

DITO ANUROGO

LECTURER, WRITER

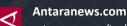
Address

Graha Surandar Permai 02 / E-25 Gowa, South Sulawesi, Indonesia

Place, Date of Birth Semarang, 23 July 1983

Email dito.anurogo@med.unismuh.ac.id

Mobile Phone Π +62 81 22 44 22 693



 \checkmark

antaranews.com/tag/dito-anurogo

Linkedin in linkedin.com/in/dito-anurogo-73b92529

Facebook web.facebook.com/dr.dito

EDUCATION

2015 - 2017

GADJAH MADA UNIVERSITY MASTER OF SCIENCE (M.Sc.) **BIOMEDICAL SCIENCES** : 3.75 out of 4.00 GPA

2002 - 2009

MEDICAL FACULTY UNISSULA **MEDICAL DOCTOR (MD) GPA** : 2.98 out of 4.00

INTEREST

- Reading, Research, Teaching
- Optogenetics, Technology
- **Classical Literature**
- Polyglot, Philanthropist
- Organization, Leadership
- Journalism, Digital Literacy
- Stem Cells, Molecular Medicine
- Nanoimmunobiotechnomedicine
- Creative and Scientific Writing

BOOKS AND PUBLICATION

Books: > 22 books Popular Publication: > 333 articles Scientific Publication: > 88 manuscripts



LANGUAGES

MANDARIN	•••••
JAPANESE	•••••
ARABIC	••••
ENGLISH	•••••
INDONESIAN	•••••

EXPERIENCES

2018 – Present

Lecturer at Universitas Muhammadiyah Makassar

2017 - 2018

Researcher at Center of Islamic Bioethics and Islamic Medical Laws, Medical Faculty, Universitas Islam Indonesia, Yogyakarta

2013 - 2014

2012 - 2013

Medical Doctor of a coal mining company at PT BUMA, East Kalimantan.

2011 - 2017Professional health consultant at detik.com.

Lecturer and assistant of researcher at Brain Circulation Institute of Indonesia (BCII), Neuroscience sub-departement, Comprehensive Herbal Medicine Institute (CHMI), Center for Robotic and Intelligent Machines (CRIM), Surya University, Indonesia.

COURSES

- Scientific Journal Writing and Journalism 1.
- Molecular Biology Techniques and Immunology 2. Technique Course (ELISA, FACS Analysis, Western Blotting, Immunohistochemistry)
- 3. **Bioinformatics and Computational Biology**
- 4 TCD (Transcranial Doppler)
- 5. Advanced Trauma Life Support (ATLS)
- Advanced Cardiac Life Support (ACLS) 6. 7.
- Advanced Neurology Life Support (ANLS) 8. ACTION (Asian Collaborative Training on
- Infectious Disease, Outbreak, Natural Disaster, and Refugee Management)
- 9 Exchange Programme (comprehensive reproductive health, HIV/AIDS education and skills building for medical students)
- Research Exchange Programme "The Role of 10. Endoglin in Colon Carcinoma"



Gadjah Mada Awards 2015

The Most Inspiring and The Best Writer Student

Seed Grant Award 2015

Blended Learning batch II, Health Management Policy Center, Medical Faculty, Gadjah Mada University.

First Winner, World Young Doctors' Organization (WYDO)

HOLY Award 2008

Second Winner, HOKI Online Literary (HOLY) Awards, Netherlands, 24 November 2008.

WYDO Award 2013

Essay Contest Award.

Profil Naratif



dr. Dito Anurogo, M.Sc.

Dokter literasi digital, pembelajar-pemerhati multidisiplin ilmu (stem cells, nanomedicine / *nanotechnology*, *optogenetics*, neurosains, neurologi, neurolinguistik, *neuroherbalmedicine*, neuroetik, hematopsikiatri, *medicopomology*, farmakogenomik-farmakogenetik, dsb), penikmat sastra, berkarya di detik.com, pernah aktif di IYHPS (Indonesian Young Health Professionals' Society). Memiliki sertifikasi CME (dari Harvard, Oxford University, dsb), ACLS, ATLS, ANLS, Hiperkes, Battra (herbal), grafologi dasar, wartawan muda. Alumnus FK UNISSULA Semarang. Tahun 2007 menjadi delegasi (riset-pelatihan) Indonesia ke Italia dan Hungaria. Tahun 2011-2012 berkarya di RS. Keluarga Sehat Pati. Tahun 2012 menjadi dokter paruh-waktu di RSI PKU Muhammadiyah sekaligus menjadi staf ahli rektor Universitas PGRI Palangka Raya. Pernah menjabat sebagai dokter di perusahaan tambang batubara, PT BUMA Kaltim. Tahun 2013-2014 berkarya di bagian neurosains, Brain Circulation Institute of Indonesia (BCII), Surya University. Tahun 2014 membantu di bagian Comprehensive Herbal Medicine Institute (CHMI) dan Center for Robotic and Intelligent Machines (CRIM), Surya University, Indonesia. Penulis puluhan buku, seperti: "45 Penyakit dan Gangguan Saraf" dan "The Art of Medicine" (Gramedia, 2016, dipromosikan di Amazon.com). Tahun 2017, ia lulus dari S-2 Ilmu Kedokteran Dasar Biomedis Fakultas Kedokteran Universitas Gadjah Mada Yogyakarta. Saat ini berprofesi sebagai dosen tetap di Fakultas Kedokteran dan Ilmu Kesehatan Universitas Muhammadiyah (FKIK Unismuh)

Makassar. Ia merupakan penggagas utama NiBTM (*Neuro-nanoimmunobiotechnomedicine*) berkolaborasi dengan Arli Aditya Parikesit dan Taruna Ikrar.

Publikasinya tentang *neuropharmacogenomics epilepsy* berhasil menembus jurnal bergengsi internasional. Karya-karyanya berhasil menghiasi berbagai semi jurnal, majalah, tabloid, media massa cetak lokal hingga nasional.

Buku "5 Menit Memahami 55 Problematika Kesehatan", karyanya telah dijadikan koleksi dan rujukan di *National Library Board* di Singapura (URL: http://www.nlb.gov.sg/biblio/200178433). Karya terbarunya bersama Dr. dr. H. Muchlis AU Sofro, SpPD-KPTI, FINASIM, berjudul: "Praktis Dan Jitu Atasi Penyakit, Infeksi, Dan Problematika Kesehatan, The Art Of Infections Diseases" dapat diakses di URL: http://andipublisher.com/produk-0119006909-praktis-dan-jitu-atasi-penyakit-infeksi-.html.

Di keorganisasian, aktif sebagai pembina *Network–Preneur Initiative Center*, CEO/Founder Sahabat Literasi Indonesia [Indonesia Literacy Fellowship], inisiator Indonesia Menulis (Writenesia). Saat ini ia terdaftar sebagai anggota di Ikatan Dokter Indonesia (IDI), anggota Primer Koperasi Ikatan Dokter Indonesia (Primkop IDI), Perhimpunan Dokter Umum Indonesia (PDUI) Cabang Jawa Tengah, divisi Penakes IYHPS (*Indonesian Young Health Professionals' Society*), Muhammadiyah, Forum Lingkar Pena (FLP) Ciputat dan Semarang, anggota dan Editor Forum Aktif Menulis (FAM), Jaringan Pena Ilma Nafia (JPIN), Masyarakat Linguistik Indonesia. Kesibukannya saat ini adalah sebagai kepala LP3AI ADPERTISI, pengurus Forum Lingkar Pena (FLP) Makassar Sulawesi Selatan, *Director networking* IMA *Chapter* Makassar, pengurus APKKM (Asosiasi Pendidikan Kedokteran dan Kesehatan Muhammadiyah),

Saat SMP dan SMU aktif di berbagai organisasi: OSIS, Rohis, Pramuka, Majalah Sekolah, *English Club*, dsb. Pernah menjabat sebagai LORE (*Local Officer Research Exchange*) CIMSA UNISSULA. Perintis Medical Study Club (MSC) di FK UNISSULA.

Berbagai penghargaan dan prestasi yang pernah diukir olehnya, seperti: duta literasi Sulawesi Selatan 2019, kontributor terbaik Desember 2016 di Ummi online. Peraih ''Gadjah Mada Awards'' 2015 kategori mahasiswa terinspiratif dan penulis terbaik. Tahun 2015 menjadi peserta terpilih program Menyapa Negeriku [salah satu tim ke Raja Empat dari total seleksi 47.523 orang] yang diselenggarakan oleh Direktorat Jenderal Sumber Daya Ilmu Pengetahuan Teknologi dan Pendidikan Tinggi [Ditjen SDID]. "Penulis Terpilih" dan "Juara Kedua" Lomba Kepenulisan 2015, diselenggarakan oleh Ellunar Publisher. Peserta Terbaik di

Sarasehan Jurnalistik Ramadan, Masjid Agung Jawa Tengah (MAJT), Semarang, 2014. Juara pertama "2013 *World Young Doctors' Organization (WYDO) Indonesia Essay Contest Award*". Nominator Lomba Cipta Puisi Tingkat Nasional 2012, FAM Indonesia, 1 September 2012. Peserta Terbaik di Sarasehan Jurnalistik Ramadan 2010 "Membudayakan Santri Menulis", Suara Merdeka, MAJT Semarang, 2010. Pemenang Kedua HOKI Online Literary Awards (HOLY) 2008, Netherlands, 2008. Pemenang I Lomba Menulis Surat Cinta 2008 dari HOKI (Harian Online Kabar Indonesia), 2008. Reporter of the Month, Dec 2007 dari Kabar Indonesia, 2007. Juara Harapan Unissula *English Contest*, 2005.

Ia berpengalaman sebagai pengasuh rubrik kesehatan di media online ternama, seperti: https://health.detik.com/konsultan/dr.%20Dito%20Anurogo) detik.com (URL: sejak 4 2011 hingga 13 Oktober 2017. hellosehat.com (URL: Agustus https://hellosehat.com/expert/dito-anurogo/), Kampus Desa Indonesia (URL: http://kampusdesa.or.id/author/dito-anurogo/).

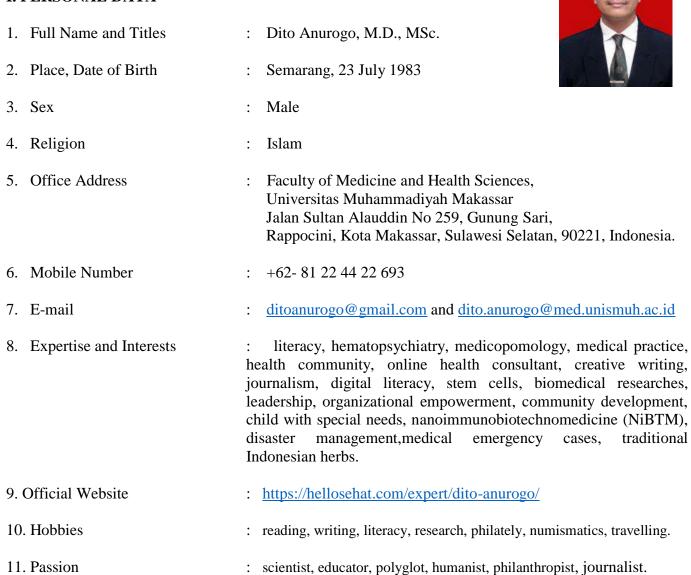
Alumnus terbaik Madrasah Takhashushiyah di Pondok Pesantren Modern Islam Assalaam (PPMIA) Sukoharjo Indonesia tahun 1999. Delegasi SMU Negeri 1 Semarang untuk Olimpiade Matematika hingga tingkat Internasional. Siswa Berprestasi SMP Negeri 3 Semarang, tahun 1996. Bintang Kelas, Ebta, dan Ebtanas PERTAMA se-SDN Sompok 1,2,3,4 Semarang tahun 1995. Juara II Putra Pemilihan Siswa Teladan SD Tingkat Kotamadia Semarang, tahun 1994. Juara I Lomba Menata Perangko, SDN Sompok Semarang, 19 Desember 1992.

Profil inspiratif Dito Anurogo sempat dinarasikan oleh sahabatnya, seperti di: <u>http://muhammadjanu.blogspot.com/2015/02/dito-anurogo-dokter-online-kaya-prestasi.html</u> dan <u>https://guyubmitra.wordpress.com/2015/01/22/menyelami-romantisme-dokter-</u> berprestasi-dito-anurogo/.

Senantiasa *tawadhu*, zuhud, dan mensyukuri nikmat Allah SWT, menjadikan pria yang dianggap *multitasking*-multitalenta oleh para sahabatnya ini, selalu mau berbagi ilmu pengetahuan dan pengalaman. Silakan menghubungi via email: <u>ditoanurogo@gmail.com</u> dan <u>dito.anurogo@med.unismuh.ac.id</u> atau Instagram: @ditoanurogo.

CURRICULUM VITAE

I. PERSONAL DATA



II. EDUCATIONAL BACKGROUND

1. Formal Education

NO.	LEVEL	INSTITUTION	FIELD OF STUDY	YEAR OF ENTRANCE AND GRADUATION
1	Elementary School	SDN Sompok Semarang		1989 – 1995
2	Junior High School	SMPN 3 Semarang		1995 – 1998
3	Senior High School	SMUN 1 Semarang	Natural Sciences	1999 – 2002
4	University			
	a. Bachelor (S1)	Medical School UNISSULA Semarang	Medicine	2002 - 2007
	b. Profession (GP)	Medical School UNISSULA Semarang	Medicine	2007 - 2009
	c. S2	Gadjah Mada University Yogyakarta	Basic Medicine and Biomedical Sciences	2015 – Oct 2017
5	Other	Islamic Boarding School, As-Salam, Sukoharjo	Religious and Islamic Studies	1998 – 1999

2. Courses, Training

No	Name	Time	Place
1	Immunology Technique Course (ELISA,	10-12 Feb 2016	FK UGM, Yogyakarta
	FACS Analysis, Western Blotting, Immunohistochemistry)		
2	Workshop "Scientific Journal Writing"	23-24	Grand Zuri Hotel,
	Batch II Held by UGM	November 2015	Yogyakarta
3	Advanced Neurology Life Support (ANLS)	23-24 August	National Brain
		2014	Center Hospital,
			Jakarta
4	Workshop on Bioinformatics and	14-17 April 2014	Swiss German
	Computational Biology: Next Generation		University
	Sequencing and Vaccine and Drug Design	42.42.5 - 2042	
5	Workshop Hand on Practice: Stroke Model	12-13 Sep 2013	Surya University,
	and TTC Staining Techniques, Neural Tracer and Immunohistochemistry		Tangerang, Indonesia
	Techniques		indonesia
6	Course and Practical Work: Molecular	13 – 15 Feb	Medical Faculty,
	Biology Techniques	2012	UGM, Yogyakarta
7	TCD (Transcranial Doppler) Training	13-14 August	Wisma Hasanah
		2011	Srondol, Semarang
8	Advanced Trauma Life Support (ATLS)	4 – 6 Feb 2011	Kariadi Hospital
			Semarang
9	Advanced Cardiac Life Support (ACLS)	22 – 24 Jan 2010	Semarang
10	IFMSA (International Federation of Medical Students' Associations) Exchange	30 July – 27	Hungary (Budapest,
	Programme providing comprehensive	August 2007	Pécs, Szeged,
	reproductive health and HIV/AIDS education and skills building for medical		Debrecen)
	students.		
11	IFMSA (International Federation of	5 – 26 March	Università degli
	Medical Students' Associations) Research	2007	Studi di Torino, Italy
	Exchange Programme "The Role of		
	Endoglin in Colon Carcinoma"		
12	ACTION (Asian Collaborative Training on	19 – 24 March	Jakarta
	Infectious Disease, Outbreak, Natural	2006	
	Disaster, and Refugee Management)		

III. PROFESSIONAL JOBS AND ORGANIZATION

1. Jobs Experiences

- 1. February 2018 present: lecturer of Medical Faculty of Muhammadiyah University (FK Unismuh) Makassar.
- 2. August 2017– February 2018: member of researcher at Center of Islamic Bioethics and Islamic Medical Laws (Biohuki), Medical Faculty, Universitas Islam Indonesia, Yogyakarta.
- 3. August 2011 October 2017: digital/online doctor (voluntary health consultant) at detik.com.
- 4. August October 2017: Reporter of EFKAGAMA (Official Magazine of FK UGM)
- 5. July 2014 August 2015: clinical doctor in Semarang.
- 6. May 2014 June 2014: Assistant Researcher at Comprehensive Herbal Medicine Institute (CHMI), Center for Robotic and Intelligent Machines (CRIM), Surya University, Indonesia.
- 7. 1 May 2013 30 April 2014 : lecturer, researcher at Brain Circulation Institute of Indonesia (BCII), Neuroscience sub-departement, Surya University.
- 8. December 2012 April 2013 : Company medical doctor at PT BUMA Kaltim.
- 9. 2 June 2012 November 2012 : specialist staff of Rector at PGRI University, Palangka Raya.
- 10. 17 April 2012 November 2012: Doktor (part-time) at PKU Muhammadiyah Hospital, Palangka Raya, Central Kalimantan.

- 11. 19 September 2011 16 March 2012: TCD operator (medical doctor) at Keluarga Sehat Hospital, Pati.
- 12. 1 March 2011 16 March 2012: Medical doktor (full-time) at Keluarga Sehat Hospital, Pati, Central Java.
- 13. November 2009 February 2011: Medical Doktor at Great Mosque Central Java's clinic (klinik Masjid Agung Jawa Tengah; MAJT), Semarang, Central Java, Indonesia.

2. Organization

- Patron of Sci.id Patron of Menusa Community
- 3.
- 4.
- Founder and Initiator Indonesia Menulis (Writenesia) Founder and Initiator Indonesia Menulis Online Leader / Head of LP3AI ADPERTISI (Alliance of Indonesian Private University Lecturers) Commitee of Muhammadiyah Medical and Health Education Association (Asosiasi Pendidikan 6.
- Kedokteran dan Kesehatan Muhammadiyah, APKKM) Commitee of Indonesian Stem Cell Association (Asosiasi Sel Punca Indonesia, ASPI) The Governing Board of Network-Preneur Initiative Center (NPIC) 7
- 8.
- 9. Founder and Initiator Srikandi Forum Indonesia
 10. Founder and CEO Sahabat Literasi Indonesia (*Indonesia Literacy Fellowship*)
 11. Leader of UKM Jurnal Paradigma UGM
 12. Member of International Indonesia Scientists Association (I-4; Ikatan Ilmuwan Indonesia Internasional)
 13. Member of FISH (Forum Ilmu Social Humaniora) UGM

- 13. Member of FISH (Forum Ilmu Sosial Humaniora) UGM
 14. Member of FOST (Forum Sains dan Teknologi) UGM
 15. Member of HIMMPAS UGM
 16. Member of Himpunan Mahasiswa Pascasarjana Universitas Gadjah Mada (HMP UGM)
 17. Member of International Language Center Universitas Gadjah Mada (ILC UGM)
 18. Member of Ikatan Dokter Indonesia (IDI).
 19. Member of Primer Koperaci Ikatan Dokter Indonesia (Primkon IDI)

- Member of Ikatan Dokter Indonesia (IDI).
 Member of Primer Koperasi Ikatan Dokter Indonesia (Primkop IDI).
 Member of Perhimpunan Dokter Umum Indonesia (PDUI), Jawa Tengah Branch.
 Member of IYHPS (*Indonesian Young Health Professionals' Society*).
 Member of Muhammadiyah.
 Member of Keating Health Care Community.

- Member of Munammadiyan.
 Member of Karima Health Care Community
 Member of The Islamic Movie Lovers Community [Komunitas Pecinta Film Islami; KOPFI]
 Member of Forum Lingkar Pena (FLP) Ciputat, Semarang, Makassar.
 Member and Editor of Writing Active Forum (Forum Aktif Menulis, FAM)
 Member of Pen Networking (Jaringan Pena Ilma Nafia, JPIN)
 Member of Indonesian Linguistic Society (Masyarakat Linguistik Indonesia, MLI)

3. Achievement

- 1. National Ambassador of Literacy 2019, based on the selection and decision of the Language Development and Development Agency, Ministry of Education and Culture, in Jakarta, April 8-14, 2019.
- 2. National First Champion, National Scientific Poster Presentation, National Scientific Meeting and Work Conference 2018 organized by: the Association of Indonesian Doctors for HIV AIDS, 30 November – 1 December 2018.
- 3. Best Contributor at Ummi Online January 2017.
- Best Contributor at Ummi Online December 2016. 4.
- 5. The Most Inspiring Student "Gadjah Mada Awards" 2015.
- The Best Writer Student "Gadjah Mada Awards" 2015. 6.
- Seed Grant Award Blended Learning batch II year 2015 from Health Management Policy 7. Center, Medical Faculty, Gadjah Mada University.
- The Indonesian delegation to the "Saying to My Country" or "Menyapa Negeriku" 8. program (1 of 47523 registrants) was held by the Directorate General of Science Technology and Higher Education Resources, 2015.
- The Best Winner, science category, national essay competition, AGRINOVA forum, held by HIMMPAS IPB 2015.
- 10. "The Selected Writer" and "Second Winner" Writing Competition 2015, held by: Ellunar Publisher.
- 11. The Best Participant in Ramadan Journalistic Training, held by Suara Merdeka, in Semarang, 3 July 2014.
- 12. First Winner "2013 World Young Doctors' Organization (WYDO) Indonesia Essay Contest Award".
- 13. Nominee National Poetry Competition 2012, FAM Indonesia, 1 September 2012.
- 14. The Best Participant in Ramadan Journalistic Training, held by Suara Merdeka, in Semarang, 28 August 2010.
- 15. Second Winner, HOKI Online Literary Awards (HOLY) 2008, Netherlands, 24 Nov 2008.
- 16. First Winner, Love Letter Writing Competition 2008, HOKI (Harian Online Kabar Indonesia), 14 Feb 2008.
- 17. Indonesian Delegation for Research at University Degli Studi de Turino, Italy, 2007. Supported by: The International Federation of Medical Students Associations (IFMSA) and Indonesian government.

- Indonesian Delegation for Training HIV AIDS, Blood Bank, and Reproductive Health in Hungary, 2007. Supported by: The International Federation of Medical Students Associations (IFMSA) and Indonesian government.
- 19. Reporter of the Month, Dec 2007, Kabar Indonesia, online newspaper, 11 December 2007.
- 20. Hope Champion, Unissula English Contest, 28 September 2005.
- 21. The Best Pupil, Madrasah Takhashushiyah, Modern Islamic Boarding School, Assalaam (PPMIA) Sukoharjo Indonesia, 10 June 1999.
- 22. The Paragon Student of SMP 3 Semarang, 1996.
- 23. First Rank and The Best in Ebta-Ebtanas, SDN Sompok 1,2,3,4 Semarang, 1995.
- 24. The Second Paragon Elementary School Student, Semarang city, 1994.
- 25. First winner, Stamp Competition, in SDN Sompok Semarang, 19 December 1992.

IV. PUBLICATION

Scientific Publication

- 1. **Anurogo D**, Parikesit AA, Ikrar T. LncRNAs in CONDBITs Perspectives, From Genetics towards Theranostics. Malaysian Journal of Health Sciences. 2019;17:2. URL: <u>http://ejournal.ukm.my/jskm/article/view/16808</u>
- Anurogo D, Soesatyo MHNE. The Neuropharmacogenetics of Angelman Syndrome. Ethical Digest No. 169 Year XV March 2018 pp 40-45
- Anurogo D. Effects Mesenchymal Stem Cells Conditioned Medium on Creatinine Level, Tubular Injury, and Tubular Proliferation in Mice Model of Ischaemic Reperfusion Injury. Thesis. Universitas Gadjah Mada. Yogyakarta. Indonesia. 2017.
- 4. Anurogo D, Parikesit AA, Ikrar T. Bionanomedicine: A "Panacea" In Medicine? Makara J Health Res 2017;21(2):42-48.
- 5. Anurogo D. The Art of Neuroreligenomics in Autism. Ethical Digest No.165 Year XIV Nov 2017 pp 42-45.
- 6. Parikesit AA, **Anurogo D**, Putranto RA. The utilization of bioinformatics in the field of agriculture and health. Menara Perkebunan 2017;85(2):105-115.
- 7. **Anurogo D**, Parikesit AA, Marsetyawan HNES, Ikrar T. The Onconeurobioimmunotranscriptomics (ONBITs) of Klotho. First International Seminar on Biotechnology October 7th, 2017. Universitas Gadjah Mada, Yogyakarta, Indonesia. Poster Presentation.
- 8. **Anurogo D.** Ikrar T. Treatment of Epilepsy: Background and Future Directions. Progress and Communication in Sciences. 2014(1):27-41.
- Anurogo D, Ikrar T. Neuropharmacogenetics of Autism. 3rd International Seminar on Autism and Fragile-X Syndrome; 28-29 August 2013. UC Davis USA - IDI - UNDIP CEBIOR Semarang, Indonesia. Proceeding Book ISBN: 978-602-097-394-4.
- Anurogo D, Ikrar T. Mediconeurophenomenology of Savant Syndrome. Oral Presentation. The 3rd ACIKITA International Conference on Science and Technology (AICST). Jakarta, August 25-27, 2013. Proceedings. ISBN: 978-602-1372-11-1. Page 1-20. Full paper.
- Anurogo D, Ikrar T. The Tourette Toddlers: To Treat or Not to Treat? Oral Presentation. The 3rd ACIKITA International Conference on Science and Technology (AICST). Jakarta, August 25-27, 2013. Proceedings. ISBN: 978-602-1372-11-1. Page 21-51. Full paper.
- 12. Anurogo D. The Science of "Tindihan" Phenomenon. ACIKITA International Conference of Science and Technology (AICST), August 26-28, 2012. Proceeding. ISBN: 978-602-18102-1-7. Page 139-148. Full paper.
- Anurogo D, Satriotomo I. Futurology of Biomarker for Stroke: A Review. ACIKITA International Conference of Science and Technology (AICST), July 26-27, 2011.Proceeding. ISBN: 978-979-16415-9-3. Page 264-277. Full paper.
- 14. **Anurogo D**, Nurani W, Ikrar T. Neurolinguistics of Asperger Syndrome. Neurona, Suplemen Volume 30 No.4 September 2013, page 14. Full paper had been presented on Jakarta Neurology Exhibition, Workshop, and Symposium, Jakarta, 30 Jan-2 Feb 2014.
- Anurogo D, Nurani W, Ikrar T. The Art of Multiple Sclerosis Management. Neurona, Suplemen Volume 30 No.4 September 2013 halaman 13. Full paper had been presented on Jakarta Neurology Exhibition, Workshop, and Symposium, Jakarta, 30 Jan-2 Feb 2014.
- Nurani W, Anurogo D, Ikrar T. Nucleic Acid Aptamers as Novel Promising Therapeutic Agents for Multiple Sclerosis. Neurona, Suplemen Volume 30 No.4 September 2013 halaman 12. Full paper had been presented on Jakarta Neurology Exhibition, Workshop, and Symposium, Jakarta, 30 Jan-2 Feb 2014.
- 17. **Anurogo D**, Ikrar T. Brain Card Games as the Art of Neuroedutainment. Poster presentation, First National Conference of Neuroscience Indonesia, 14-15 Sep 2013, Jakarta, Indonesia.
- 18. Anurogo D. Tension Type Headache. Cermin Dunia Kedokteran (CDK)214 Vol41 No3 Th2014 pp186-191.
- 19. Anurogo D. Diagnosis dan Manajemen Amyotrophic Lateral Sclerosis. CDK204 vol40 No5 Th2013 pp352-356.
- 20. Anurogo D. Penatalaksanaan Migren. CDK 198 vol.39 No. 10 Th.2012 pp 731-737.
- 21. Anurogo D. Demensia dan Demensia Alzheimer. Ethical Digest No.134 Thn XII April 2015 pp 70-74.
- 22. Anurogo D. Shaken Baby Syndrome. Ethical Digest No.130 Thn XI Des 2014 pp 64-65.
- 23. **Anurogo D**, Ikrar T. The Art of Neuropsychocreativity and Neuroedutainment. Ethical Digest No.125 Thn. XI July 2014, pp 67-69.
- 24. Anurogo D, Ikrar T. The Neuroscience of Glutamate. Ethical Digest No.120 Thn.X February 2014, pp 55-61.
- 25. Anurogo D. Manajemen Meningitis. Ethical Digest No.110 Thn.X April 2013 pp 62-64.
- 26. Anurogo D. Infeksi Cytomegalovirus. Ethical Digest No.108 Thn. X Feb 2012 pp 62-63.
- 27. **Anurogo D,** Supartiningsih. Fenomena Shaken Baby Syndrome. Kongres Nasional Ikatan Ahli Kesehatan Masyarakat Indonesia [KONAS IAKMI] XIII. 4 Nov 2016, Hotel Four Points Makassar. Oral Presentation.
- Anurogo D, Ikawati Z. Pedoman Tatalaksana Infeksi Virus Zika. Kongres Nasional Ikatan Ahli Kesehatan Masyarakat Indonesia [KONAS IAKMI] XIII. 4 Nov 2016, Hotel Four Points Makassar. Oral Presentation.

- 29. **Anurogo D**. Strategi Efektif Pembelajaran Neuroetik di Indonesia. Kongres Nasional Ikatan Ahli Kesehatan Masyarakat Indonesia [KONAS IAKMI] XIII. 4 Nov 2016, Hotel Four Points Makassar. Oral Presentation.
- 30. **Anurogo D**, Kencanasari SP. Healthedutainment, Sehat melalui Game: Prototipe Game Interaktif ''Fight the Diseases'' Sebagai Strategi Efektif untuk Sosialisasi Penyakit. Kongres Nasional Ikatan Ahli Kesehatan Masyarakat Indonesia [KONAS IAKMI] XIII. 4 Nov 2016, Hotel Four Points Makassar. Oral Presentation.
- 31. **Anurogo D**, et al. LNC RNAs in CONDBITs Perspectives, from Genetics towards Theranostics. 1st International Conference on Health Science [ICHS], 28 29 Oct 2016, UGM Yogyakarta, oral presentation, full paper.
- 32. **Anurogo D,** Ikrar T. Optogenetics, A Futuristic Panacea in Genetics. Trans-Academic Cancer Genetics [TACG] 2 Symposium and Workshop "When Clinicians Meet Genetics" GENETICS; Application from bench to bedside and community. 19 – 21 August 2016. Poster Presentation.
- 33. **Anurogo D,** Arfian N, Harjana SM. MicroRNAs in Stem Cells: Beauty and the Behaviour. The 1st Makassar International Conference on Stem Cells and Regenerative Medicine, 28-29 May 2016, Clarion Hotel, Makassar, Poster Presentation.
- 34. **Anurogo D,** Lazuardi L, Ikrar T. Nanoimmunobiotechnomedicine [NiBTM]: The Futurology of Stem Cells. The 1st Makassar International Conference on Stem Cells and Regenerative Medicine, 28-29 May 2016, Clarion Hotel, Makassar, Best Poster Presentation.
- 35. Anurogo D, Soesatyo M HNE. Mesenchymal Stem Cells and Exosomes in Sepsis: Foes Instead or Friends Indeed? The 1st Makassar International Conference on Stem Cells and Regenerative Medicine, 28-29 May 2016, Clarion Hotel, Makassar, Poster Presentation.
- 36. Anurogo D, Purnami N. The Futurology of Tinnitus: Neurootogenetics Perspectives. 5th International Joint Symposium on Biomedical Sciences. Translational Neuroscience: Bridging the Gaps between Basic Medical and Clinical Sciences. 11 – 12 December 2015. FK UGM Yogyakarta. Poster Presentation.
- 37. Anurogo D, Sunariani J, Ikrar T. The Neuropathodentistry of Aquaporins: Their Roles in Diseases and Potential Treatment. 5th International Joint Symposium on Biomedical Sciences. Translational Neuroscience: Bridging the Gaps between Basic Medical and Clinical Sciences. 11 – 12 December 2015. FK UGM Yogyakarta. Oral Presentation.
- 38. **Anurogo D**. Being the Best and Ideal Doctor through PBL: Philosophical Concepts. 5th Asia-Pasific Association on Problem Based Learning in Health Sciences Conference.Surabaya. 15-17 November 2006. Poster Presentation.
- Anurogo D. Paremiology: the Art of Understanding Indonesian's Community Characteristic through Proverbs. Second International Graduate Student Conference on Indonesia 2010. 3-4 November 2010. Oral presentation. Full paper.
- 40. **Anurogo D**, Huda AN. Hematopsychiatry: Relationship between Blood Type and Depression. Biennial Scientific Meeting of Indonesian Psychiatric, Palembang. 3-5 July 2007.
- 41. **Anurogo D**. Biohematopsychiatry: Genomics as A Link Between Hematology and Psychiatry. Biennial Scientific Meeting of Indonesian Psychiatric, Palembang. 3-5 July 2007.
- 42. **Anurogo D**, Ikrar T. Pharmacogenetics and Pharmacogenomics: The Art of Bipolar Disorder Management. First Bipolar National Conference, 9-10 March 2012, Sheraton Hotel, Surabaya. Poster Presentation.
- 43. **Anurogo D**. Psychosexual Medicine: The Futurology of Female Sexual Dysfunction. First National Congress Women's Mental Health, 26-27 Nov 2011.
- 44. **Anurogo D**. Orgasmology: The Art of Artistic Kamasutra. First National Congress Women's Mental Health, 26-27 November 2011.
- 45. **Anurogo D**, Ikrar T. Vitiligo. CDK 220 Vol.41 No.9 Th 2014 pp 666-675.
- 46. Anurogo D. Memahami Dispareunia. CDK 206 vol.40 No.7 Th.2013 pp 508-515.
- 47. Anurogo D. Ejakulasi Dini. CDK 199 vol.39 no. 11 Th.2012 pp 823-828
- 48. Anurogo D. Broken Heart Syndrome. CDK 192 vol.39 no. 4 Th.2012 pp 256-260
- 49. Anurogo D. Probiotics, Medika (Indonesian Medical Journal), Edisi No.10, Vol.XL, 2014.
- 50. Anurogo D, Ikrar T. Manajemen Sariawan. Ethical Digest No.132 Thn.XI Feb 2015 pp 66-69.
- 51. Anurogo D, Ikrar T. Tatalaksana Angiofibroma. Ethical Digest No.131 Thn.XI Jan 2015 pp 72-75.
- 52. Anurogo D. Herbal Forest as Futuristic Forest. National Seminary and Conggres XI IMAHAGI, 9 March 2010, Auditorium UNNES Sekaran, Semarang. Full paper.
- Anurogo D. Effective Strategy in Developing Golden Generation. National Seminary and Book Launching "Character Education in Implementing 2013 Curriculum". Education Science Faculty, IKIP PGRI Semarang, 5 January 2014. Proceeding. ISBN: 978-602-8047-91-3, page 94-104.
- 54. **Anurogo D**. Graphoanthropology: The Art of Changing the World through Words and Love. Literary Talkshow "Masterpiece for Nation" FLP (Forum Lingkar Pena) Sekaran UNNES Semarang. 31 Oct 2010. Full paper.

Published Books (Indonesian Language)

- 55. Anurogo D, Sofro MAU. The Miracle of Medicine. (2020, In Progress)
- 56. Anurogo D. Encyclopedia of Diseases and Disorders. Penerbit Pustaka Setia Bandung. 2020. (In Progress)
- 57. Anurogo D, Sofro MAU, Problematika Infeksi dan Solusinya. Penerbit ANDI Yogyakarta. 2019.
- 58. **Anurogo D,** Ikawati Z. Tata Laksana Terapi Penyakit Sistem Syaraf Pusat. Bursa Ilmu, Yogyakarta. ISBN: 978-602-1578-10-0.
- 59. Anurogo D. The Art of Medicine. Gramedia. Jakarta. 2016. ISBN: 9786020321554.
- Anurogo D, Usman FS. 45 Penyakit dan Gangguan Saraf. Rapha Publishing, Penerbit Andi. Yogyakarta. 2014. ISBN: 978-979-29-2123-6.
- 61. Sofro MAU, Anurogo D. 5 Menit Memahami 55 Problematika Kesehatan. Penerbit D- Medika, DIVA Press. Yogyakarta. May 2013. ISBN: 978-602-7933-45-3.
- Anurogo D, Wulandari A. 45 Penyakit yang Banyak Ditemukan di Masyarakat. Penerbit Andi. Yogyakarta. 2013. ISBN: 978-979-29-3059-7.
- Anurogo D, Wulandari A. 45 Penyakit Aneh dan Khusus. Penerbit Andi. Yogyakarta. 2011. ISBN: 978-979-29-2665-1.

- 64. Anurogo D, Wulandari A. *Cara Jitu Mengatasi Nyeri Haid*. Penerbit Andi. Yogyakarta. 2011. ISBN: 978-979-29-2660-6.
- 65. Anurogo D, Wulandari A. *Cara Jitu Mengatasi Impotensi*. Penerbit Andi. Yogyakarta. 2011. ISBN: 978-979-29-2556-2.
- 66. Anurogo D. 123 Penyakit dan Pengobatannya. Penerbit Ide Media. Semarang. 2008. ISBN: 978-979-25-2757-5.
- 67. Anurogo D, et al. Second Glance. Ellunar Publisher. Bandung. 2015. ISBN: 978-602-72139-3-7.
- 68. Anurogo D, Jonru. Sembuh dan Sukses dengan Terapi Menulis. Indie Pro Publishing. ISBN: 978-602-9142-86-0

Editor of Book (Indonesian Language)

- 69. Suprapto TD. Teguh Menyambut Maut. Pustaka Pelajar, Yogyakarta. 2020 (in progress).
- 70. Ikrar T. Ilmu Neurosains Modern. Pustaka Pelajar. Yogyakarta. 2015.

Antology (Indonesian Language)

- 71. Menuju Cahaya Kebaikan (Diandra Kreatif, 2018)
- 72. Berani Bermimpi (Penerbit Mizania, 2014)
- 73. Pelangi Jiwa (Poems Antology, ebook, 2008)
- 74. Catatan Sang Pemenang (Penerbit Elex Media Komputindo, Jakarta, 2013)
- 75. Lerak (Penerbit FAM Publishing, Kediri, East Java, March 2013)

Self - Publishing Books

- 76. Asthabrata: Javanese Leadership (English edition, 2007)
- 77. Pearl from Indonesia (English edition, 2007)
- 78. Da Dito con Amore (Italian English Language, 2007)
- 79. Atlas Dermatologi (for internal use, 2006)
- 80. Atlas Malaria (for internal use, 2006)

Scientific - Popular Publication

(Newspapers, Magazines, etc in Local, Regional, National Level)

- Anurogo D. Hantu Narkoba Merajalela. Majalah Parlementaria. Edisi 153 Tahun XLVII 2017 Hlm 74-75. ISSN 1979-5912.
- Anurogo D. Mulutku Sehat Tubuhku Kuat. Majalah Parlementaria. Edisi 152 Tahun XLVII 2017 Hlm 74-75. ISSN 1979-5912.
- Anurogo D. Diet Sehat di Era Digital. Majalah Parlementaria. Edisi 151 Tahun XLVII 2017 Hlm 74-75. ISSN 1979-5912.
- Anurogo D. Menguak Misteri dan Solusi Kanker Serviks. Majalah Parlementaria. Edisi 150 Tahun XLVII 2017 Hlm 74-75. ISSN 1979-5912.
- Anurogo D. Taktik Agar Kolesterol Tak Bikin Dongkol. Majalah Parlementaria. Edisi 149 Tahun XLVII 2017 Hlm 74-75. ISSN 1979-5912.
- 86. Anurogo D. Hobi Selfie Berujung Tragis. Majalah Parlementaria. Edisi 148 Tahun XLVII 2017 Hlm 74-75. ISSN 1979-5912.
- 87. Anurogo D. Gerakan Senam Bahagia Sambil Bekerja. Majalah Parlementaria. Edisi 147 Tahun XLVII 2017 Hlm 78. ISSN 1979-5912.
- Anurogo D. Mencegah Kanker Jiwa Merajalela. Majalah Parlementaria. Edisi 146 Tahun XLVII 2017 Hlm 76-77. ISSN 1979-5912.
- Anurogo D. Neuroimunobioseismologi Perspektif Baru Gempa Bumi. Majalah Parlementaria. Edisi 145 Tahun XLVI 2017 Hlm 76-77. ISSN 1979-5912.
- 90. Kepemimpinan Ideal Era Digital, Opini, Harian Fajar, 20 January 2018, page 8.
- 91. Strategi Efektif Menilai Berita, Opini, Harian Fajar, 27 November 2017, page 8.
- 92. Gagal Ginjal Akut, Siapa Takut? Opini, Harian Fajar, 14 September 2017, page 8.
- 93. Solusi Sakit Kepala Saat Berpuasa, Opini, Harian Fajar, 6 June 2017, page 8.
- 94. Sindrom Lelah Kronis, Opini, Harian Fajar, Tuesday, 14 March 2017, page 8.
- 95. Nutrigenomik, Diet ala Genetik nan Futuristik, Opini, Harian Fajar, Tuesday, 31 January 2017, page 8.
- 96. Paremiologi, Peribahasa Pencerah Peradaban, Opini, Harian Fajar, Thursday, 18 August 2016, page 8.
- Vaccinomics, Era Baru Vaksin, Opini, Harian Fajar, Tuesday, 26 July 2016, page 8.
- Simalakama Lupus, Opini, Harian Fajar, Tuesday, 10 May 2016, page 8.
- 99. Menaklukkan Virus Zika. Harian Fajar. 11 Feb 2016
- 100. Menguak Misteri Akromegali. Harian Fajar. 9 January 2016.
- 101. Hipersomnia Idiopatik "Si Tukang Tidur", Opini, Harian Fajar, Wednesday, 2 December 2015, page 8.
- 102. Jurnalisme Sains, Harian Fajar, 24 October 2015
- 103. Silaturahmi dan Kesehatan Otak, Opini, Harian Fajar, Saturday, 25 July 2015.
- 104. Misteri Sindrom Balint, Koran Sindo, 26 June 2015
- 105. Paremiomedikoetik, Paradigma Baru Bioetik, Koran Sindo, 2 October 2015
- 106. Cara Cerdas Atasi Alzheimer, Koran Sindo, 6 March 2015
- 107. Fibromialgia, "Hantu Nyeri" Wanita, Koran Sindo, 28 August 2015
- 108. Menguak Misteri Herbal Korea dan Khasiatnya, Koran Sindo, 17 April 2015
- 109. Bell's Palsy Menyerang Siapa Saja (Suara Merdeka, 18 March 2015)
- 110. Cara Cerdas Atasi Alzheimer (Koran Sindo, 6 March 2015)
- 111. Bahaya Infeksi Bakteri Listeria (Koran Sindo, 20 Februari 2015)
- 112. Menguak Misteri Broken Heart Syndrome (Koran Sindo, 13 Februari 2015)
- 113. Sakit Kepala Serasa Disambar Petir (Koran Sindo, 6 Februari 2015)
- 114. Darah Rendah Bikin Resah (Majalah Kesehatan Sinergi Sep-Okt 2014, hlm 16-17)
- 115. Dia Superherbal (Trubus 529 Desember 2013/XLIV, hlm 84-85)
- 116. 10 Menit Deteksi Dini Sindrom Tourette (Majalah Sains Indonesia, hlm 90-92, Vol 19, July 2013)

- 117. Osteoporosis "Si Koruptor Tulang" (Suara Merdeka, 27 March 2013)
- 118. (Profil) Prof. dr. Zainal Muttaqin, SpBS(K), Ph.D.: Pakar Bedah Epilepsi Indonesia Bereputasi Internasional.CDK2013;204;40(5):393-4.
- 119. (Profil) Endah Rahmawati, MD, MA: Srikandi Bioetik Indonesia. CDK-203/Vol.40 No.4 Th.2013 hlm 312-4.
- 120. (Profil) dr. H. Muchlis AU Sofro, SpPD-KPTI: Jenius nan Religius. CDK-202/Vol.40 No.3 Th.2013 hlm 232-3.
- 121. (Profil) Irawan Satriotomo, M.D., Ph.D.: Pakar Neurosains Indonesia. CDK-201/Vol.40 No.2 Th.2013 hlm 151-3.
- 122. (Profil) dr. Taruna Ikrar, MD., MPharm., PhD.: Ilmuwan Penemu Mekanisme Terapi Epilepsi. CDK-198/Vol.39 No.10 Th.2012 hlm 785-7.
- 123. Depresi Dapat Dicegah (Suara Merdeka, 24 October 2012)
- 124. Di Balik Tragedi Taman Sari (Suara Merdeka, 24 October 2012)
- 125. Hentikan Tangis dengan Mengguncang (Suara Merdeka, 12 September 2012)
- 126. Mengguncang Bayi Bisa Berakibat Fatal (Suara Merdeka, 12 September 2012)
- 127. Mewaspadai Flu Singapura (Suara Merdeka, 29 August 2012)
- 128. Manfaat Kolak Pisang bagi Kesehatan (Suara Merdeka, 15 August 2012)
- 129. Kopi Penyembuh atau Pembunuh? (Suara Merdeka, 25 July 2012)
- 130. Sindrom Alice in Wonderland (Suara Merdeka, 2 May 2012)
- 131. Melasma Wajah Mirip Topeng (Suara Merdeka, 2 May 2012)
- 132. Bipolar: Penyakit Galau Penduduk Risau (2) [Rubrik Opini Kalteng Pos, 28 April 2012]
- 133. Bipolar: Penyakit Galau Penduduk Risau (1) [Rubrik Opini Kalteng Pos, 27 April 2012]
- 134. Hamil Kosong Akibat Kelainan Gen (Suara Merdeka, 14 March 2012)
- 135. Terjadinya Kembar Siam (Suara Merdeka, 14 March 2012)
- 136. Mewaspadai Penyakit Musiman (Suara Merdeka, 29 Februari 2012)
- 137. Pneumonia: Penyakit Pancaroba (Suara Merdeka, 30 November 2011)
- 138. Mewaspadai Stres di Otot Jantung (Suara Merdeka, 2 November 2011)
- 139. ITP, Penyakit Kelainan Darah (Suara Merdeka, 06 October 2011)
- 140. Pseudomembranous Colitis Penyakit Akibat Antibiotik (Suara Merdeka, 15 Sep 2011)
- 141. Tak Sulit Taklukkan Selulit (Suara Merdeka, 08 September 2011)
- 142. Khasiat Kurma untuk Kesehatan (Suara Merdeka, 11 August 2011)
- 143. Asperger Syndrome, Anak Berkebutuhan Khusus (Suara Merdeka, 28 July 2011)
- 144. Penyakit Akibat E. coli: Perlukah Antibiotik (Suara Merdeka, 30 June 2011)
- 145. Kematian akibat Syok Jantung (Suara Merdeka, 26 May 2011)
- 146. Solusi Mengatasi Alergi Ulat Bulu (Suara Merdeka, 05 May 2011)
- 147. Dampak Nuklir bagi Kesehatan Manusia (Suara Merdeka, 24 March 2011)
- 148. Ataxia Friedreich: Bukan Lumpuh Biasa (Suara Merdeka, 7 April 2011)
- 149. Metode "Atraktif" Mencegah Antraks (Suara Merdeka, 10 March 2011)
- 150. Terkontaminasi Bakteri *E Sakazakii* (Suara Merdeka, 24 Februari 2011)
- 151. Tempe: Antikanker dan Awet Muda (Suara Merdeka, 30 Januari 2011)
- 152. Tifus: Penyakit Mirip Gayus (Suara Merdeka, 27 Januari 2011)
- 153. GERD akibat "Muntahan" Asam Lambung (Suara Merdeka, 27 Januari 2011)
- 154. Mewaspadai Penyakit Hirschsprung (Suara Merdeka, 20 Januari 2011)
- 155. "Minum Obat dan Periksa ke Dokter Apakah Menakutkan?" (Suara Merdeka, 9 Januari 2011, sebagai narasumber)
- 156. Terapi Sehat dengan Jeruk (Suara Merdeka, 19 Desember 2010)
- 157. Penyakit Bernuansa Batik (Suara Merdeka, 11 November 2010)
- 158. Mewaspadai si Buram Malam (Suara Merdeka, 21 October 2010)
- 159. Waspadai Sindrom Iritasi Usus (Suara Merdeka, 14 October 2010)
- 160. Memahami Perilaku Anak Indigo (Suara Merdeka, 7 October 2010)
- 161. Mengatasi Alergi Susu Sapi (Suara Merdeka, 19 September 2010)
- 162. Sendiri Itu Seni (Suara Merdeka, 29 August 2010)
- 163. Cara Cerdas Mengatasi Kejang Demam (Suara Merdeka, 19 August 2010)
- 164. Menguak Misteri Hamil Anggur (Suara Merdeka, 25 July 2010)
- 165. Misteri "si Belang Putih" Vitiligo (Suara Merdeka, 22 July 2010)
- 166. Mewaspadai Tuberkulosis pada Anak (Suara Merdeka, 8 July 2010)
- 167. Misteri "Keroncong Lambung" Dispepsia (Suara Merdeka, 27 June 2010)
- 168. Anak Manja "Sindrom Peter Pan" (Suara Merdeka, 24 June 2010)
- 169. Cara Cerdas Mengatasi Rambut Rontok (Suara Merdeka, 4 June 2010)
- 170. "Hantu Tangan" Sindrom Terowongan Karpal (Suara Merdeka, 3 June 2010)
- 171. Mengatasi Nyeri Menstruasi (Suara Merdeka, 2 May 2010)
- 172. Menguak Misteri Tidur Berjalan (Suara Merdeka, 15 April 2010)
- 173. Memahami Derita Bilqis: Atresia Bilier (Dokter Kita Edisi 4 Thn V April 2010)
- 174. Cara Cerdas Atasi Disfungsi Ereksi (Suara Merdeka, 25 March 2010)
- 175. Menguak Misteri Penyakit Ainhum (Suara Merdeka, 11 March 2010)
- 176. Cara Cerdas Mengenali Anak Hiperaktif (Suara Merdeka, 11 Februari 2010)
- 177. Hukum Bermata Elang (Suara Merdeka, 25 Januari 2009)
- 178. Ayat-ayat Cinta VS Ayat-ayat Setan Mana yang Anda Suka (Rubrik Perilaku, Majalah Psikologi Plus Vol VI No.9 March 2012)
- 179. 10 Kiat Berkomunikasi Efektif (Rubrik Beranda, Majalah Psikologi Plus Vol VI No.6 Desember 2011)
- 180. Donald Bebek Pelipur Stres Penemu Pijat Gusi (Rubrik Tamu Kita, Majalah Psikologi Plus Vol VI No.4 October 2011)
- 181. Pepaya Lezat Bermanfaat (Rubrik Tips, Majalah Psikologi Plus Vol VI No.3 September 2011)
- 182. Rendah Hati Induk Segala Kreativitas (Rubrik Tamu Kita, Majalah Psikologi Plus Vol VI No. 3 September 2011)
- 183. 7 Kecupan Bikin Istri Serasa di Nirwana (Rubrik Perilaku, Majalah Psikologi Plus Vol VI No. 3 September 2011)
- 184. 9 Langkah Pernikahan Abadi (Rubrik Teropong, Majalah Psikologi Plus Vol VI No. 2 August 2011)
- 185. SMART Mengelola Angpao Lebaran (Rubrik Stop Press, Majalah Psikologi Plus Vol VI No. 3 September 2011)
- 186. Solusi Sederhana Menjaga Keutuhan Keluarga (Rubrik Oase, Majalah Psikologi Plus Vol VI No. 1 July 2011)

- 187. Keluarga Sehat Hospital Melesat Berkat Kepemimpinan Cinta Kasih (Rubrik Tamu Kita, Majalah Psikologi Plus Vol V No.11 May 2011)
- 188. 7 Prinsip Dokter Cinta (Rubrik Teropong, Majalah Psikologi Plus Vol V No.11 May 2011)
- 189. Seni Memahami Bahasa Jiwa (Rubrik Sketsa, Majalah Psikologi Plus Vol V No.10 April 2011)
- 190. Post-traumatic Disorder Musuh Utama Wanita (Rubrik Psikologia, Majalah Psikologi Plus Vol V No.10 April 2011)
- 191. Banyak Obat Skizofrenia Pilih yang Berisiko Minimal (Majalah Psikologi Plus Vol V No.9 March 2011)
- 192. 5 Langkah Ubah Dunia (Rubrik Perilaku, Majalah Psikologi Plus Vol V No.7 Januari 2011)
- 193. Memahami Gangguan Kepribadian Antisosial (Rubrik Psikologia, Majalah Psikologi Plus Vol V No.7 Januari 2011)
- 194. Skizofrenia: Hubungan Interpersonal Hambar Pemicunya (Rubrik Psikologia, Majalah Psikologi Plus Vol V No.6 Des 2010)
- 195. (Wawancara) Wahai Pemimpin, Belajar dari Seks, Dong... (Majalah Psikologi Plus, Volume V No. 5, November 2010)
- 196. (Artikel) Anak Indigo Pewaris Mata Ilahi (Majalah Psikologi Plus, Volume V No.5, November 2010)

Online Publication and Profile

- 197. https://www.antaranews.com/tag/dito-anurogo
- 198. http://health.detik.com/indekskanal/759/1/
- 199. http://www.suryaresearch.com/person-detail/brain-circulation-institute-of-indonesia-bcii/dito-anurogo/343
- 200. www.kompasiana.com/dito
- 201. http://kampusgw.com/tag/dito-anurogo
- 202. http://netsains.net/author/dito-anurogo/
- $203.\ www.global indonesian voices.com/author/dito-anurogo/$
- 204. http://www.noormuslima.com/tag/dokter-dito-anurogo/
- 205. https://id.linkedin.com/pub/dito-anurogo/29/925/73b
- $206. www.researchgate.net/profile/Dr_Dito_Anurogo/info$
- 207. www.slideshare.net/DitoAnurogo

 $208.\ http://muhammadjanu.blogspot.co.id/2015/02/dito-anurogo-dokter-online-kaya-prestasi.html$

V. SCIENTIFIC ACTIVITIES

No	Nome of A stinit	Dele	Time	Organized by	Diago
No 1.	Name of Activity General Health Consultation	Role Health	2011 – present	Organized by Detik.com	Place Detik.com
1.	in online media	consultant	2011 present	Deuk.com	Detrk.com
2.	Online Health Consultation	Consultant	2009 - 2014	Netsains.net	Netsains.net
3.	Penyusunan Dokumen Analisis Situasi Ibu dan Anak (ASIA) Kab. Biak Numfor	Executor	10 Oct 2014 – 10 Dec 2014	Badan Perencanaan Pembangunan Daerah Kabupaten Biak Numfor	Kabupaten Biak Numfor
4.	Seminar Nasional dan Bedah Buku "Pendidikan Karakter dalam Implementasi Kurikulum 2013"	Speaker	5 Jan 2014	Fakultas Ilmu Pendidikan IKIP PGRI Semarang	IKIP PGRI Semarang
5.	International Symposium Integrating Research and Action on Dengue	Presenter and participant	29-30 Nov 2013	FK UGM	Yogyakarta
6.	Research Day "The Neuropharmacogenetics of Autism"	Speaker	15 Nov 2013	Surya University	Universitas Surya, Tangerang
7.	Launching Buku "100 Plus Herbal Indonesia: Bukti Ilmiah dan Racikan"	Speaker	5 Oct 2013	PT Trubus Swadaya – Gramedia	Gramedia Matramaı Jakarta
8.	1 st National Conference of Neuroscience Indonesia	Presenter	14 – 15 Sep 2013	IBRC Surya University – PP PERDOSSI – PDSKJI – MNI – IDI	Jakarta
9.	Life Chat	Resource Person	13 Sep 2013	Detik.com	Detik.com
10.	The 3 rd International Seminar and Workshop on Autism and Fragile –X Syndrome	Presenter	28 – 29 August 2013	CEBIOR FK UNDIP	Semarang
11.	The 3 rd Acikita International Conference on Science and Technology	Presenter	25 – 27 August 2013	ACIKITA – BKKBN	Jakarta
12.	Keep Healthy and Keep Smile "45 Penyakit Aneh dan Khusus"	Speaker	24 August 2013	Penerbit ANDI – Gramedia	Gramedia Mall Alan Sutera Tangerang
13.	Penyuluhan Sex Education	Resource Person	10 – 11 June 2013	SURE INDONESIA	SIP Surya Tangerang
14.	Sosialisasi Program TB ke Masyarakat	Resource Person	26 Sep 2012	Aisyiyah Jateng – R&GFATM	Semarang
15.	The 2 nd Acikita International Conference on Science and Technology	Presenter	26 – 28 August 2012	ACIKITA – RRI	Jakarta
16.	Konferensi Nasional Bipolar ke-1	Presenter (Poster)	9 March 2012	PDSKJI	Surabaya
17.	Konferensi Nasional I "Women's Mental Health"	Presenter	26 – 27 Nov 2011	FK UNAIR – RSUD DR. SOETOMO	Surabaya
18.	Orientasi Mitra Baru	Speaker	26 July – 6 August 2011	RS Keluarga Sehat	Pati
19.	Acikita International Conference on Science and Technology (AICST)	Presenter	25 – 27 July 2011	ACIKITA – Kemendiknas – RISTEK	Jakarta
20.	The 2 nd International Graduate Student Conference on Indonesia	Presenter	3 – 4 Nov 2010	UGM	Yogyakarta
21.	Talkshow Kesusastraan "Karya Untuk Bangsa"	Speaker	31 Okt 2010	FLP Sekaran	Semarang
22.	Seminar dan Kongres Nasional XI IMAHAGI "Pembangunan Berbasis Kelingkungan sebagai Kunci Dasar dalam Mencapai Millennium Development Goals (MDGs) 2015"	Speaker	9 March 2010	Ikatan Mahasiswa Geografi Indonesia (IMAHAGI) Universitas Negeri Semarang	Semarang
23.	5 th Asia – Pacific Association on Problem Based Learning in Health Sciences Conference	Presenter	15 – 17 Nov 2006	MERSDU FK UNAIR	Surabaya
24. *	CIMSA May Meeting "Stop Drugs Abuse & Against HIV/AIDS"	Committee	25 – 28 May 2006 Neurology	CIMSA UNISSULA	Semarang
25.	Simposium "World Stroke Day"	Participant	1 Nov 2014	SMF Neurologi RSUP Dr. Kariadi	Semarang
26.	Workshop "Understanding Pain and Headache"	Participant	23 August 2014	PERDOSSI	Jakarta
27.	Jakarta Neurology Exhibition, Workshop And Symposium (JakNews)	Presenter and Participant	30 Jan-2 Feb 2014	Dept Neurologi FK UI, IDI, PERDOSSI	Jakarta
28.	First National Conference of Neuroscience Indonesia	Participant	14-15 Sep 2013	Surya university, IBRC	Jakarta
29.	Management of Pain and Epilepsy	Participant	11 Des 2011	PERDOSSI, IDI	Semarang
30.	Mini Symposium "Intractable Pain"	Participant	16 April 2011	PDUI, IDI	Semarang
31.	Workshop "Current Management in Pediatric Gastrohepatology, Cardiology and Neurology"	Participant	28 Feb-1 Mar 2011	IDAI, Undip, RSUP Dr. Kariadi	Semarang
32.	Symposium Neurogeriatri Update	Participant	12 June 2010	PERDOSSI, Undip	Semarang
33.	Symposium and Workshop "Early Detection on Neurodevelopmental Disorders"	Participant	1 Sep 2007	IDAI-FK UNDIP- RSDK	Semarang

34.	Seminar "LUMPUH, APAKAH PASTI POLIO?"	Participant	29 June 2005	FK Unissula-RSISA	Semarang
35.	Seminar Kesehatan Nasional 2005 "Optimalisasi Kecerdasan Otak Mencapai E.S.I.Q. yang Berkualitas	Participant	21 May 2005	FK UNISSULA	Semarang
2.5	serta Strategi Pencapaiannya"		25.5. 2004		
36.	Seminar Profesi Dokter "Penatalaksanaan Stroke secara Komprehensif"	Participant	25 Sep 2004	RS.St. Elisabeth	Semarang
37.	Simposium Nasional AIDS, Tuberkulosis, dan Malaria		19 Sep 2004	ISMKI dan BEM FK UNDIP	Semarang
*			dicine (Outside Neurolo		
38	Forum Nasional V Jaringan Kebijakan Kesehatan Indonesia	Participant	25 Sep 2014	Kemenkes RI, AIPHSS, Australian Aid	Bandung
39.	Simposium dan Workshop HIV/AIDS 2013	Participant	12 Des 2013	PDPAI, PT Kimia Farma	Jakarta
40.	Seminar "Illumina: the Next Genome Sequencing"	Participant	20 Nov 2013	Surya University	Tangerang
41.	Increasing Quality of Life Through Cell Therapy	Participant	9 Nov 2013	Kalbe and the Stem Cell and Cancer Institute	Jakarta
42.	Simposium "The Role of New Antifungal in The Treatment of Critical III Patient"	Participant	12 July 2013	Mayapada Hospital, IDI	Tangerang
43.	Public Lecture: Vaccine Design & Bioimaging Probe	Participant	25 May 2013	Dept of Chemistry University of	Jakarta
				Indonesia	
44.	Pelatihan HIPERKES dan Keselamatan Kerja	Participant	17-21 Des 2012	Universitas Yarsi	Jakarta
45.	"New Trends and Emergencies in Internal Medicine"	Participant	28 – 30 Sep 2012	PIT XVI 2012 PAPDI Semarang	Semarang
46.	Sixth Scientific Meeting on Hypertension, "Hypertension Syndrome: The Challenge to Improve Cerebro-Cardio-Renal Outcome"	Participant	24-26 Feb 2012	Indonesian Society of Hypertension (InaSH)	Jakarta
47.	Praktikum Teknik Biologi Molekuler	Participant	15 Feb 2012	FK UGM	Yogyakarta
48.	Kursus Teknik Biologi Molekuler	Participant	13-14 Feb 2012	FK UGM	Yogyakarta
49.	Leadership Workshop: Mental Health Program Development	Participant	9 Okt 2011	Perhimpunan Dokter Spesialis Kedokteran Jiwa Indonesia	Jakarta
50.	Konferensi Nasional	Participant	7-9 Okt 2011	Perhimpunan Dokter	Jakarta
	Kebijakan Kesehatan Jiwa I Konferensi Nasional Psikiatri Komunitas II			Spesialis Kedokteran Jiwa Indonesia	
51.	Seminar Sehari "Konsep Sehat Sakit dari Sudut Pandang Nanobiologi: Aplikasi Klinik, Progres, dan Masa Datang"	Participant	23 July 2011	Undip, IAPI, IDI	Semarang
52.	Seminar Radiologi "Peran CT-Scan Multislice (MSCT) sebagai Alat Penunjang Diagnosa"	Participant	26 March 2011	RSU Rembang, IDI	Rembang
53.	Second International Seminar and Workshop on Fragile-X, Autism and Related Disorders	Participant	7 August 2010	CEBIOR, UNDIP in collaboration with MIND Institute, UC Davis, USA	Semarang
54.	Symposium "Update on Rheumatic"	Participant	5 June 2010	IDI, RS. St. Elisabeth, PERDOSRI	Semarang
55.	Seminar Inisiasi Menyusui Dini (IMD)	Participant	22 May 2010	Maternity Hospital	Semarang
56.	Seminar Sehari "Kiat-kiat Menunda Penuaan Dini"	Participant	12 Des 2009	RSUD Kota Semarang	Semarang
57.	Pelatihan "Optimalisasi Siaga Bencana"	Participant	7-8 Nov 2009	FK UMY, PMI	Yogyakarta
58.	Seminar Penanggulangan Demam Berdarah	Participant	28 June 2009	Bulan Sabit Merah Indonesia	Semarang
59.	Symposium "Current Comprehensive Management in Allergy"	Participant	3 May 2009	FK UGM, IDI	Yogyakarta
60.	Participant in Guest Lecture "Surgical Ablation as a Treatment of Atrial Fibrillation"	Participant	1 Des 2008	FK UNISSULA	Semarang
61.	Workshop Radiologi "Basic Understanding of Plain Photo and Head CT-Scan Imaging on Clinical Settings"	Participant	31 August 2008	FK UGM, IDI	Yogyakarta
62.	Seminar Nasional "Excellent and Competence Doctor's for Indonesia Health"	Participant	6 Nov 2008	FK UMY, IDI	Yogyakarta

63.	Seminar Post Disaster Syndrome	Participant	19 May 2007	CIMSA FK Unair	Surabaya
64.	Agopuntura e Medicina non convenzionale in Ginecologia ed Ostetricia	Participant	24 March 2007	Prospettive di sviluppo nella Sanita Pubblica	Torino, Italy
65.	Convegno Prostata 2007: Le attuali terapie del tumore prostatico.	Participant	16 March 2007	Università degli Studi di Torino, Italy	Torino, Italy
66.	Skin Care Training	Participant	23 Des 2006	Synergy WorldWide	Jakarta
67.	Seminar dan Talkshow Kesehatan Nasional "HIV/AIDS & Narkoba"	Participant	27 May 2006	CIMSA UNISSULA	Semarang
68.	Diskusi Panel "Kortikosteroid: Aplikasi Rasional dalam Klinik"	Participant	30 July 2005	FK UNISSULA- RSISA	Semarang
69.	Seminar "Korelasi Pola Hidup Modern dengan Stres"	Participant	3 May 2005	Universitas AKI	Semarang
70.	Seminar Pemeriksaan Penunjang di Bidang Oftalmologi untuk Mencegah Kebutaan	Participant	11 Des 2004	FK UNDIP/RSUP Dr.Kariadi	Semarang
71.	Talkshow "Living without Drugs"	Participant	Tanpa Tahun	AMSA-FK UNDIP	Semarang
*			Medicine and Health		
72.	Seminar Sehari Pemahaman Aturan Pendirian Klinik Kesehatan	Participant	23 August 2014	PDUI – IDI	Semarang
73.	Pelatihan EKG Dasar Bagi Praktik Dokter Umum	Participant	15 Feb 2014	PDUI – IDI	Semarang
74.	Seminar "Penatalaksanaan Gangguan Berkemih, Hipertrofi Prostat dan Terapi CAPD pada Pasien Gagal Ginjal"	Participant	24 Nov 2012	Ikatan Ahli Urologi – RSISA	RSISA Semarang
75.	Seminar Tatalaksana Kasus Malaria "Menuju Kalteng Bebas Malaria 2018"	Participant	5 May 2012	Dinkes-IDI	Palangkaraya
76.	Seminar Profesi Kedokteran "Management of Emergency Multiple Trauma"	Participant	18 June 2011	PDGI, IDI	RS Keluarga Sehat, Pati
77.	Seminar "Manajemen Rujukan dan Penanganan Awal Pre Eklamsia-	Participant	28 May 2011	IBI	RS Keluarga Sehat Pati
78.	Eklamsia" Symposium & Workshop "Update in Growth and Development Social Pediatric Endocrinology and Nutrition Metabolic"	Participant	30-31 Oct 2010	IKA FK UNDIP- RSDK	Semarang
79.	Symposium "The Role of Probiotics and Antibiotic for Children"	Participant	25 Sep 2010	IDAI-FK UNDIP	Semarang
80.	Evidence Based Medicine (EBM) Workshop	Participant	24-25 July 2010	IDAI-FK UNDIP- RSDK	Semarang
81.	Simposium dan Workshop "Update Demam Berdarah Dengue pada Anak"	Participant	12-13 June 2010	IDAI JATENG-IKA FK UNDIP	Semarang
82.	Sosialisasi Pengembangan Pendidikan Keprofesian Berkelanjutan (P2KB) dan Workshop Pengisian Borang	Participant	29 Nov 2009	IDI Cabang Kota Semarang	Semarang
83.	Simposium dan Workshop "Current Management of Antimicrobial Therapy in Pediatric"	Participant	25-26 July 2009	FK UNDIP-RSDK	Semarang
84.	Seminar Nasional Pencegahan Dini Osteoporosis	Participant	18 June 2009	FKM UNIMUS	Semarang
85.	Seminar Sehari "Dampak Pergaulan Bebas terhadap Kesehatan Reproduksi"	Participant	6 June 2009	IBI, FKM Undip	Semarang
86.	Seminar "Etik Medikolegal, Hubungan Terapetik Dokter- Pasien"	Participant	2 August 2008	FK Undip-RSDK	Semarang
~ -	Seminar and Workshop	Participant	31 May 2008	CEBIOR-FK UNDIP- RSDK, IDAI Jateng	Semarang
87.	"The Role of Professional and Parents in Caring Children with Mental Retardation and Autism"				

	"What are drugs and free				
	sex? Agama sebagai Media Terapi"				
89.	Participant in Guest Lecturer of "Surgical Ablation as a treatment of atrial fibrillation"	Participant	29 Nov 2007	UNISSULA	Semarang
90.	Seminar dan Pelatihan Hidup Sehat dengan Shalat Tahajjud	Participant	10-11 Nov 2007	Majelis Taklim Insan Mulya	Semarang
91.	Diskusi Bulanan "Dasar- dasar Pemikiran Pengembangan Ilmu Kedokteran ditinjau dalam Perspektif Islam"	Participant	31 January 2007	FP IPTEK UNISSULA	Semarang
92.	Penyegaran Ilmiah Kegawatdaruratan Mata	Participant	1 July 2006	RSU William Booth	Semarang
93.	One Day Training "Islamic Holistic Health"	Participant	8 April 2006	BAI FK UNISSULA	Semarang
94.	Seminar Nasional "Doa dan Dzikir sebagai Obat Atasi Problematika Fisik- Psikis"	Participant	27 Sep 2005	FK UNISSULA- RSISA	Semarang
95.	Seminar Sehari "Pengaruh Minuman Berenergi terhadap Gizi dan Kesehatan"	Participant	31 Sep 2005	Dinkes	Semarang
96.	Seminar Hemofilia dalam Perspektif Medis dan Fiqh	Participant	18 June 2005	MUI Jateng	Semarang
97.	Seminar Pencegahan Kebutaan akibat Diabetes Mellitus	Participant	18 June 2005	RSISA - FK UNISSULA	Semarang
98.	Talk Show "Free Sex and the EFFECT"	Participant	17 May 2005	BEM PT UNISSULA- BEM FK UNISSULA-CIMSA FK UNISSULA	Semarang
99. 100.	Seminar Autisme Workshop	Participant Participant	28 August 2004 28 August 2003	UNDIP, IDAI Jateng FK UNDIP-IDAI	Semarang Semarang
	"Neurodevelopmental Assessment in Young Children, the Importance of Subtle Signs and Symptoms of Developmental Problems"			Jateng	
* 101.	Sarasehan Jurnalistik Ramadan 2014	Participant	Writing and Journalism 3 July 2014	Suara Merdeka	Masjid Agung Jawa Tengah (MAJT), Semarang
102.	Pelatihan Penulisan Artikel Ilmiah dan HAKI	Participant	18-19 Okt 2013	DP2M Dikti	Swiss German University
103.	Program Pendidikan dan Pelatihan Tahap Dasar Sekolah Jurnalisme Indonesia	Participant	18 Okt – 1 Nov 2012	PWI Pusat, Kemendikbud, UNESCO	Gedung Pers Jateng Semarang
104.	Book Writing Revolution	Participant	17-18 Dec 2011	Akademi Penulis Indonesia	Yogyakarta
105.	Workshop "Peka dan Kritis melalui Tulisan di Media Massa"	Participant	23 Oct 2010	KOMPAS-UPT UNIKA Soegijapranata, Semarang	UNIKA Semarang
106.	Sarasehan Jurnalistik Ramadan 2010	Participant	28 August 2010	Suara Merdeka	MAJT Semarang
107. 108.	One Day Workshop Menulis Workshop "Mahir Menulis:	Participant Participant	18 July 2010 19 June 2010	Mata Pena Writer FE UNNES	Tangerang UNNES Semarang
108.	Kiat Jitu Menulis Artikel Opini, Kolom, dan Resensi Buku"	Participant	19 June 2010	FE UNNES	UNNES Semarang
109.	Workshop Jurnalistik dan Penulis Plus	Participant	8 June 2008	ICRC DIY – Jateng	Universitas Negeri Yogyakarta
110.	Pelatihan Kiat Cepat Menulis Artikel di Media Tingkat Lanjut untuk Umum	Participant	17 – 18 March 2008	Lembaga Pendidikan Wartawan PWI Jawa Tengah	Gedung Pers Jateng Semarang
111.	Workshop Penulisan Sastra: Puisi, Cerpen, Teenlit	Participant	28 Dec 2007	Suara Merdeka-DKJT	Suara Merdeka, Semarang
112.	Talk Show "Menulis dengan Hati dan Pikiran"	Participant	10 June 2007	KALAM ROHIS FE UNDIP	Semarang
113.	Workshop Karya Ilmiah Mahasiswa	Participant	15 March 2005	Lembaga Penelitian UNISSULA	FTI UNISSULA, Semarang
*	Deletiber M. P. L'	Dent	Additional Activities	EID LINIDID DOD	
114.	Pelatihan Media Literasi tentang Fenomena Bahasa dalam Pers di Jawa Tengah Bakti Sosial Pelayanan	Participant	11 October 2014	FIB-UNDIP, BSF, LeSPI	Semarang
115.		Medical	15 May 2014	Puskesmas Pd. Aren	Bintaro

112	sekitarnya	D	11.4 1.0011		T 1 .
116.	Uji Kompetensi Battra Ramuan Tingkat Pratama	Participant (Kompeten)	11 April 2014	Lembaga Sertifikasi Kompetensi Battra Ramuan Indonesia	Jakarta
117.	Refressing Uji Kompetensi Battra Ramuan Tingkat Pratama	Participant	10 April 2014	Lembaga Kursus dan Pelatihan "Sekar Peni"	Depok
118.	Pelatihan Matematika GASING (gampang, asyik, menyenangkan) SD	Participant	3-7 March 2014	Surya University	Tangerang
119.	Bakti sosial sunatan masal, pengobatan gratis, sembako murah	Medical Doctor	23 February 2014	KIMMI (Komunitas Mitra Medis Indonesia)	Marunda, Cilincing Jakarta Utara
120.	Workshop "Wireless Cellular Network and Its Challenges"	Participant	11 Feb 2014	Surya University	Tangerang
121.	Diskusi Panel "Indonesiaku, Indonesiamu, Indonesia Kita"	Participant	4 Feb 2014	Surya University	Tangerang
122.	Seminar Pendidikan Akbar "Memajukan Pendidikan dan Riset Indonesia Melalui Kerjasama Internasional"	Participant	25-27 Aug 2013	ACIKITA, BKKBN	Jakarta
123.	Pelatihan "5 Langkah Mudah Memahami Dasar Grafologi"	Participant	22–23 June 2013	New Spirit Psychology Professional, Grafologi Indonesia	Jakarta
124.	Technopreneurship : "Build Your Own"	Participant	21 May 2013	UMN	Serpong, Tangerang
125.	Good Communicator : "Being Comfortable in Every Situation"	Participant	20 May 2013	UMN	Serpong, Tangerang
126. 127.	"Seminar Fotografi" Bedah 3 Buku	Participant Participant	7 Okt 2012 23 Sep 2012	Nikon BAI FK UNISSULA	Semarang Balaikota Semarang
127.	"Journey of Love" Kegiatan Sosialisasi Undang Undang Nomor 3 tahun 2005 Tentang Sistem Keolahragaan	Participant	22 June 2012	Pemerintah Provinsi Kalimantan Tengah	Kalimantan Tengah
129.	Nasional Motivation Achievement Training: Membangun Budaya Kerja Profesional	Participant	15 June 2012	RSI PKU Muhammadiyah, Palangka Raya	Palangka Raya
130.	Turnamen Golf Memperingati HUT KALTENG ke-55	Leader of Medical team	11 June 2012	Universitas PGRI Palangkaraya	Palangka Raya
131.	Seminar Pendidikan Akbar "Memajukan Pendidikan dan Riset Indonesia Melalui Keriasama Internasional"	Participant	25-27 July 2011	ACIKITA Foundation – Kemendiknas	Jakarta
132.	"How to be a Great Public Speaker", PR Community Gathering	Participant	23 Des 2010	PR Community, Bank Indonesia	Semarang
133.	Seminar "How to Get Overseas Scholarship" + TOEFL Workshop and Test	Participant	4-5 Des 2010	FK Undip	Semarang
134.	The Climate Change Action Training	Participant	28 Oct 2010	The Climate Project Indonesia	Jakarta
135.	Seminar Nasional Pendidikan Karakter Seminar Qur'ani "Qur'an for Gen"	Participant	9 October 2010	FBS UNNES	Semarang
136. 137.	Kegiatan Mobil Unit untuk	Participant Leader of	29 August 2010 31 July 2010	Remaja Islam MAJT PMI Semarang	Semarang Semarang
1071	rekrutmen donor	Mobile Unit Team	-	1 m Sommany	
138.	Caraka Festival Kreatif "Burn Your Box!!"	Participant	17-19 June 2010	PPPI PENGDA JATENG, Suara Merdeka	Semarang
139.	Wisuda Akbar Indonesia Menghafal bersama Ustadz Yusuf Mansur	Participant	8 May 2010	PPPA DAARUL QUR'AN	Jakarta
140.	Seminar Awam "Apa yang dapat perempuan lakukan untuk mencegah kanker serviks"	Participant	20 Februari 2010	RSB Gunung Sawo	Semarang
141.	The International Seminar on Disaster: Theory, Research, and Policy	Participant	20 – 22 Oct 2009	UGM	Yogyakarta
142.	Musyawarah Nasional II Forum Lingkar Pena (Seminar-Workshop Nasional)	Committee	14-16 August 2009	Forum Lingkar Pena (FLP)	Surakarta
143.	International Seminar "Business, Property and Public Interest: Legal Perspective in Asian Countries	Participant	5 August 2009	Toyo University-UNDIP	Semarang
144.	Talkshow Mengasuh Anak Hebat	Participant	19 July 2009	BSMI	Semarang
145.	Seminar Enterpreneurship Goes to Campus	Participant	8 June 2009	BEM FAI UNISSULA	Semarang
146.	Seminar Nasional Quantum Cinta "Recharge Your Love"	Participant	14 March 2009	UKM-FSA UNISSULA	Semarang
147.	Seminar Nasional "The Fourth Annual Training for	Participant	20 – 21 Des 2008	BAI, FK UNISSULA,	Semarang

	Better Organization and Islamic Health Conference"			FULDFK, IDI	
148.	Seminar Interaktif	Participant	1 Des 2008	FE UNISSULA	Semarang
149.	"Cara Cerdas Cari Uang" Talk Show Mind Set "Open and Manage Your Mind, Get Your Future"	Participant	26 March 2008	BEM Fakultas Psikologi UNISSULA	Semarang
150.	Kelas Introduksi "Cara EDAN: Bicara Percaya Diri Saat Memimpin, Menjual, dan Berpresentasi"	Participant	18 Nov 2007	School of Motivational Communication	Semarang
151.	Seminar Nasional "Membangun Sinergi Berbasis Spiritualitas"	Participant	6 Sep 2007	UNDIP	Semarang
152.	Seminar Nasional Quo Vadis Pendidikan: Menelisik Kasus Kekerasan dalam Praksis Pendidikan di IPDN	Participant	14 June 2007	IKA UNNES	Semarang
153.	May Meeting 2007	Participant	17 – 20 May 2007	CIMSA-FK UNAIR	Surabaya
154. 155.	Youth of Nation Summit Seminar Nasional Pasar	Participant Participant	13 May 2007 2007	AIESEC UNDIP KSPM-UNDIP	Semarang Semarang
156	Modal	-	2 4 5 1 2007		-
156.	Seminar "Preparing Medical Muslim Generation Facing Indonesian's Future Phenomena"	Participant	3 – 4 Februari 2007	FK UGM	Yogyakarta
157.	"September Meeting" Standing Committee of Research Exchange	Delegation	30 Sep-1 Oct 2006	SCORE CIMSA, UGM-UMY	Yogyakarta
158.	Volunteer BSMI (Bulan Sabit Merah Indonesia) untuk Gempa Bumi Klaten	Volunteer	30 May-25 June 2006	BSMI	Klaten
159.	ESQ Leadership Training	Participant	25-26 Feb 2006	ESQ Leadership Center	Semarang
160.	Seminar Nasional "Menumbuhkan Jiwa Enterpreunership"	Participant	22 Des 2005	FTI UNISSULA	Semarang
161.	Seminar Multilevel Marketing dalam Perspektif Islam	Participant	20 August 2005	MUI Jateng	Semarang
162. 163.	Seminar Keperawatan Seminar Pengembangan	Participant Participant	18 June 2005 4 June 2005	RS St. Elisabeth UNISSULA	Semarang Semarang
164.	Peradaban Islam Seni Menata Hati Menuju	Participant	29-30 Jan 2005	LEMBKOTA	Semarang
	Insan Kamil Seminar Nasional	•			
165.	Biophytofarmaca	Participant	18 Des 2004	UNDIP	Semarang
166.	Harunyahya International: Invitation to the Truth	Participant	Sep 2002	Harunyahya International	Semarang
167.	Belajar Bahasa Jepang Kelas Dasar 1A selama 40 jam	Participant	2014	Pandan College	Tangerang
168. 169.	Research Day Batch III Pelayanan Kesehatan di Klinik SuRE	Participant Dokter	17 Des 2013 10-13 June 2013 3-5 June 2013 27-31 May 2013 21-24 May 2013	Surya University PT. SURE INDONESIA	Tangerang Tangerang
170.	Love Poetry Valentine Day 2010	Tim Dewan Juri	21 Feb 2010	Harian Online Kabar Indonesia	Netherlands
171.	The Product Promotion	Participant	15 March 2000	IBEC-British Council-	Semarang
172.	Competition Lomba Karya Cipta '99	Participant	10 Feb-1 March 1999	UNIKA Organisasi Pelajar PPMIA	Sukoharjo
173.	Lomba Penelitian Ilmiah Remaja ke-21 Tahun 1997	Participant	20 August 1997	DepDikBud	Jakarta
174.	Penulisan buku "Kisah 25 Ilmuwan Indonesia yang Mendunia"	Mentor	1 Januari 2015 – finished	Ikatan Ilmuwan Indonesia Internasional (I-4), Masyarakat Nano Indonesia (MNI), Nano World Indonesia (NWI)	Indonesia
175.	Pendidikan Operator Komputer Berbasis Windows	Participant	15 Des 2014 – 23 Jan 2015	Lembaga Pendidikan Alfabank	Semarang
176.	Pengobatan Massal CARDIAC 4	Medical Doctor	1 Februari 2015	CIMSA UNISSULA	Demak
177.	CME Online: Assessment and Treatment of Depression in the Primary Care Setting	Participant	9 April 2010	Harvard Medical School, Boston, Massachusetts	Online
178.	Lomba Penulisan Tayangan Film Televisi di Mata Remaja	Participant	23 Nov 1996	PKBI – Depdikbud	Semarang
179.	Pengobatan Massal CARDIAC 5	Medical Doctor	21 Feb 2016	CIMSA UNISSULA	Demak
180.	National Seminary "Introducing and Understanding Self-Potential	Main Speaker	22 Nov 2015	Himabio – UNNES	Semarang
181	through Genetics" National Congress and	Poster	6 – 7 Feb 2016	ASPI	Bogor

	Seminary ASPI II	presenter			
182	Computer Course 40 hours:	Participant	15 Dec 2014 – 23 Jan	ALFABANK	Semarang
	Computer Operator Windows-		2015		
	Based				
183	Seminar Forum Kebijakan	Speaker	24 – 26 August 2015	FJKKI – FKKI	Minang
	Kesehatan Indonesia VI				
184	National Seminary Sastra	Participant	27 Feb 2016	Forum Lingkar Pena	FBS UNY Yogya
	Santun di Era Digital			(FLP)	
185	Seminar Akademik	Participant	1 Des 2015	PPIE FEB UI	Jakarta
	Pembangunan Ekonomi				
	Indonesia 2015				
186	Nobel Prize Committee: Prof.	Participant	2-4 Nov 2015	FK UGM	Yogyakarta
	Anders Liljas. Special				
	Lectures Series Agendas				
187	5 th International Joint	Oral and Poster	11 – 12 Dec 2015	FK UGM	Yogyakarta
	Symposium on Biomedical	Participant			
	Sciences: Translational				
	Neuroscience				
188	Workshop "Scientific Articles	Participant	24 Feb 2016	LPPM UGM	Yogyakarta
	Writing for International				
	Journals Publication"				

ЪT		Activities 2016 – 2017	
No	Name of Activity	Time, Place	Role
1	Public Discussion: Srikandi Forum Indonesia 2017 ''Women, Stem Cells, Nanomedicine, Hematopsychiatry''	29 April 2017, Syuhada Mosque, Yogyakarta	Speaker and Founder/Initiator
2	Nationality Dialogue: Religion Indonesian Perspective; Humanism in Differences.	Wednesday, 26 April 2017, UIN Suka Yogyakarta	Participant
3	Workshop Creative Writing by Learning Indonesia	11-12 March 2017, Meeting Room, Rumah Kreatif Jogja, Jalan Sagan 123 Yogyakarta.	Main Speaker
4	Workshop Springer Nature [Database Springer, Quality of Journal, How to Submit]	Tuesday, 14 Feb 2017, Library UGM Yogyakarta	Participant
5	National Seminary ''Controversy, Revision, Implementation UU No. 11 Tahun 2008 about ITE [Information and Electronic Transaction].	28 Dec 2016, Yogyakarta	Participant
6	Voluntary Activity [Bakti Sosial]	Wed, 21 Dec 2016, Dusun Dukuh, Sidomoyo, Godean, Sleman.	Medical Doctor
7	Seminary ''Maximum Achievement with Mind Technology''	15 Dec 2016, Sekolah Pascasarjana UGM, Yogyakarta	Participant
8	Author Talk: How to Succeed in Publishing at International Academic Journals	28 Nov 2016, UGM Library	Participant
9	International Seminar on Character Education: Living Values Education [LVE] Approach.	21 Nov 2016, Convention Hall, UIN Sunan Kalijaga, Yogyakarta	Participant
10	Mini Workshop; CV, Personal Branding, Interview Strategies for Working	16 Nov 2016 Library FT UGM	Participant
11	Monthly Online Seminar [MOS] # 10 about Writing Scientific Paper	10 Nov 2016, Sahabat Beasiswa	Speaker
12	Kongres Nasional Ikatan Ahli Kesehatan Masyarakat Indonesia [KONAS IAKMI] XIII	3 – 5 Nov 2016, Makassar	Oral Presenter
13	Workshop Kepenulisan Kreatif Pra Kongres Nasional Ikatan Ahli Kesehatan Masyarakat Indonesia [Pra KONAS IAKMI] XIII	1 – 2 Nov 2016, Ruang K225 Lantai 2 Gedung FKM Unhas, Makassar	Speaker [Pemateri]
14	Call for Essay Competition: Creating Youth with National Culture towards International	5 Nov 2016, Universitas Sebelas Maret, Surakarta	Participant

Scientific	Activities	2016 -	2017

15	1 st International Conference on Health	28 – 29 Oct 2016, UGM	Speaker
	Science [ICHS] 2016	Yogyakarta	-
16	Dr. Boenjamin Setiawan Distinguished	Saturday, 15 Oct 2016, Faculty of	Participant
	Lecture Series 2016 Anti-Ageing	Medicine, Auditorium - UGM	
	Revolution A Scientific Breakthrough of Stem Cell Therapy		
17	Islamic Civilization and Thought Seminary	Universitas Darussalam Gontor	Participant
18	Pertemuan Ilmiah Nsional Tahunan Agromedis [PINTAR I] Update on Management of Dermatovenereology Problems in Primary Health Care	25 Sep 2016, Aston Hotel – FK Universitas Jember	Presenter Poster
19	Experimental Animal Training [Pelatihan Pengenalan Hewan Coba]	21 Sep 2016, LPPT UGM Yogyakarta	Participant
20	Introduction to EEWOWW: A tool to support research best practices	30 August 2016, UGM Library	Participant
21	Reference Manager and Sway Training; Sway Training	25 August 2016, Library FK UGM	Participant
22	Reference Manager and Sway Training; Mendeley Training	24 August 2016, Library FK UGM	Participant
23	Trans-Academic Cancer Genetics [TACG] 2 Symposium and Workshop ''When Clinicians Meet Genetics'' GENETICS; Application from bench to bedside and community	19 – 21 August 2016, Royal Ambarukmo, Yogyakarta	Delegate and Poster Presentator
24	Seminar ''Potency of Herbal Immunomodulator to Maintain Health''	14 August 2016, Auditorium Kampus III, Universitas Ahmad Dahlan, Yogyakarta	Participant
25	Seminary and Workshop ''Improving Health Quality by Changing the Future Using Your Fingertips'' by Indonesian Young Health Professionals Society [IYHPS].	16 July 2016, Al Kindi Building, FK UNISSULA Semarang	Speaker
26	General Lecture ''Molecular Targeting of Boron Delivery Agents for Neutron Capture Therapy of Brain Tumors in the Genomic Era''	Monday, 16 May 2016, Ruang Sidang unit V, Faculty of Pharmacy UGM	Participant
27	Advanced Immunology Course XVII: Immunology of Sepsis	28 – 29 April 2016, Departemen Histologi dan Biologi Sel FK UGM, Yogyakarta	Committee
28	Seminar "Application Stem Cells on	13 April 2016, Rumah Sakit Umum	Participant
	Various Medical Cases'' 10 hours @ 45 minutes	Pusat [RSUP] Dr. Sardjito Yogyakarta	[6 SKP]
29	Menulis Itu Asyik: Jurus Jitu Taklukkan Jurnal Internasional Terindeks Scopus	Tuesday, 12 April 2016, Pharmacy Faculty, UGM, Yogyakarta	Leader of Committee
30	Islamic Psychology Intensive Course [KIPI] by DR. Bagus Riyono and Prof. Subandi, M.A., Ph.D.	30 March – 18 May 2016 [8 weeks], Islamic Psychology Learning Forum [IPLF] Universitas Gadjah Mada [UGM]	Best Participant
31	Annual Scientific Meeting; Sustainable Development Goals [SDGs], Non- Communicable Diseases [NCD], and Neglected Tropical Diseases [NTD]	3 March 2016, FK UGM	Participant [16 SKP]

References

References are available upon request.







nn

MODEL UNITED NATIONS



This certificate is proudly presented to

DITO ANUROGO

As The Best Position Paper of UN Women in

IMUN ONLINE CONFERENCE 56.0

from May 8th to 9th, 2021

Mohineesh Bhandwy

Mohneesh Bhardwaj **Executive Chairman**



Australian Embassy

Best of

IMUN

Vietnam & Thailand

Gralip Akhand

Galib Akhand Academic Advisor





IS AWARDED TO

dr. Dito Anurogo, M.Sc.

as Trainer at BASC 2021 Workshop Series "PENERBITAN BUKU AJAR"

Virtual, 24 April 2021

FULL-DAY Meeting + 100 HOURS Exclusive Consultation

Universitas YARSI, Rector



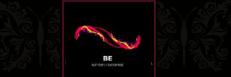
Prof. dr. Fasli Jalal, Ph.D

BASC 2021, Chair

Dr. Samsul Mustofa

	informatics and	
CERTI	FICATE	
	IT APPRECIATION	
Prese	ent to	
dr. Dito Anurogo, M.Sc		
for Sharing Valuable Knowledge in the WEBINAR COVID-19 "MENGENAL CORONAVIRUS SECARA SAINTIFIK AGAR TIDAK PANIK" Saturday, 7 March 2020		
Director of	Vice Committee Workshop Life Science	
Didik Huswo Utomo, M.Si	Evi Octaviany, S.Pd., M.Si	







BUTTERFLY ENTERPRISE AWARDED THIS CERTIFICATE TO

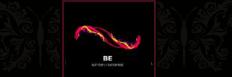
dr. DITO ANUROGO, M.Sc.

No.: 07.19/III-I/H-BBP/BUTTERFLY/VII/202

for being The Speaker of "PENANGANAN KECANDUAN GADGET PADA ANAK & REMAJA" on July 19th, 2021 at BINCANG "BARENG YENI DEWI SIAGIAN PSIKOLOG TV" YOUTUBE CHANNEL

Jakarta, July 19th, 2021

YENI DEWI SIAGIAN, PSIKOLOG®, NCLT®, NCLTDO®, NCLPMA® Managing Director





BUTTERFLY ENTERPRISE AWARDED THIS CERTIFICATE TO

dr. DITO ANUROGO, M.Sc.

No.: 07.07/II-I/H-BBP/BUTTERFLY/VII/2021

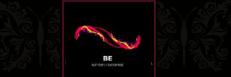
for being The Speaker of "PERILAKU SADISME"

on July 7th, 2021

at "BINCANG BARENG YENI DEWI SIAGIAN PSIKOLOG TV" YOUTUBE CHANNEL

Jakarta, July 7th, 2021

YENI DEWI SIAGIAN, PSIKOLOG®, NCLT®, NCLTDO®, NCLPMA® Managing Director





BUTTERFLY ENTERPRISE AWARDED THIS CERTIFICATE TO

dr. DITO ANUROGO, M.Sc.

No.: 07.04/I-I/H-BBP/BUTTERFLY/VII/202

for being The Speaker of "RAHASIA AWET MUDA, CANTIK & BAHAGIA TANPA OPERASI PLASTIK" on July 4th, 2021

at BINCANG "BARENG YENI DEWI SIAGIAN PSIKOLOG TV" YOUTUBE CHANNEL

Jakarta, July 4th, 2021

YENI DEWI SIAGIAN, PSIKOLOG®, NCLT®, NCLTDO®, NCLPMA® Managing Director



SERTIFIKAT

No: 0034/ADPI- PKMOSA-5/II/2021

Diberikan Kepada:

dr. Dito Anurogo, M.Sc.

Sebagai Plenary Speaker

yang telah mengikuti dan berperan aktif dalam kegiatan:

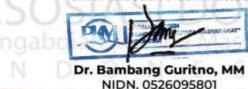
Pengabdian Dosen Lintas Bidang 16 Provinsi se-Indonesia

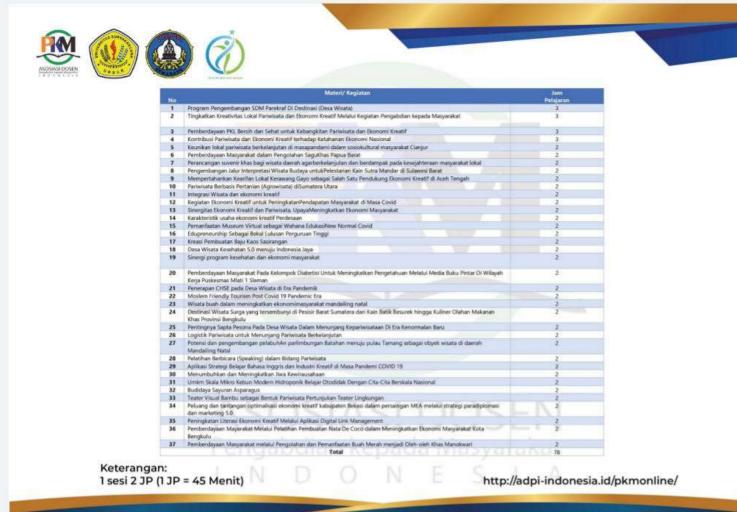
"Tingkatkan Kreativitas Lokal Pariwisata dan Ekonomi Kreatif Melalui Kegiatan Pengabdian kepada Masyarakat"

Yang dilaksanakan pada tanggal 26 - 28 Maret 2021

Padang, 28 Maret 2021

Chief Executive Committee











he 18th International Virtual Conference of Asia acific Association of Surgical Tissue Bank 2021 convetion with nd International Meeting in Regenerative Medicine th Annual Meeting Indonesian Tissue Bank Association rd Annual Meeting Indonesian Association of Tissue Engine and Cell Therapy Oth Annual Meeting Indonesian Stem Cell Association

Certificate of Participant

Dito Anurogo

Has participated as **Presenter of Oral Paper Competition** in the **APASTB** (The 18th International Virtual Conference of Asia Pacific Association of Surgical Tissue Bank 2021) **Young Investigator Awards**, on March 19-20, 2021



Heri Suroto, MD, PhD

Chairman of Committee -President of Asia Pacific Association of Surgical Tissue Banking Assoc Prof. Ferdiansyah Mahyudin, MD, PhD

President of Indonesian Tissue Bank Association

Bintang Soetjahjo, MD, PhD

President of Indonesian Association of Tissue Engineering and Cell Therapy (IATECT) / REJASELINDO

Assoc Prof. Rahyussalim, MD, PhD

President of Indonesian Association of Tissue Stem Cell (IASC) / ASPI



SERTIFIKAT

diberikan kepada dr. Dito Anurogo, M.Sc

Telah menyelesaikan program Online Course INBIO Batch VIII dengan topik "Understanding Epigenetics Cancer Pathway and its Bioinformatic Analysis" selama 6 kali pertemuan dengan total waktu 12 jam pada tanggal 17 - 27 Maret 2021



Evi Octaviany, S.Pd., M.Si. GENERAL MANAGER INBIO INDONESIA



Didik H. Utomo, M.Si. DIREKTUR INBIO INDONESIA



Nilai Peserta

90

Predikat: 85 - 100 : A 75 - 84 : B 60 - 74 : C < 59 - 0 : D



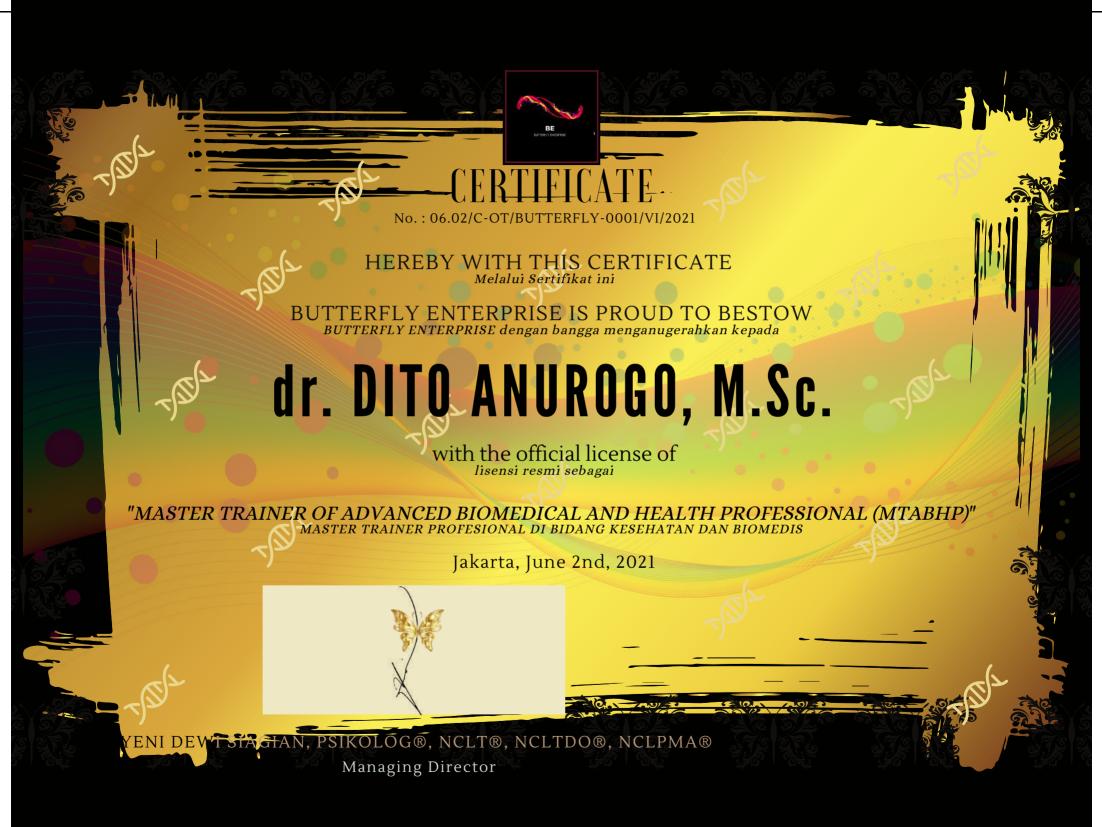
RUNDOWN INBIO INDONESIA ONLINE COURSE

"UNDERSTANDING EPIGENETICS CANCER PATHWAY AND ITS BIOINFORMATIC ANALYSIS"

17 - 27 Maret 2021

Waktu	Materi
021 09.00 - 11.00 WIB	Pengenalan dan konsep dasar kanker epigenetik
	Pembuatan "research pipeline" pada topik kanker epigenetik
	Pengenalan Database untuk penelitian kanker epigenetik
09.00 - 11.00 WIB	Pengolahan, filter, dan pengunduhan data genomics untuk kanker epigenetik (data gene expression,
	DNA methylation and miroRNA)
	Format data genomik untuk kanker epigenetik
et 2021 09.00 - 11.00 WIB	Analisis Data kanker epigenetik (differential gene expression, differential DNA methylation expression,
	differential miRNA expression)
09.00 - 11.00 WIB	Analisis Data kanker epigenetik (check mutation or epigenetic cancer pathway, correlation analysis, dan
	network analysis)
09.00 - 11.00 WIB	Drafting manuscript penelitian
09.00 - 11.00 WIB	Review dari pemateri terhadap draft manuskrip dari peserta
	09.00 - 11.00 WIB 09.00 - 11.00 WIB 09.00 - 11.00 WIB 09.00 - 11.00 WIB 09.00 - 11.00 WIB







THE ACADEMY OF MODERN APPLIED PSYCHOLOGY

CERTIFICATE OF COMPLETION

AWARDED TO

Dito Anurogo

DIPLOMA IN MODERN APPLIED PSYCHOLOGY

The holder of this certificate has successfully completed a Diploma certificate course in Modern Applied Psychology on Udemy.



Kain Ramsay Director of Training

February 20, 2021

Date



IEEEL INSTITUTE

Indonesia Excellent Education For Excellent Life



Hereby With This Certificate We Are Proud To Entitle

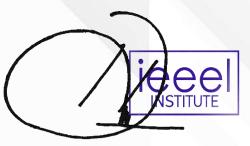
Dito Anurogo

Having satisfactorily completed the course of study is herewith and henceforth recognized as

CERTIFIED BUSINESS OPERATIONS ASSOCIATE (CBOA)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of our Participants as Certified Business Operations Associate.

July 16th, 2021



DR. HENDY TANNADY

DIRECTOR

Certificate Number : CBOA-001072021





No. 02/EMM2-STMI/VII/2020

THIS CERTIFICATE IS PROUDLY PRESENTED TO :

Dito Anurogo, C.EMM

Has Successfully completed online training on :

Certified Event Management Mastery Batch #02

Which was held on July 3rd, 2021, From 10.00 AM – 12.00 PM



Jakarta, July 3rd, 2021

Saktisyahputra, S.Ikom, M.I.Kom, Headmaster of STMI

Coach Irma Ramadhani, S.E. TRAINER







Hereby With This Certificate We Are Proud To Entitle



Certificate Number : CETP-201062021

Having satisfactorily completed the course of study is herewith and henceforth recognized as

CERTIFIED EXCELLENT TRAINER PROFESSIONAL (CETP)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of our Participants as Certified Excellent Trainer Professional.

June 21st, 2021





No. 10/GL4-STMI/VI/2021

THIS CERTIFICATE IS PROUDLY PRESENTED TO :

Dito Anurogo, C.GL

Has Successfully completed online training on :

Certified Great Leadership Batch #04

Which was held on June 1st, 2021, From 09.00 AM – 11.00 AM



Jakarta, June 1st, 2021



Dr. Ir. Hendy Tannady, ST. MT. MM. MBA Dipl.PM. TRAINER Great Leadership





IEEEL INSTITUTE

Indonesia Excellent Education For Excellent Life

Hereby With This Certificate We Are Proud To Entitle



Having satisfactorily completed the course of study is herewith and henceforth recognized as

CERTIFIED LEADERSHIP MANAGEMENT ASSOCIATE (CLMA)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of our Participants as Certified Leadership Management Associate.

May, 29th 2021



Certificate Number : CLMA-019052021

1	
(* * *	/ideel
	HEEEI MISTITUTE

DR. HENDY TANNADY DIRECTOR

CERTIFICATE OF COMPLETION

No. 26/PDM3-STMI/VI/2021

THIS CERTIFICATE IS PROUDLY PRESENTED TO :

Dito Anurogo, C.PDM

Has Successfully completed online training on :

Certified Personality Development Mastery

Which was held on June 12th, 2021, From 09.00 PM – 12.00 PM



Headmaster of STMI

Jakarta, June 12th, 2021



Widya Amata

Widya Amata TRAINER



CERTIFICATE OF COMPLETION

No. 05/PS19-STMI/VI/2021

THIS CERTIFICATE IS PROUDLY PRESENTED TO :

Dito Anurogo, C.PS

Has Successfully completed online training on :

Certified 17 Rahasia Public Speaking 100% Total

Which was held on June 20th, 2021, From 07.00 PM to 10.00 PM

Jakarta, June 20th, 2021

Saktisyahputra, S.Ikom, M.I.Kom,

C.NLP, CM.NLP, CH, CHt, CPS, CMSP, CSTS, CESQ, CTHRNLP





Hereby With This Certificate We Are Proud To Entitle



Having satisfactorily completed the course of study is herewith and henceforth recognized as

CERTIFIED SYSTEM OPERATING PROCEDURE ANALYST (CSOPA)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of Our Participants as Certified System Operating Procedure Analyst.

July21st, 2021





DR. HENDY TANNADY

DIRECTOR

Certificate Number : CSOPA-007072021





No. 05/STMI277-STMI/VI/2021

THIS CERTIFICATE IS PROUDLY PRESENTED TO :

Dito Anurogo, C.STMI

Has Successfully completed online training on :

Certified School of Trainer and Motivator Indonesia

Which was held on June 20^{th} , 2021, From 02.30 PM to 10.00 PM

Jakarta, June 20th, 2021



Saktisyahputra, S.Ikom, M.I.Kom,

C.NLP, CM.NLP, CH, CHt, CPS, CMSP, CSTS, CESQ, CTHRNLP











IEEEL INSTITUTE Indonesia Excellent Education For Excellent Life

Hereby With This Certificate We Are Proud To Entitle



Certificate Number : CSRP-017072021

Having satisfactorily completed the course of study is herewith and henceforth recognized as

CERTIFIED SELECTION & RECRUITMENT PROFESSIONAL (CSRP)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of Our Participants as Certified Selection & Recruitment Professional.

July 26th, 2021



DIRECTOR

Part of Certifications and Achievements

Dito Anurogo, M.D., M.Sc.

No	Attainment	Date	Comittee / Organizer
1	Practice in Rehabilitation and Cardiopulmonary Exercise	21 Nov 2019	Taipei Medical University (OpenEdu)
2	Pulmonary Rehabilitation	21 Nov 2019	Taipei Medical University (OpenEdu)
3	The 3D MS THRIVE Initiative: Patient-Centered Management for Optimal Outcomes in Multiple Sclerosis and is awarded 1.0 AMA PRA Category 1 Credits™	11 August 2018	Med Learning Group
4	Rational Approach for Clinical Practice in HIV/AIDS Treatment	30 Nov – 1 Dec 2018	Indonesian HIV / AIDS Concerned Doctors Association
5	The Art of Medicine (Copyright Certificate)	25 Jan 2016	Ministry of Law and Human Rights
6	Acupressure – Miracle Points	01 Nov 2019	Udemy
7	Free Fab Body Course Bundle	25 Nov 2019	Accredited CPD Activity
8	Understanding Anxiety, Depression and CBT	07 Nov 2019	Future Learn, University of Reading
9	Digital Skills: Artificial Intelligence	10 Nov 2019	Future Learn, Accenture
10	Blended Learning Essentials: Digitally – Enriched Apprenticeships	2 Dec 2019	Future Learn, University of Leeds and UCL Institute of Education
11	Diploma in Nutrition	25 Nov 2019	Fob Academy Fabulous Body Inc, California, United States
12	Good Brain, Bad Brian: Parkinson's Disease	27 Nov 2019	Future Learn – University of Birmingham
13	Genomic Technologies in Clinical Diagnostics: Molecular Techniques	11 Nov 2019	Future Learn – ST GEORGE'S, University of London
14	Pulmonary Rehabilitation	21 Nov 2019	Taipei Medical University (OpenEdu)
15	Sleep and Respiratory Care	21 Nov 2019	Taipei Medical University (OpenEdu)
16	Understanding Autism	8 Dec 2019	Future Learn, University of Kent
17	Advanced Good Pharmacy Practice	4 Dec 2019	Taipei Medical University (OpenEdu)
18	Moderate Good Pharmacy Practice	4 Dec 2019	Taipei Medical University (OpenEdu)
19	How to Succeed at: Writing Applications	3 Dec 2019	Future Learn, University of Sheffield

20	Advanced Google Analytics	Expires 09 Nov 2022	Google Analytics Academy
21	Google Analytics for Beginners	Expires 08 Nov 2022	Google Analytics Academy
22	Fully Accredited Professional Child Psychology Diploma	07 Nov 2019	Udemy
23	Internationally Accredited Diploma Certificate in Nutrition	26 Nov 2019	Udemy
24	The Art of Artistic Writing Training	13 May 2017	CIMSA (Center for Indonesian Medical Students' Activities)
25	Online Seminary with 1000 Participant Awareness of Bipolar: "Confussion Diseases in Digital Era"	01 Nov 2019	The Champion Community
26	Professional Child Psychology Diploma Course	7 Nov 2019	Diploma of Professional Study (KEY ACADEMY)
27	Reviewer	2 Dec 2019	Journal An-Nafs
28	Good Pharmacy Practice	5 Dec 2019	Taipei Medical University (OpenEdu)
29	Pulmonary Medicine and Rehabilitation	5 Dec 2019	Taipei Medical University (OpenEdu)
30	Advanced Cardiac Life Support (ACLS)	22 - 24 Jan 2010	Indonesian Heart Association (PERKI)
31	Advanced Trauma Life Support (ATLS)	4 - 6 Feb 2011	Committee on Trauma, Indonesian Surgeons Association (IKABI)
32	Licensed Writer in Non-fiction Book Writing	31 May 2019	Indonesian Professional Certification Authority
33	Empowering Indonesia Through Digital Literacy	12 Dec 2018	Makassar Digital Valley
34	Improvement of Lecturer Competence in Learning Based on Information and Communication Technologies (PembaTIK) Literacy Level (32 hours) – South Sulawesi Province	20 – 21 April 2019	Ministry of Education and Culture
35	Technical Guidance for Read-Write Instructors at National Level Literacy (67 hours)	8 – 14 April 2019	Board of Language Development and Coaching, Ministry of Education and Culture
36	Overcoming Challenges for Children and Adolescents with MS: A Comprehensive Review for Pediatric Clinicians of MS Symptoms, Ddiagnosis, Treatment, and Coordination of Care	11 August 2018	The Consortium of Multiple Sclerosis Centers (CMSC). CMSC is accredited by the Accreditation Council for Continuing Medical Education.
37	Practical Tips for Recognizing 123 Diseases (Copyright Certificate)	20 August 2008	Ministry of Law and Human Rights, Republic of Indonesia
38	Biofest 4.0	8 Jan 2019	Universitas Muhammadiyah Makassar

39	Training of Writing Recruitment (TOWR)	15 – 16 June 2019	Forum Lingkar Pena, Universitas Muslim Indonesia
40	Literacy as a Movement Towards a Golden Generation 2045	2 July 2019	Selayar Islands Student Association
41	Scientific Training XIII, Institute for Student Scientific Creativity, "Intellectualization of Integrity and Competitive Young Generation to Achieve Quality Research"	7 Feb 2019	Research and Reasoning Student Scientific Creativity Institute (LKIM-PENA) Universitas Muhammadiyah (Unismuh) Makassar
42	BAJURI : Baca Jurnal Ilmiah (Read the Scientific Journal)	12 Oct 2018	Medical Ar-Razi Research Community (MARC) Unismuh Makassar
43	Recruitment MARC FK Unismuh 2018	2018	Faculty of Medicine, Unismuh, Makassar
44	Sharing Knowledge "How to give soul to an article"	28 July 2018	Indonesian Writers Association (IPI)
45	TOEFL Prediction Test	17 June 2019	Universitas Muhammadiyah Makassar
46	Chinese Upper Beginner Supplementary Online Course	3 Dec 2019	Udemy
47	Psychodynamic Psychology	09 Nov 2019	Udemy
48	ISO 14001:2015 - Awareness on Environment Management (EMS)	12 Nov 2019	Udemy
49	Mastering Selections and Masks in Photoshop	13 Nov 2019	Udemy
50	Polite English in Forty Minutes	19 Oct 2019	Udemy
51	Motivate yourself	20 Nov 2019	Udemy
52	Basic Science of Oncology	22 Sep 2019	Udemy
53	Learn to Unlock Your Full Potential	24 Sep 2019	Udemy
54	Beginner's Mandarin Chinese	28 Sep 2019	Udemy
55	Gadjah Mada Award: The Best Writer Student Category	11 Dec 2015	Universitas Gadjah Mada, Yogyakarta
56	Gadjah Mada Award: The Most Inspiring Student Category	11 Dec 2015	Universitas Gadjah Mada, Yogyakarta
57	College Mandarin Chinese Course on Your Own - Beginning Level (18.5 hours)	3 Oct 2019	Udemy
58	[Publication] Anurogo D, Parikesit AA, Ikrar T. LncRNAs in CONDBITs Perspectives, From Genetics towards Theranostics. Malaysian Journal of Health Sciences. 2019;17:2. URL: <u>http://ejournal.ukm.my/jskm/article/view/16808</u>	2019	Malaysian Journal of Health Sciences

59	[Publication] Anurogo D, Parikesit AA, Ikrar T. Bionanomedicine: A "Panacea" In Medicine? Makara J Health Res 2017;21(2):42-48. URL: <u>http://journal.ui.ac.id/index.php/health/article/viewArticle/6524</u>	2017	Makara Journal of Health Research, Universitas Indonesia
60	[Publication] Anurogo D. The Neuropharmacogenomical Perspectives of Bipolar Disorders. CDK 243. 2016;43(8):587-591. URL: <u>http://www.cdkjournal.com/index.php/CDK/article/view/93</u>	2016	Cermin Dunia Kedokteran
61	[Publication] Anurogo D. Ikrar T. Treatment of Epilepsy: Background and Future Directions. Progress and Communication in Sciences. 2014(1):27-41. URL: <u>http://ojs.unsysdigital.com/index.php/pcs/article/view/149</u>	2014	Progress and Communication in Sciences





successfully completed

Practice in Rehabilitation and Cardiopulmonary exercise

a course of study offered by **TMUx** an online learning initiative of **Taipei Medical University** throught OpenEdu

Jiunn-Horng Kang Chair Taipei Medical University CERTIFICAT



This is to certify Dito Anurogo MD MSc

successfully completed

Pulmonary Rehabilitation

a course of study offered by **TMUx** an online learning initiative of **Taipei Medical University** throught OpenEdu

shu-chuan Ho

Shu-Chuan Ho Associate Professor Taipei Medical University



CERTIFICAT

Med Learning Group

certifies that

Dito Anurogo, M.D.

has participated in the enduring activity titled

The 3D MS THRIVE Initiative: Patient-Centered Management for Optimal Outcomes in Multiple Sclerosis

and is awarded

1.0AMA PRA Category 1 Credits™

Date Completed: August 11, 2018 Maximum Credits: 1.0 Total Credits Reported: 1.0

Med Learning Group is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

Med Learning Group designates this enduring activity for a maximum of 1.0 AMA PRA Category 1 Credit(s)™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

ning NOW OF DUPMANE AVAILABLE ACKNEED

KWitch

Lauren Welch VP of Outcomes and Accreditation Med Learning Group

Dr. Sudirman Katu, SpPD-KPTI

Ketua Panitia

Prof. DR. Dr. Samsuridjal Djauzi, SpPD

m

Perhimpunan Dokter Peduli HIV/AIDS Indonesia

Ketua Badan Pengurus

Hotel Sahid Jaya Makassar, 30 November - 1 Desember 2018 Akreditasi IDI No. 0035/PB/A, 4/11/2018 Peserta 10 SKP, Pembicara 12 SKP, Instruktur 4 SKP dan Panitia 2 SKP

"Rational Approach for Clinical Practice in HIVIAIDS Treatment"

PERTEMUAN ILMIAH NASIONAL & KONFERENSI KERJA 2018 **PERHIMPUNAN DOKTER PEDULI HIV/AIDS INDONESIA** Peserta Poster Presentation dan Standing Banner

Sertifikat

dr. Dito Anurogo, M.Sc

sebagai

Diberikan kepada

REPUBLIK INDONESIA KEMENTERIAN HUKUM DAN HAK ASASI MANUSIA

SURAT PENCATATAN CIPTAAN

Dalam rangka pelindungan ciptaan di bidang ilmu pengetahuan, seni dan sastra berdasarkan Undang-Undang Nomor 28 Tahun 2014 tentang Hak Cipta, dengan ini menerangkan:

Indonesia

Indonesia

: Buku

: Dr Dito Anurogo MSc

: Dr Dito Anurogo MSc

: The Art Of Medicine

Nomor dan tanggal permohonan

: EC00201808953, 12 April 2018

Pencipta

Nama

Alamat

Kewarganegaraan

Pemegang Hak Cipta

Nama

Alamat

Kewarganegaraan

Jenis Ciptaan

Judul Ciptaan

Tanggal dan tempat diumumkan untuk : 25 Januari 2016, di Jakarta pertama kali di wilayah Indonesia atau

Jangka waktu pelindungan

Berlaku selama hidup Pencipta dan terus berlangsung selama 70 (tujuh puluh) tahun setelah Pencipta meninggal dunia, terhitung mulai tanggal 1 Januari tahun berikutnya.

JL. Cinde Barat No. 4, Semarang, Jawa Tengah, 50256

: JL. Cinde Barat No. 4, Semarang, Jawa Tengah, 50256

Nomor pencatatan

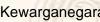
000105420 1

adalah benar berdasarkan keterangan yang diberikan oleh Pemohon. Surat Pencatatan Hak Cipta atau produk Hak terkait ini sesuai dengan Pasal 72 Undang-Undang Nomor 28 Tahun 2014 tentang Hak Cipta.



a.n. MENTERI HUKUM DAN HAK ASASI MANUSIA DIREKTUR JENDERAL KEKAYAAN INTELEKTUAL

> Dr. Freddy Harris, S.H., LL.M., ACCS. NIP. 196611181994031001



di luar wilayah Indonesia

Certificate of Completion

This is to certify that Dito Anurogo successfully completed 38 mins of ACUPRESSURE - Miracle Points online course on Nov. 1, 2019

Annette Reilly

Annette Reilly, Instructor

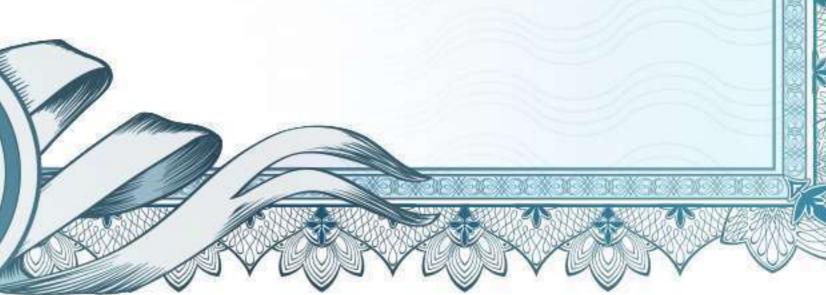


#BeAble

Certificate no: UC-I3RYBYE8 Certificate url: ude.my/UC-I3RYBYE8









Fab Academe Division of Fabulous Body Inc California. United States www.fabulousbody.com

FREE FAB BODY COURSE BUNDLE

Has successfully completed this Internationally Accredited CPD Activity May you Inspire Others with your exemplary performance





The CPD Standards Office CPD PROVIDER: 50138 2018-2020 www.cpilstandards.com

This is to certify that

DITO ANUROGO



Certificate of Achievement

Dito Anurogo

has completed the following course:

UNDERSTANDING ANXIETY, DEPRESSION AND CBT

UNIVERSITY OF READING

This course explored anxiety and depression; dispelling common myths and stereotypes around these disorders. It also explored how CBT targets the vicious cycles which keep these difficulties going, by sharing the expertise of CBT therapists and patients who have experienced CBT first hand.

5 weeks, 3 hours per week

Dr. Michelle Lee Project Support Officer University of Reading





The person named on this certificate has completed the activities in the attached transcript. For more information about Certificates of Achievement and the effort required to become eligible, visit futurelearn.com/proof-of-learning/certificate-of-achievement.

This learner has not verified their identity. The certificate and transcript do not imply the award of credit or the conferment of a qualification from University of Reading.



Dito Anurogo

has completed the following course:

UNDERSTANDING ANXIETY, DEPRESSION AND CBT UNIVERSITY OF READING

This course explored anxiety and depression; dispelling common myths and stereotypes around these disorders. It also explored how CBT targets the vicious cycles which keep these difficulties going, by sharing the expertise of CBT therapists and patients who have experienced CBT first hand.

STUDY REQUIREMENT

5 weeks, 3 hours per week

LEARNING OUTCOMES

- Describe the key signs and symptoms of depression and identify how a depressive disorder differs from simply feeling low or down
- Describe how a depressive disorder is diagnosed and identify an appropriate assessment tool
- Describe the key signs and symptoms of the most frequently occurring anxiety disorders and identify how anxiety disorders differ from simply feeling worried or nervous
- Describe how anxiety disorders are diagnosed and identify an appropriate assessment tool
- Identify the most common stereotypes surrounding anxiety and depression and evaluate them on the basis of current knowledge
- Describe how Cognitive Behavioural Therapy can be delivered and identify the types of difficulties that it can help with
- Summarise how what we know about perception (making sense of the world around us) can help us to understand the CBT approach better
- Identify the key components of a Cognitive Behavioural approach to understanding anxiety and depression

• Describe how specific kinds of behaviours and thought pattern can maintain difficulties in anxiety and depression and identify key CBT techniques which are used to address these in therapy

SYLLABUS

- Week 1 provides an introduction to how we perceive the world around us and how this relates to the Cognitive Behavioural approach to anxiety and depression. It explores how CBT can be delivered and the types of difficulties if can help.
- Week 2 looks at depression within a CBT framework, exploring what depression is (and is not) as well as highlighting commonly held myths and stereotypes around depression.
- Week 3 explores anxiety within a CBT framework. It covers the function and positive role of 'normal' anxiety exploring the difference between 'normal' anxiety and anxiety disorders.
- Week 4 focuses on how behaviour changes in anxiety and depression, how these changes can maintain difficulties and how CBT techniques are used in therapy to address them.
- Week 5 focuses on 'cognitions' or thoughts; specifically the types of thoughts which commonly occur in anxiety and depression, how they maintain difficulties and what CBT techniques are used in therapy to address them.



For more information about transcripts visit futurelearn.com. Issued 7th November 2019. futurelearn.com/certificates/pbxumkx



Certificate of Achievement

Dito Anurogo

has completed the following course:

DIGITAL SKILLS: ARTIFICIAL INTELLIGENCE

ACCENTURE

This online course helped discover the potential of Artificial Intelligence (AI) and how it can change the workplace. It enhanced understanding of AI with interesting facts, trends, and insights, and helped to explore the working relationship between humans and AI.

3 weeks, 2 hours per week



accenture



The person named on this certificate has completed the activities in the attached transcript. For more information about Certificates of Achievement and the effort required to become eligible, visit futurelearn.com/proof-of-learning/certificate-of-achievement.

This learner has not verified their identity. The certificate and transcript do not imply the award of credit or the conferment of a qualification from Accenture.

accenture

Dito Anurogo

has completed the following course:

DIGITAL SKILLS: ARTIFICIAL INTELLIGENCE ACCENTURE

This online course helped discover the potential of Artificial Intelligence (AI) and how it can change the workplace. It enhanced understanding of AI with interesting facts, trends, and insights, and helped to explore the working relationship between humans and AI.

STUDY REQUIREMENT

3 weeks, 2 hours per week

LEARNING OUTCOMES

- Describe the origins and advent of Al
- Explain the relationship between AI and Automation
- Reflect on the application of AI to your own context
- Identify key shifts in the workplace influenced by AI
- Assess the impact shifts in the workplace may have on roles and responsibilities
- Identify how the relationship has changed between AI and humans
- Identify future skills required to work and interact with AI
- Produce an action plan to adapt your skills for the future

SYLLABUS

Week 1: Introduction to Artificial Intelligence

- What is Artificial Intelligence and where did it come from?
- Al in Action
- What does this mean for me?

Week 2: Artificial Intelligence in Industry

- Impact of AI on Individuals
- What does this mean for me?

Week 3: Adapting your skills to work with Artificial Intelligence

90%

AVERAGE TEST SCORE

- How has the relationship changed between Al and Humans?
- Imagining the Future





Certificate of Achievement

Dito Anurogo

has completed the following course:

BLENDED LEARNING ESSENTIALS: DIGITALLY-ENRICHED APPRENTICESHIPS

UNIVERSITY OF LEEDS AND UCL INSTITUTE OF EDUCATION

This online course helped teachers and trainers develop an understanding of how digital technology can be used to enrich their apprenticeship programmes.

This course has been accredited by the CPD Certification Service, which means it can be used to provide evidence of your continuing professional development.

Diana Laurillard Professor of Learning with Digital Technology, UCL Institute of Education. UCL

Dr Bronwen Swinnerton Research Fellow in Digital Learning University of Leeds







The person named on this certificate has completed the activities in the attached transcript. For more information about Certificates of Achievement and the effort required to become eligible, visit futurelearn.com/proof-of-learning/certificate-of-achievement.

ى ا

This learner has not verified their identity. The certificate and transcript do not imply the award of credit or the conferment of a qualification from University of Leeds and UCL Institute of Education.







Dito Anurogo

has completed the following course:

BLENDED LEARNING ESSENTIALS: DIGITALLY-ENRICHED APPRENTICESHIPS UNIVERSITY OF LEEDS AND UCL INSTITUTE OF EDUCATION

This online course helped teachers and trainers develop an understanding of how digital technology can be used to enrich their apprenticeship programmes.

STUDY REQUIREMENT

2 weeks, 4 hours per week

LEARNING OUTCOMES

- Explore the role of the trainer in apprenticeships in the digital age
- Describe the role of digital in preparing for a trainer's or organisation's readiness for the apprenticeship programme
- Develop plans for using digital tools in the delivery of an apprenticeship programme
- Investigate the use of digital tools for supporting learners and apprentices
- Identify good practice in using digital tools for collecting evidence
- Explain the potential in using digital tools for the end-point assessment

SYLLABUS

- Preparation: staff and organisational readiness
- Planning the apprentice journey
- Planning the apprentice programme to support delivery
- Digital for developing learner support
- Digital for supporting evidence collection
- End-point assessment (EPA)

ACCREDITATION

This course has been accredited by the CPD Certification Service, which means it can be used to provide evidence of your continuing professional development.



-0

Fab Academy Fabulous Body Inc California, United States www.fabulousbody.com

DIPLOMA IN NUTRITION

This Certificate is Proudly Presented to



The CPD Standards Office CPD Provides: 10138 2016-1020 Www.construction.com





Dito Anurogo, M.d., M.sc.

Grade: Distinction Has successfully completed this Internationally Accredited CPD Activity May you Inspire Others with your exemplary performance

25 November 2019

DATE

Altoh Schront

AUTHORIZED SIGNATORY





Certificate of Achievement

Dito Anurogo

has completed the following course:

GOOD BRAIN, BAD BRAIN: PARKINSON'S DISEASE

UNIVERSITY OF BIRMINGHAM

This course on Parkinson's disease covered the fundamentals of pathology, symptoms, treatment and research.

3 weeks, 3 hours per week

Dr Alison Cooper Senior Lecturer University of Birmingham

UNIVERSITY^{OF} BIRMINGHAM



The person named on this certificate has completed the activities in the attached transcript. For more information about Certificates of Achievement and the effort required to become eligible, visit futurelearn.com/proof-of-learning/certificate-of-achievement.

This learner has not verified their identity. The certificate and transcript do not imply the award of credit or the conferment of a qualification from University of Birmingham.

UNIVERSITY^{OF} BIRMINGHAM

Dito Anurogo

has completed the following course:

GOOD BRAIN, BAD BRAIN: PARKINSON'S DISEASE UNIVERSITY OF BIRMINGHAM

This course on Parkinson's disease covered the fundamentals of pathology, symptoms, treatment and research.

STUDY REQUIREMENT

3 weeks, 3 hours per week

LEARNING OUTCOMES

- Identify the key regions of the brain involved in movement control
- Explain how disruption to basal ganglia function can lead to the signs and symptoms of Parkinson's disease
- Investigate the rationale behind current areas of research
- Apply a knowledge of the pathology of Parkinson's disease to explain how current therapies work
- Explore some of the current areas of active research

SYLLABUS

- Neurobiology of movement
- Pathology of Parkinson's disease
- Symptoms of Parkinson's disease
- Treatments for Parkinson's disease
- Current research for Parkinson's disease





Certificate of Achievement

Dito Anurogo

has completed the following course:

GENOMIC TECHNOLOGIES IN CLINICAL DIAGNOSTICS: MOLECULAR TECHNIQUES ST GEORGE'S, UNIVERSITY OF LONDON

This online postgraduate level course explored how genomic technologies are used in healthcare to investigate genetic disorders. The course covered a wide range of molecular genetic and cytogenetic techniques with learning firmly embedded in the clinical setting.

3 weeks, 5 hours per week

Kitamen Brann

Kate Tatton-Brown Consultant and Reader in Clinical Genetics St George's, University of London

Katie Snape Consultant and Senior Lecturer in Clinical Genetics St George's, University of London



Accredited by



The person named on this certificate has completed the activities in the attached transcript. For more information about Certificates of Achievement and the effort required to become eligible, visit futurelearn.com/proof-of-learning/certificate-of-achievement.



This learner has not verified their identity. The certificate and transcript do not imply the award of credit or the conferment of a qualification from St George's, University of London.







Dito Anurogo

has completed the following course:

GENOMIC TECHNOLOGIES IN CLINICAL DIAGNOSTICS: MOLECULAR TECHNIQUES ST GEORGE'S, UNIVERSITY OF LONDON

This online postgraduate level course explored how genomic technologies are used in healthcare to investigate genetic disorders. The course covered a wide range of molecular genetic and cytogenetic techniques with learning firmly embedded in the clinical setting.

STUDY REQUIREMENT

3 weeks, 5 hours per week

LEARNING OUTCOMES

- Demonstrate knowledge and applicability of the molecular principles behind PCR/Sanger sequencing; Next Generation Sequencing; MLPA/ MS_MLPA; Southern blotting; array CGH; FISH; karyotyping; the extraction and analysis of cell free fetal DNA and QF-PCR
- Evaluate which laboratory investigation(s) is(are) most suitable for a given clinical scenario
- Demonstrate an in-depth understanding of the methodology of at least four molecular genetic techniques

SYLLABUS

- Polymerase chain reaction (PCR)
- Sanger sequencing
- Southern blotting
- Multiplex ligation probe amplification (MLPA)
- Array comparative genomic hybridisation (array CGH)
- Karyotyping
- Fluorescent in situ hybridisation (FISH)
- Quantitative fluorescent PCR (QF-PCR)
- Single nucleotide polymorphism (SNP) genotyping and genome wide association studies (GWAS)

• The extraction and analysis of cell free fetal DNA, including non-invasive prenatal testing (NIPT).

ACCREDITATION

The course has been approved for distancelearning continuing professional development (CPD) by the Royal College of Pathologists (RCPath): for 15 CPD credits.



TRANSCRIPT



This is to certify
Dito Anurogo

successfully completed

Pulmonary Rehabilitation

a course of study offered by **TMUx** an online learning initiative of **Taipei Medical University** throught OpenEdu

shu-chuan Ho

Shu-Chuan Ho Associate Professor Taipei Medical University CERTIFICAT



This is to certify
Dito Anurogo

successfully completed

Sleep and Respiratory Care

a course of study offered by TMUx an online learning initiative of Taipei Medical University

throught OpenEdu

HSIN- ONTIEN LEE

Hsin-Chien Lee Director Taipei Medical University Shuang Ho Hospital



CERTIFICAT



Certificate of Achievement

Dito Anurogo

has completed the following course:

UNDERSTANDING AUTISM

THE UNIVERSITY OF KENT

This online course explored autism, including diagnosis, the autistic spectrum, and life with autism. The course was presented in the context of addressing the 'big question': how do we know that autism exists?

4 weeks, 3 hours per week

Dr Jill Bradshaw Lead Educator, and Lecturer in Learning Disability The University of Kent





The person named on this certificate has completed the activities in the attached transcript. For more information about Certificates of Achievement and the effort required to become eligible, visit futurelearn.com/proof-of-learning/certificate-of-achievement.

This learner has not verified their identity. The certificate and transcript do not imply the award of credit or the conferment of a qualification from The University of Kent.

University of Kent

Dito Anurogo

has completed the following course:

UNDERSTANDING AUTISM THE UNIVERSITY OF KENT

This online course explored autism, including diagnosis, the autistic spectrum, and life with autism. The course was presented in the context of addressing the 'big question': how do we know that autism exists?

STUDY REQUIREMENT

4 weeks, 3 hours per week

LEARNING OUTCOMES

- Explain what autism is, and evaluate whether it really exists
- Identify social communication skills and explain what happens if they do not develop as expected
- Summarise knowledge of sensory and repetitive behaviours, and whether such behaviours are advantages or disadvantages
- Explain why many people on the autism spectrum have co-occurring conditions
- Identify the origins of strengths and difficulties experienced by people on the autism spectrum
- Explore and discuss lived experiences of people on the autism spectrum

SYLLABUS

- What is autism
- Social communication skills
- Sensory sensitivities and repetitive behaviours
- Co-occurring conditions
- Strengths and difficulties of people on the autism spectrum
- Lived experiences of people on the autism spectrum







This is to certify **Dito Anurogo**

successfully completed

Advanced Good Pharmacy Practice

a course of study offered by **TMUx** an online learning initiative of **Taipei Medical University** throught OpenEdu

Yhth

Yuh-Lih Chang Division Chief Taipei Veterans General Hospital



CERTIFICAT



This is to certify **Dito Anurogo**

successfully completed

Moderate Good Pharmacy Practice

a course of study offered by **TMUx** an online learning initiative of **Taipei Medical University** throught OpenEdu

Chia-Lin Chou

Mei-Tu Chen

Chia-Lin Chou Chief pharmacist Taipei Veterans General Hospital

Mei-Yu Chen Clinical pharmacist Taipei Veterans General Hospital

Fan Hsiu Chao

Fan-Hsiu Chao Clinical pharmacist Taipei Veterans General Hospital

Ju-Chieh Wun

CERTIFICAT

Ju-Chieh Wung Clinical pharmacist Taipei Veterans General Hospital

Date of issue: 2019-12-04



Certificate of Achievement

Dito Anurogo, M.D., M.Sc.

has completed the following course:

HOW TO SUCCEED AT: WRITING APPLICATIONS

THE UNIVERSITY OF SHEFFIELD

This online course explored how to produce a successful CV (or résumé), application and online profile to apply for a job or course.

3 weeks, 3 hours per week

S. R. Davie

Stephen Davie Information Systems Manager The University of Sheffield





The person named on this certificate has completed the activities in the attached transcript. For more information about Certificates of Achievement and the effort required to become eligible, visit futurelearn.com/proof-of-learning/certificate-of-achievement.

This learner has not verified their identity. The certificate and transcript do not imply the award of credit or the conferment of a qualification from The University of Sheffield.



Dito Anurogo, M.D., M.Sc.

has completed the following course:

HOW TO SUCCEED AT: WRITING APPLICATIONS THE UNIVERSITY OF SHEFFIELD

This online course explored how to produce a successful CV (or résumé), application and online profile to apply for a job or course.

STUDY REQUIREMENT

3 weeks, 3 hours per week

LEARNING OUTCOMES

- Improve your chances of success in getting a job or securing a place on a university course
- Apply best practice techniques when applying for jobs, apprenticeships, placements and university courses, from preparing to apply, to writing CVs and completing application forms
- Identify what recruiters are looking for by analysing job adverts and researching employers and institutions, to find out how to adapt your offer to suit their requirements
- Develop a better understanding of your strengths and skills to tackle applying for your dream job or course with confidence
- Improve the way you promote yourself effectively through positive writing and a strong personal brand, creating an identity that looks impressive to a recruiter, whether that's an employer or admissions tutor

SYLLABUS

Understanding your skills

- Analysing job adverts and course descriptions
- Researching the organisation
- Promoting yourself through positive writing
- Mastering applicant tracking systems
- Creating a personal brand
- Dealing with gaps in your application

CVs and covering letters

Making a positive impression

- Creating an effective CV
- Developing a professional online profile
- Selling yourself in your covering letter
- Exploring sample CVs and covering letters

Application forms and personal statements

- How to approach application forms
- Structuring your responses with the STAR technique
- Responding to competency-based, strengthbased, motivational and situational judgement questions
- How to write a brilliant personal statement



This transcript should be read alongside the accompanying Certificate of Achievement. For more information about transcripts visit futurelearn.com. Issued 3rd December 2019. futurelearn.com/certificates/rcdxh2r Google Analytics Academy

Advanced Google Analytics Certificate of Completion

Dito Anurogo

Awarded for successfully completing the course "Advanced Google Analytics"

Certificate expires November 9, 2022

Google Analytics Academy

Google Analytics for Beginners Certificate of Completion

Dito Anurogo

Awarded for successfully completing the course "Google Analytics for Beginners"

0

Certificate expires November 8, 2022

This is to certify that Dito Anurogo successfully completed 1 hour of Fully Accredited Professional Child Psychology Diploma online course on Nov. 7, 2019

Dr Karen & Wells

Dr Karen E Wells, Instructor

& Udemy

#BeAble

Certificate no: UC-SWL6G044 Certificate url: ude.my/UC-SWL6G044



This is to certify that Dito Anurogo successfully completed 3 hours of Internationally Accredited **Diploma Certificate in Nutrition online course on** Nov. 26, 2019

Akash Sehrawat, Instructor

Akash Sehrawat Fabulous Body Teaching Assistant

Fabulous Body, Instructor



Certificate no: UC-LZPM6S0S Certificate url: ude.my/UC-LZPM6S0S

#BeAble



Teaching Assistant, Instructor





CENTER FOR INDONESIAN MEDICAL STUDENTS' ACTIVITIES



THIS CERTIFICATE IS AWARDED TO

dr. Dito Anurogo

FOR HIS VALUABLE CONTRIBUTION AS A SPEAKER OF

"THE ART OF ARTISTIC WRITING" TRAINING

ON Local Leadership Summit 2017 BY CIMSA UNISSULA

SEMARANG, MAY 13" 2017

LOCAL COORDINATOR CIMSA UNISSULA



KOKO AGUNG TRI WIBOWO

SECRETARY GENERAL

CIMSA UNISSULA

RIZKA HIDYA TIFFANI





Sertifikat

Nomor : 0034/KSJ/And/XI/2019

diberikan kepada

dr. Dito Anurogo, M.Sc

atas partisipasinya sebagai - NARASUMBER dalam acara Seminar Nasional Online Batch 34 yang diikuti 1.000 peserta dengan tema : "Sadar Bipolar : Penyakit Galau Zaman Now"

yang diselenggarakan pada hari Jum'at, 1 November 2019

Founder Komunitas Sang Juara

Moh. Ilham, S.Sos.I., MM.

CEO Andonesia.id Group

Andonesia.id

Is Your Partner For Your Event

Ibnu

Diploma Of Professional Study

This certifies that

Dito Anurogo

has successfully completed the training program requirement for

PROFESSIONAL CHILD PSYCHOLOGY DIPLOMA COURSE

Date

07/11/2019



Karen E Wells - Instructor

The KEW TRAINING ACADEMY -Accredited by CTAA - Complementary Therapists Accreditation Association









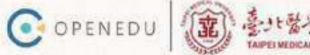
of Reviewing

Volume 4 Issue 2 December 2019 Awarded to

Dito Anurogo, M.D., M.Sc.

in recognition of an outstanding contribution to the quality of the journal

SINTA 3 SK. 30/E/KPT/2019 Reviewer Recognition Kediri, 02 December 2019 Journal An-Nats Journal An-Nats Kajian Powelitian Poilologi M. Arif Khoiruddin, M.Pd.I Editor in Chief



CERTIFICATE of ACHIEVEMENT

Dito Anurogo

successfully completed all courses in the Series Course

Good Pharmacy Practice

a series of four courses offered by TMUx through OpenEdu.

Ing Hom Uh

V Director Taipei Medical University

Chia-Sin Chou

Chief pharmacist Taipei Veterans General Hospital

Division Chief
 Taipei Veterans General Hospital



CERTIFICATE of ACHIEVEMENT

Dito Anurogo

successfully completed all courses in the Series Course

Pulmonary medicine and rehabilitation

a series of four courses offered by TMUx through OpenEdu.

HSIN- ONTIEN LEE

Director Shuang Ho Hospital

shu-chuan Ho

Associate Professor Taipei Medical University

Taipei Medical University Hospita

INDONESIAN HEART ASSOCIATION



THIS IS TO CERTIFY THAT

Dito Anurogo, MD

has succesfully completed the course of

ADVANCED CARDIAC LIFE SUPPORT

Diklat P2PNFI, Ungaran January 22 - 24 (2010

AND QUALIFIED TO PERFORM ADVANCED CARDIAC LIFE SUPPORT IN CONFORMITY WITH STANDARD AND PROCEDURE OF AMERICAN HEART ASSOCIATION THIS CERTIFICATE IS VALID FOR 3 YEARS

Sunarya Soerianata, MD, FIHA PRESIDENT



Anna Ulfah Rahajoe, MD, FIHA SECRETARY GENERAL

Accreditation of Indonesian Medical Association No: 0931/PB/A 7/05/2009 Participant 14 SKP, Instructor 7 SKP

Reg. No: 09/1/2010

ATLS 022790 **KOMISI TRAUMA** Committee On Trauma PERHIMPUNAN DOKTER SPESIALIS BEDAH INDONESIA Indonesian Surgeons Association "IKABI" Certificate ADVANCED TRAUMA LIFE SUPPORT Diberikan kepada This is to certify that Dr. Dito Anurogo Telah menyelesaikan lind successfully completed PELATIHAN ADVANCED TRAUMA LIFE SUPPORT The Advanced Trauna Life Support Course dengan baik sesuai standard American College Of Surgeons Committee on Trauma. according to the standards established by the Anerican College Of Surgeons Committee on Trauma Disclenggarakan pada tanggal / On ... 4 s.d. 6 Pebruari 2011 Di Kola / At Semarang, RS Dr. Kariadi Dr. Bagyo S. Winoto Dr. Warko Karnadiharaha Direktur Latihan Ketua Course Director Chairman



BADAN NASIONAL SERTIFIKASI PROFESI INDONESIAN PROFESSIONAL CERTIFICATION AUTHORITY

SERTIFICATE OF COMPETENCE

No. 58110 26411 0 0001098 2019

Dengan ini menyatakan bahwa, This is to certify that,

dr. Dito Anurogo, M.Sc.

No. Reg. KOM.1446.01900 2019

Telah memenuhi persyaratan dan kompeten pada kualifikasi: Meet the requirements and competent for the below qualification:

Penulisan Buku Nonfiksi Non-fiction Book Writing

Pada Bidang Pekerjaan: In the area of:

Penulis Buku Nonfiksi Non-fiction Book Writer

Sertifikat ini berlaku untuk: 3 (tiga) Tahun This certificate is valid for: 3 (three) Years

Jakarta, 31 Mei 2019

Atas Nama Badan Nasional Sertifikasi Profesi On Behalf of Indonesian Professional Certification Authority

Lembaga Sertifikasi Profesi Penulis dan Editor Profesional Professional Certification Body for Professional Writer and Editor



Bambang Trimansyah Direktur

Director



4882066

A REAL PROPERTY AND A REAL PROPERTY AND A

CERTIFICATE OF APPRECIATION

indigo

Abor assor digited in volley

This is presented to

dr. Dito Amurogo, M.Sc

for being speaker of the Startup AtoZ Event "Membangun Indonesia Melalui Literasi Digital" on December 12, 2018.

S. ARYANI

(TULE)

General Manager Makassar Digital Valley



KEMENTERIAN PENDIDIKAN DAN KEBUDAYAAN

SERTIFIKAT

Nomor : 14307/I2.3/PP/2019

Diberikan kepada :

dr Dito Anurogo MSc

(Fakultas Kedokteran Universitas Muhammadiyah Makassar)

telah berperan aktif sebagai :

Peserta

dalam kegiatan "Peningkatan Kompetensi Guru dalam Pembelajaran Berbasis TIK (PembaTIK) Level Literasi – Provinsi Sulawesi Selatan"

yang dilaksanakan oleh Pusat Teknologi Informasi dan Komunikasi Pendidikan dan Kebudayaan Kementerian Pendidikan dan Kebudayaan pada tanggal 20 Maret - 21 April 2019 secara daring

NEW PARKAGE



Jakarta, 12 Juni 2019 Yeyala Pusat Teknologi Informasi dan Komunikasi Pendidikan dan Kebudayaan

Gogot Suharwoto, Ph.D NIP. 197102111993011002

Peningkatan Kompetensi Guru dalam Pembelajaran Berbasis TIK (PembaTIK) Level Literasi – Provinsi Sulawesi Selatan

Materi Pelatihan

No.	Materi/Kegiatan	Alokasi waktu/jam pelatihan		
		Teori	Praktik	
1	Fitur-fitur Portal Rumah Belajar dan Cara Pemanfaatannya	4	4	
2	Pembelajaran Abad 21	2	2	
3	Portal Rumah Belajar untuk Meningkatkan Kecakapan Pembelajaran Abad 21	2	4	
4	Mengenal Perangkat Keras Komputer	2	2	
5	Penggunaaan Perangkat Lunak untuk Pembelajaran	2	2	
6	Pemanfaatan Internet untuk Pembelajaran (Internet dan Peramban, Mesin Pencari, Email, Kompresi File, Cloud Storage, Etika Berinternet)	2	4	
Sub. Total		14	18	
Total			32	



SERTIFIKAT

Nomor: 0123/SPbS/2019

Kepala Badan Pengembangan dan Pembinaan Bahasa Kementerian Pendidikan dan Kebudayaan memberikan sertifikat ini kepada

dr. Dito Anurogo, M.Sc.

sebagai peserta Bimbingan Teknis Instruktur Literasi Baca-Tulis Tingkat Nasional yang diselenggarakan di Jakarta pada tanggal 8—14 April 2019.

Jakarta, 14 April 2019

Prof. Dr. Dadang Sunendar, M.Hum. NIP 196310241988031003

No.	Materi	Pakar/Narasumber	Jumlal Jam
the second second	Kelajakan GLN Kementerian Pendidikan dan Keladayaan	Prof. Dr. Muhadjir Effendy, M.A.P.	4
1	Upaya Pembinaan Bahasa melalui Pembudayaan Literaa paca-	Prof. Dr. Dadang Sunendar, M.Hum.	2
2	Tulis dan Bernalar Aras Tinggi (BAT)	Prof. Dr. Marsudi Wahyu Kisworo	2
3.	Pernanfaatan Literasi Siber/Multimedia dalam Literasi Baca-Tulia Hubungan Literasi Baca-Tulis dengan Kemampuan Bernalar Araa Tinggi (BAT), STEM, dan 4K	DrHurip Danu Ismadi, M.Pd.	2
5.	Pemahaman Berbagai Jenis Teks dalam Pembelajaran Laterasi Baca Tulis	Prof. Emi Emilia, M.Ed., Ph.D.	4
	Proses Kreatif Menulis Karya Inspiratif	Habiburrahman El Shirazy	3
6.	Metodologi Pengajaran Literasi Baca-Tulis	Drs Krisanjaya, M.Hum.	3
8.	Gerakan Literasi Masyarakat dan Cara Pengelolaan Komunitas	Melvi	4
	Literasi Mencipinkan Kreaai dan Inovasi Literasi Baca-Tulis di Masyarakat	Dr. Firman Hadiansyah, M.Hum.	5
9	Mencipingan Areasi dan Inovasi Energan	Bambaog Trimansyah, S.S.	3
10.	Jeris, Strategi, dan Teknik Membaca Praktik Membaca Berbagai Jenis Teks	Bambang Trimansyah, S.S.	3
11.	Meringkas, Menulis Ulang, Menceritakan Kembali, Mengonversi, dan Merekonstruksi Tel.s	Drs. Krisanjaya, M.Hum.	2
13.	Praktik Meringkas, Menulis Ulang, Mengonversi, dan	Dra Krisanjeya, M.Hum.	3
14	Teknik Menangkap ide dan Menulis Kreatif Serbagai Jenir Teks	Gol A. Gong	2
15		Gol A. Gong	
16		Gol A. Gong	2
17		Gol A. Gong	2
1	Rear Talan	Gol A. Gong. Dr. Firman Hediarsyah, M.Hum., Dr. Tengku Syarfina, M.Hum., Fetno Utami, M.Hum.	20
-	Jumlah		

MATERI BIMBINGAN TEKNIS INSTRUKTUR LITERASI BACA-TULIS TINGKAT NASIONAL

Jakarta, 14 April 2019

Dr. Tengalu Syarfina, M.Hum. Kepala Bidang Pembulajaran



MULTIPLE SCLEROSIS CENTERS

certifies that

Dito Anurogo, M.D.

has participated in the enduring activity titled

Overcoming Challenges for Children and Adolescents with MS: A Comprehensive Review for Pediatric Clinicians of MS Symptoms, Diagnosis, Treatment, and Coordination of Care

at freeCME.com® or CMEUniversity on August 11, 2018

and is awarded 1.5 AMA PRA Category 1 Credit(s)TM.

CMSC is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

Laurie Scudder, DNP, NP Director, Continuing Professional Education



SURAT PENCATATAN CIPTAAN

Dalam rangka pelindungan ciptaan di bidang ilmu pengetahuan, seni dan sastra berdasarkan Undang-Undang Nomor 28 Tahun 2014 tentang Hak Cipta, dengan ini menerangkan:

Nomor dan tanggal permohonan : EC00201847005, 26 September 2018 Pencipta Dr Dito Anurogo MSc Nama Alamat Perum Graha Surandar Permai 02 Blok E-25, RT 02 RW 05, Paccinongang, Somba Opu, Kabupaten Gowa, Provinsi Sulawesi Selatan, Indonesia Kode Pos 92113, Kabupaten Gowa, Sulawesi Selatan, 92113 Kewarganegaraan Indonesia **Pemegang Hak Cipta** Nama **Dr Dito Anurogo MSc** Perum Graha Surandar Permai 02 Blok E-25, RT 02 RW 05, Alamat Paccinongang, Somba Opu, Kabupaten Gowa, Provinsi Sulawesi Selatan, Indonesia Kode Pos 92113, Kabupaten Gowa, Sulawesi Selatan, 92113 Kewarganegaraan Indonesia **Buku Saku** Jenis Ciptaan Judul Ciptaan Tips Praktis Mengenali 123 Penyakit 20 Agustus 2008, di Semarang Tanggal dan tempat diumumkan untuk 1 pertama kali di wilayah Indonesia atau di luar wilayah Indonesia Jangka waktu pelindungan Berlaku selama hidup Pencipta dan terus berlangsung selama 70 (tujuh puluh) tahun setelah Pencipta meninggal dunia, terhitung mulai tanggal 1 Januari tahun berikutnya. Nomor pencatatan 000118687 -

adalah benar berdasarkan keterangan yang diberikan oleh Pemohon. Surat Pencatatan Hak Cipta atau produk Hak terkait ini sesuai dengan Pasal 72 Undang-Undang Nomor 28 Tahun 2014 tentang Hak Cipta.



a.n. MENTERI HUKUM DAN HAK ASASI MANUSIA DIREKTUR JENDERAL KEKAYAAN INTELEKTUAL

Dr. Freddy Harris, S.H., LL.M., ACCS. NIP. 196611181994031001

CERTIFICATE OF APPRECIATION This certificate is awarded to **dr. Dito Anurogo, M.Sc** For sharing his valuable knowledge as a guest speaker during Biofest 4.0 at Universitas Muhammadiyah Makassar on Tuesday, January 8th 2019





RANTING UNIVERSITAS MUSLIM INDONESIA SKR-003/FLP/Ran-UMI/INT/VI/2019

Diberikan Kepada :

ertifikat

dr. Dito Anurogo, M.Sc

Sebagai PEMATERI pada kegiatan Training of Writing Recruitment (TOWR) yang diselenggarakan oleh Forum Lingkar Pena Ranting Universitas Muslim Indonesia di Benteng Somba Opu pada tanggal 15 - 16 Juni 2019

Cara Terbaik Memeluk Ingatan

14 Juni 2019

Mengetahui



Sekretaris FECTOR

PIAGAM PENGHARGAAN

🦳 Di berikan kepada 🦳

dr. Dito Anurogo., M.Sc

Atas Partisipasinya Sebagai :

PEMATERI

Dalam Kegiatan Bazar dan Dialog

DEWAN PIMPINAN PUSAT HIMPUNAN PELAJAR MAHASISWA KEPULAUAN SELAYAR (DPP-HPMKS)

Tema;

" Literasi Sebagai Gerakan Menuju Generasi Emas 2045"

Mengetahui,

Makassar, 02 Juli 2019

ANDI ABRI

KETUA UMUM DPP - HPMKS

PANDI ADRIAWAN

KETUA PANITIA



PANITIA PELAKSANA DIKLAT ILMIAH XIII LEMBAGA KREATIVITAS ILMIAH MAHASISWA PENELITIAN DAN PENALARAN (LKIM-PENA) UNIVERSITAS MUHAMMADIYAH MAKASSAR



NOMOR: 003/C/PP-DIKLAT ILMIAH XIII/X/FEBRUARI/2019 M diberikan kepada:

dr. Dito Anurogo, M.Sc.

sebagai PEMATERI

pada kegiatan Indoor Diklat Ilmiah XIII Lembaga Kreativitas Ilmiah Mahasiswa Penelitian dan Penalaran (LKIM-PENA) Universitas Muhammadiyah Makassar Periode 2018-2019 pada tanggal 11-14 Februari 2019 di Aula Perpustakaan Umum Multimedia

"Intelektualisasi Generasi Muda yang Berintegritas dan Kompetitif untuk Mewujudkan Penelitian Berkualitas"

Menyetujui, Wakil Rektor III Iniversitas Muhammadiyah Makassar Afehammad Tahir, M.Si. JBM, 823 081

Mengetahui, Umum LKIM-PENA ode 2018-2019 1205.2016

Makassar, 07 Februari 2019 M 02 Jumadil Akhir 1440 H

Ketua Panifia PHOMAN Ilmiah XIII Didig Ferdiansyah 101205 2017



SERTIFIKAT PENGHARGAAN

diberikan kepada :

dr. Dito Anurogo. M,Sc

Sebagai

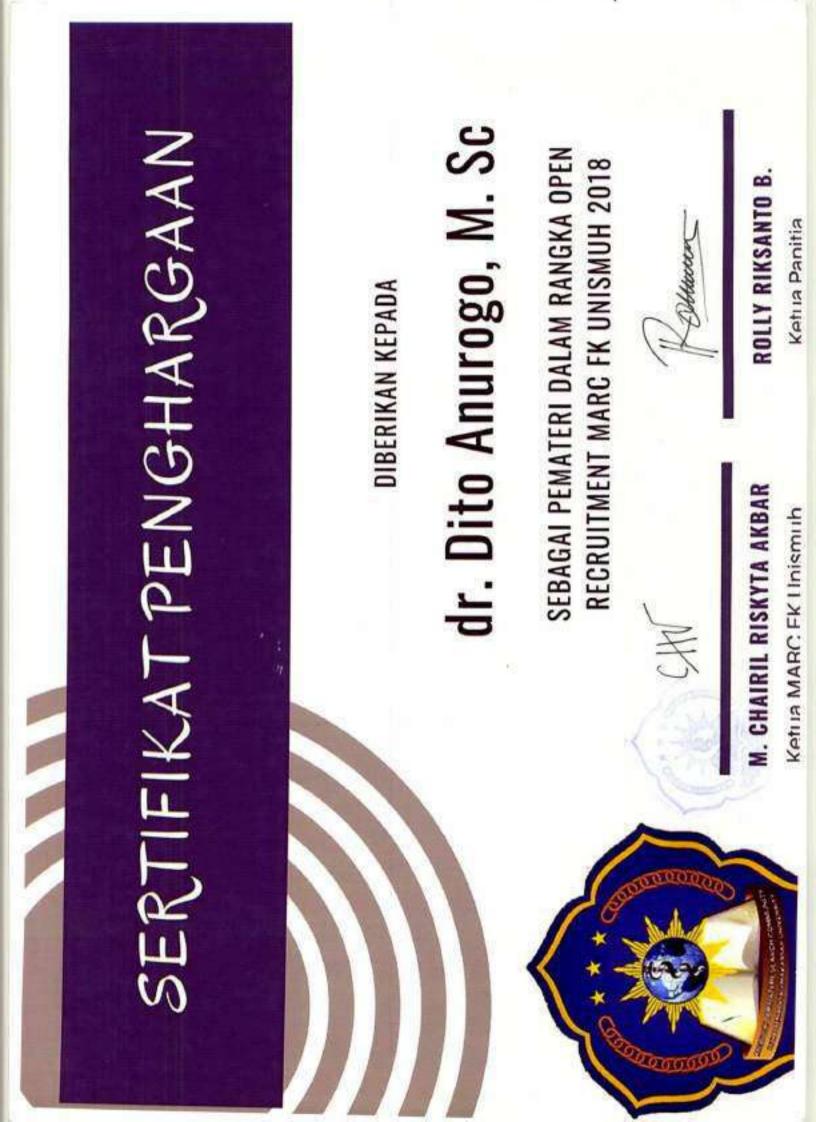
Pemateri

BAJURI : Baca Jurnal Ilmiah Fakultas Kedokteran Universitas Muhammadiyah Makassar Makassar, 12 October 2018



Att .

Rolly Riksanto B. Ketua MARC FK Unismuh Egah Auviah Ketua Bidang Scientific







Diberikan kepada

dr. Dito Churogo, M.Sc.

sebagai

Marasumber

dalam Sharing Knowledge Forum Literasi Ikatan Penulis Indonesia dengan tema "Cara Memberikan Rasa pada sebuah Tulisan" pada tanggal 28 Juli 2018.

Pekalongan, 28 Juli 2018

Penanggung Jawab Sharing Knowledge







CERTIFICATE OF ACHIEVEMENT



This is to certify that

dr. Dito Anurogo, M.Sc.

Achieved the following score on the

TOEFL PREDICTION TEST

Listening Comprehension	460
Structure & Writen Expression	490
Reading Comprehension	540
Total	497



Makassar, June 17, 2019

Afimad Yani NEA BARASA III 077 2016

This is to certify that Dito Anurogo successfully completed 1 hour of Chinese Upper Beginner Supplementary online course on Dec. 3, 2019

Winkie Wong

Winkie Wong, Instructor

& Udemy

#BeAble

Certificate no: UC-YOKSROKM Certificate url: ude.my/UC-YOKSROKM



This is to certify that Dito Anurogo successfully completed 3 hours of Psychodynamic Psychology -Certification Course. online course on Nov. 9, 2019

Glory Dimitrova

Glory Dimitrova, Instructor



#BeAble

Certificate no: UC-DKXG580W Certificate url: ude.my/UC-DKXG580W



This is to certify that Dito Anurogo successfully completed 31 mins of ISO 14001:2015 - Awareness on Environment Management (EMS) online course on Nov. 12, 2019

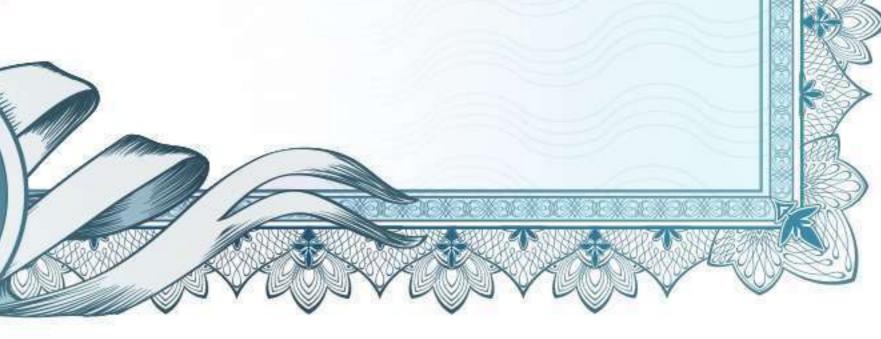


S.M. WAQAS IMAM, Instructor

#BeAble

Certificate no: UC-NQET5ORU Certificate url: ude.my/UC-NQET5ORU





This is to certify that Dito Anurogo successfully completed 1 hour of Mastering Selections and Masks in Photoshop online course on Nov. 13, 2019

Marcin Mikus

Marcin Mikus, Instructor

& Udemy

#BeAble

Certificate no: UC-10R45G00 Certificate url: ude.my/UC-10R45G00





This is to certify that Dito Anurogo successfully completed 40 mins of Polite English in Forty Minutes online course on Oct. 19, 2019

Cerys Vaughan Cerys Vaughan, Instructor



#BeAble

Certificate no: UC-MACSQ7N5 Certificate url: ude.my/UC-MACSQ7N5



This is to certify that Dito Anurogo successfully completed 41 mins of Motivate yourself online course on Nov. 20, 2019

Shai (Fedida

Shai Fedida, Instructor



#BeAble

Certificate no: UC-4TY6XUKN Certificate url: ude.my/UC-4TY6XUKN



This is to certify that Dito Anurogo successfully completed 2.5 hours of Basic Science of Oncology online course on Sept. 22, 2019

Sbdallah Adel

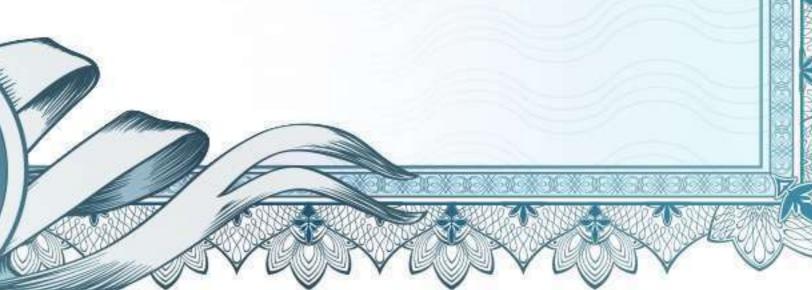
Abdallah Adel, Instructor



#BeAble

Certificate no: UC-349MI8MN Certificate url: ude.my/UC-349MI8MN





This is to certify that Dito Anurogo successfully completed 43 mins of Learn to Unlock Your Full Potential online course on Sept. 24, 2019

Karam Pal

Karam Pal, Instructor



#BeAble

Certificate no: UC-JJQPE84W Certificate url: ude.my/UC-JJQPE84W



This is to certify that Dito Anurogo successfully completed 35 mins of Beginner's Mandarin Chinese online course on Sept. 28, 2019

Jason Chan

Jason Chan, Instructor



#BeAble

Certificate no: UC-3G9A7COJ Certificate url: ude.my/UC-3G9A7COJ







AWARD CERTIFICATE

DITO ANUROGO

KATEGORI MAHASISWA TERINSPIRATIF

In Recognition of and Appreciation for the Achievement of Gadjah Mada Award 2015 Yogyakarta, Friday,December 11, 2015

Director of Student Affairs

Dr. Drs. Senawi, M.P. NIP. 19640310 199003 1 001 & Signature,

Coordinator GMA 2015

Firya Qurratu'ain 13/346019/SP/25612

This is to certify that Dito Anurogo successfully completed 18.5 hours of College Mandarin Chinese Course on Your Own--Beginning Level online course on Oct. 3, 2019



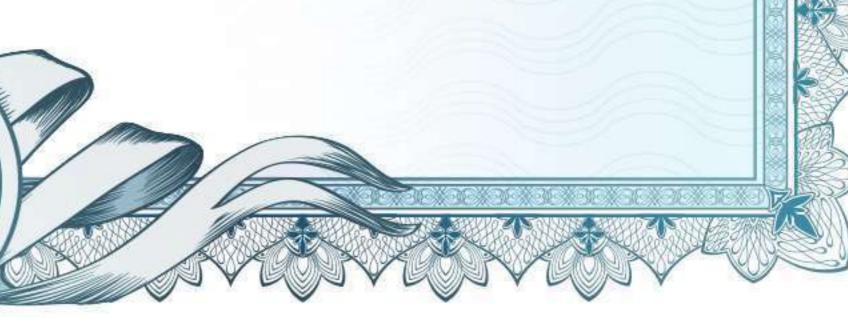
Hong Zeng, Instructor



#BeAble

Certificate no: UC-YPV68VQ8 Certificate url: ude.my/UC-YPV68VQ8





This is to certify that Dito Anurogo successfully completed 1 hour of Survival Mandarin Chinese-Get Ready for China in 1 Hour online course on Sept. 17, 2019

Francis Carlisle Francis Carlisle, Instructor

#BeAble

Certificate no: UC-667THCHQ Certificate url: ude.my/UC-667THCHQ





This is to certify that Dito Anurogo successfully completed 35 mins of Beginner's Mandarin Chinese online course on Sept. 28, 2019

Jason Chan

Jason Chan, Instructor



#BeAble

Certificate no: UC-3G9A7COJ Certificate url: ude.my/UC-3G9A7COJ



Artikel Ulasan/Review Articles

LncRNAs in CONDBITs Perspectives, From Genetics towards Theranostics (LncRNAs dalam Perspektif CONDBITs, Dari Genetik ke Theranostik)

DITO ANUROGO, ARLI ADITYA PARIKESIT & TARUNA IKRAR

ABSTRACT

LncRNAs (Long noncoding RNAs) are novel group of ncRNAs and has been discovered to be pervasively transcripted in the genome, characterized as endogenous cellular RNAs consist of more than 200 nucleotides. They are ordered in view of function, transcript length, relation with protein-coding genes and other functional DNA elements, and subcellular localization. Theranostics is a novel study in medicine that combines specific targeted biomolecules based upon molecular-based test. As novel finding in the field of molecular medicine, lncRNA is indispensable tools in theranostics based medicine that allows specific targeting of molecular pathway for diagnostics and therapeutics. LncRNAs may execute as signals, decoys, guides, and scaffolds in their natural capacities. LncRNA expression is controlled by transcriptional and epigenetic factors and processes. LncRNAs also relate detracting biological programs. Here we reviewed lncRNAs in disorders/diseasest horoughly based on CONDBITs perspectives, i.e.: cardiology, oncology, neurology and neuroscience, dermatology, the biology of molecular and bioinformatics, immunology, and technologies (related with "-omics"; transcriptomics and "nano"; nanotechnology). It was narrated the lncRNA biomarkers that abundant in cardiovascular, neurodegenerative, dermatology, and immunology perspective. However, as cancer is the most widely studied disease, more biomarkers are available for this particular case. There are abundant cancer-associated lncRNAs. The most frequent learned lncRNA molecules in cancer are HOTAIR, MALAT1, LincRNA-p21, H19, GAS5, ANRIL, MEG3, XIST, HULC. LncRNAs in cancer diagnosis and monitoring, e.g.: H19 and AA174084 (gastric), HULC (hepatocellular), PCA3 (prostate). Prognostic lncRNAs, e.g.: HOTAIR and NKILA (breast), MEG3 (meningioma), NBAT-1 (neuroblastoma), SCHLAP1 (prostate). LncRNAs predicting therapeutic responsiveness, e.g.: CCAT1 (colorectal), HOTAIR (ovarian). Thus, it is concluded that the CONDBIT perspective is useful to describe the encouraging outlook of this transcriptomics-based medicinal approach.

Keywords: LncRNAs; CONDBITs perspectives; disease hallmarks; bioinformatics; theranostics

ABSTRAK

LncRNAs (Long noncoding RNAs) ialah kumpulan ncRNA yang novel dan banyak ditranskripsikan daripada genom serta dicirikan sebagai RNA endogen yang mengandungi lebih daripada 200 nukleotida dalam sel. Spesies RNA tersebut adalah terkawal dari segi fungsi, panjang transkrip, hubungan dengan gen yang mengekodkan protein dan unsur DNA lain yang berfungsi serta lokasi dalam bahagian subsel. Theranostik pula merupakan bidang kajian yang novel dalam perubatan yang menggabungkan biomolekul sasaran khusus berdasarkan ujian molekul. Sebagai penemuan baru dalam bidang perubatan molekul, lncRNA merupakan molekul sasaran dalam bidang perubatan theranostik yang membolehkan penemuan tapak jalan molekul yang spesifik untuk tujuan diagnostik dan terapeutik. LncRNAs dapat bertindak sebagai molekul isyarat, umpan, pandu dan perancah secara semula jadi. Pengekspresan LncRNA adalah di bawah kawalan tranksripsi dan faktor serta proses epigenetik. LncRNAs juga menghubungkaitkan program biologi. Di sini, kami mengulas kefungsian lncRNAs dalam penyakit kegagalan secara terperinci dari perspektif CONDBITs iaitu kardiologi, onkologi, neurologi and neurosains, dermatologi, biologi molekul and bioinformasi, imunologi, dan teknologi (berkenaan dengan "-omik"; transkriptomik dan "nano"; nanoteknologi). Penanda biologi lncRNA dilaporkan banyak terdapat dalam perspektif kardiovaskular, neurodegeneratif, dermatologi, and imunologi. Kanser sebagai penyakit yang telah banyak dikaji, semakin banyak penanda biologi telah ditemukan untuk penyakit ini. Terdapat banyak lncRNAs yang berkait rapat dengan kanser. Antara yang kerap dikaji adalah HOTAIR, MALATI, LincRNA-p21, H19, GAS5, ANRIL, MEG3, XIST, HULC. LncRNAs yang banyak digunakan untuk diagnosis dan pengawasan kanser adalah seperti H19 and AA174084 (gastrik), HULC (hepatoselular), PCA3 (prostat). LncRNAs prognostik pula termasuk HOTAIR and NKILA (payu dara), MEG3 (meningioma), NBAT-1 (neuroblastoma), SCHLAP1 (prostat). LncRNAs yang digunakan untuk menjangka tindak balas terhadap rawatan adalah seperti CCAT1 (colorectal), HOTAIR (ovarian). Oleh itu, perspektif CONDBIT adalah sangat berguna untuk memerihalkan pendekatan yang berdasarkan transkriptomik.

Kata kunci: LncRNAs; perspektif CONDBITs; penanda penyakit; bioinformasi; theranostik

INTRODUCTION

LNCRNA ANNOTATION

LncRNAs (Long noncoding RNAs) are novel group of ncRNAs and has been discovered to be pervasively transcripted in the genome, characterized as endogenous cellular RNAs consist of more than 200 nucleotides (Mattick & Rinn 2015; Amaral & Mattick 2008). They have several general basic attributes, such as elective splicing, polyadenylation, low abundance, deficiency of protein product, and low sequence identity. They constitute a very heterogeneous group of RNA molecules that permits them to cover an expansive range of molecular-cellular functions by actualizing different modes of activity. They are ordered in view of function, transcript length, relation with proteincoding genes and other functional DNA elements, and subcellular localization.

LncRNAs may execute as signals, decoys, guides, and scaffolds in their natural capacities (Iwakiri, Hamada & Asai 2016). LncRNAs assume an imperative part in controlling gene expression at diversified levels, including chromatin alteration, transcriptional and posttranscriptional regulation, through multiple pathways that involve interplay with RNA binding proteins, subduing a major promoter of their aim gene, or performing as a co-activator of transcription factors (Sun et al. 2015). LncRNA expression is controlled by transcriptional and epigenetic factors and processes. LncRNAs also relate detracting biological programs (growth and development, the formation of cell identity, distribution of stress responses). There are 32,183 human annotated lncRNAs based on LNCipedia 2.0. Another study distinguished 6,736 lncRNA genes in the human genome (Devaux et al. 2015). In this end, IncRNA could be found on every manifestation of maladies in human. Moreover, the importance of lncRNA studies should be stated on every discussion on the molecular mechanism of the diseases. LncRNA is an indispensable aspect of theranostics-based therapy and diagnostics because it is only targeting specific molecular mechanism in the cell, in particular the transcriptomics pathway.

CARDIOVASCULAR PERSPECTIVE

LncRNAs have risen as critical regulators of cardiovascular development. LncRNAs control the differentiation of pluripotent stem cells and cardiac precursors into functional adult cardiac cells in the early phase of life. Afterward, they regulate cellular senescence and many pathways required in cardiovascular disorders (Devaux et al. 2015).

LncRNAs KCNQ1OT1 (class antisense, species human, chromosome 11) has important roles in arrhythmia and cardiac development(Korostowski, Sedlak, and Engel 2012; Bokil et al. 2010). LncRNAs Ak011347, Bvht, Fendrr (class intergenic, species mouse) have also the important role in cardiac development (Klattenhoff et al. 2013; J. G. Zhu et al. 2014; Grote et al. 2013). Additionally, lncRNAs have an imperative part of heart development. A novel lncRNA Braveheart (AK143260) required for specification of the cardiac lineage in vitro. Depletion of lncRNA (AK143260) causes loss of beating cardiomyocytes during embryonic stem cell differentiation and an inability to initiate a network of genes specifying key cardiac transcription factors and myofibril assembly components. This lncRNA is needed for interceding the transition from mesoderm to multipotent cardiac progenitors (Schonrock, Harvey & Mattick 2012).

Another class of lncRNAs, i.e. SRA transcripts, have a critical capacity as coactivators of nuclear receptor signaling, muscle differentiation, and components of gene insulator complexes. It is also connected with dilated cardiomyopathy (Friedrichs et al. 2009). One of lncRNA, namely ALC-1 antisense, from class NAT (natural antisense transcript) has a vital role in the regulation of ALC-1. It has a noteworthy association while induced in hypertrophic ventricles (Ritter et al. 1999). Inhibition of MALAT1 in vivo by oligonucleotides diminished vascularization, indicating MALAT1 as an intriguing target to control angiogenic processes (Michalik et al. 2014).

Myocardial infarction associated transcript (MIAT) was identified as lncRNA which before 2006 also known as GOMAFU, AK028326, RNCR2. It is a non-coding RNA that has a pathobiological role in the cardiovascular system. MIAT dysregulation has a critical impact on the pathogenesis of MI and atherosclerosis, as well as another microvascular dysfunction, via enigmatic pathways (Yan et al. 2015; Liao et al. 2016; Vausort, Wagner & Devaux 2014).

HEART FAILURE

Long non-coding RNAs (lncRNAs) also play an important role in heart failure (El Azzouzi, Doevendans & Sluijter 2016). Some lncRNAs have been observed to be changed in the developing or diseased heart, several single nucleotide polymorphisms (SNP) in lncRNAs have appeared to be emphatically correlated with cardiovascular disease. For instance, SNPs in myocardial infarction associated transcript (MIAT) and antisense non-coding RNA in the INK4 locus (ANRIL) will forecast the increased risk of cardiovascular disease (Carlock et al. 1985; Ishii et al. 2006). In addition, lncRNA H19 was fundamentally upregulated in fizzling murine hearts, indicating a role for hypoxia-regulated lncRNA expression in heart failure (Lee et al. 2011; Yang et al. 2014). LncRNA MT-LIPCAR (human species, chromosome M) can predict survival in patients with heart failure (Kumarswamy et al. 2014).

Actually, lncRNA levels not only responded more sensitively to LVAD (left ventricular assist device) support but their expression profile permitted to recognize left ventricular samples from patients with ischemic and nonischemic heart failure before and after LVAD support (Consortium et al. 2013; Samani et al. 2007). There are some LncRNAs with potential biomarker applications. CDKN2BAS1 (ANRIL) can be utilized as a risk factor biomarker for coronary artery disease and myocardial infarction. MIAT can be used as a risk factor biomarker for myocardial infarction (Ishii et al. 2006).

ONCOLOGY PERSPECTIVE

There are abundant lncRNAs associated with cancer, such as APL or acute promyelocytic leukemia (NEAT1), bladder cancer (GHET1, Linc-UBC1, H19, MALAT1, MEG3, SNHG16, TUG1, UCA1), breast cancer (ANRIL, BC040587, BCAR4, BCYRN1, DSCAM-AS1, GAS5, H19, HOTAIR, HOTAIRM1, IRAIN, LincRNA-BC4, LincRNA-BC5, Loc554202, LSINCT5, MALAT1, MEG3, MIR31HG, PINC, PVT1, SRA1, XIST, ZNFX1-AS1), cervical cancer (HOTAIR, GAS5), colorectal cancer (CASC2, CCAT1, CRNDE, GAS5, HULC, HOTAIR, KCNQ10T, IncRNA-422, LincRNA-p21, Lnc-LET, MALAT1, NR_015441, NR_033374, R05532, SNGH16), endometrial carcinoma (CASC2, HOTAIR, MALAT1), epithelial squamous cell carcinoma or ESCC (Taurine-upregulated gene 1 or TUG1, lincPOU3F3), gallbladder cancer (lncRNA-LET), gastric cancer (LINC00152, GAPLINC, PVT1, HOTAIR, FENDRR, AC138128.1, BRAF-activated non-coding RNA or BANCR), glioma (HOTAIR, uc.283plus, lincPOU3F3), hepatocellular carcinoma (UFC1, MT1DP, lncRNA-LET), leukemia (ANRIL, DLEU1, DLEU2, MEG3, MIR155HG, TCL6, WT1-AS), melanoma (ANRIL, BANCR, C9orf14, SPRY4-IT1), multiple myeloma (MALAT1), non-Hodgkin lymphoma (BIC), NSCLC or non-small cell lung carcinoma (RP11385J1.2, TUBA4B, PVT1, HOTAIR, MALAT1, CARLo5), osteosarcoma (MALAT1, BC040587), ovarian cancer (HOST2), pancreatic cancer (BC008363, DAPK, HOTAIR, HULC, MALAT1, MAP3K14, PPP3CB, PVT1), prostate cancer (C20orf166AS1, CBR3-AS1, CTBP1-AS, ENSG00000261777, GAS5, H19, MALAT1, NEAT1, PCA3, PCAT1, PCGEM1, PRNCR1, PTENP1, RP11-267A15.1, ucRNAs, XIST), thyroid carcinoma/cancer (AK023948, BANCR, NAMA, PTCSC3) (Eis et al. 2005; Isin & Dalay 2015; R. Zhang et al. 2016).

There are a lot of new lncRNA transcripts dysregulated in ccRCC (clear cell renal cell carcinoma) that is benefit for novel diagnostic biomarkers. The expression of lncRNAs was successfully validated for upregulated or highly overexpressed in ccRCC (lnc-BMP2-2, lnc-CPN2-1, lnc-FZD1-2, lnc-ITPR2-3, lnc-SLC30A4-1, lnc-SPAM1-6), downregulated (lnc-ACACA-1, lnc-FOXG1-2, lnc-LCP2-2, lnc-RP3-368B9, lnc-TTC34-3), and unregulated (lnc-ERCC5-1, lnc-RP11-480I12.4.1-1) transcripts using qPCR. Another lncRNAs in ccRCC are MALAT1, SPRY4-IT1 (Gutschner & Diederichs 2012; Zhang et al. 2016; Blondeau et al. 2015).

Some lncRNAs are overexpressed or decreased in multiple human cancer. ANRIL (antisense non-coding RNA in the INK4 locus) is positively correlated with

poor prognosis and considered as a risk factor in various types of human cancers, such as breast cancer, esophageal squamous cell carcinoma, gastric cancer, hepatocellular carcinoma, lung cancer, and ovarian cancer (Hua et al. 2015). BANCR (BRAF-activated noncoding RNA) is abundant in some types of human cancer, i.e. colorectal cancer, papillary thyroid carcinoma, malignant melanoma (Li et al. 2015). HOTAIR (HOX antisense intergenic RNA) is a key regulator of chromatin dynamics and gene regulation (Bhan & Mandal 2015). It appears to be disrupted in some cancers and diseases. It was downregulated in ependymomas and aortic valve calcification. It was upregulated in various carcinomas i.e. ATRTs (atypical teratoid rhabdoid tumors) such as medulloblastomas, and juvenile pilocytic astrocytomas. Breast cancer, cervical tumors/cancers, colorectal carcinomas, endometrial tumors/carcinomas, esophageal squamous cell carcinoma (ESCC), gall bladder cancers, gastric cancers, gastrointestinal stromal tumors/cancers, gliomas, hepatocellular carcinoma, laryngeal squamous cell cancer, melanoma, nasopharyngeal carcinoma, nonfunctional pituitary adenoma, non-small cell lung cancer, prostate cancer, ovarian cancers, pancreatic tumors/cancers, renal carcinomas, sarcoma, small cell lung cancer, Ta/T1 bladder cancer, urothelial carcinoma, also upregulated in osteoarthritis and pre-eclampsia (Hua et al. 2015; Qiu et al. 2015; Bhan & Mandal 2015; Hajjari & Salavaty 2015; Huang et al. 2014; Li et al. 2015). Some of lncRNAs are elucidated in Table 1 below.

NEURODEGENERATIVE PERSPECTIVE

There are a lot of long ncRNAs involved in neurological disorders. They are ANRIL, BDNF-AS, ncRNA-a, Evf-2, HTTAS_v1, SCAANT1, 116HG, ATXN80S, 17A, Gomafu, BACE1-AS, BC200, Antisense Uchl1, HAR1F, HAR1R, etc. ANRIL which do regulate transcription has INK4b/ARF/ INK4a locus as a target and associated with neural system tumors. Long ncRNAs that regulating transcription are BDNF-AS, ncRNA-a, Evf-2, HTTAS_v1, SCAANT1, 116HG. Long ncRNAs that regulating mRNA processing are ATXN80S, 17A, Gomafu. Long ncRNAs that regulating translation are BC200 and antisense Uchl1. BACE1-AS regulates mRNA stability and has an important role in pathophysiologic of Alzheimer's disease (AD). The other lncRNAs that involved in AD are 17A and BC200. ncRNA-a involved in Opitz-Kaveggia syndrome. Evf-2 that has Dlx5/6 as its target may have roles in many neurological disorders, such as autism, epilepsy, Rettsyndrome, schizophrenia, etc. SCAANT1 has Ataxin 7 as a target and involved in Spinocerebellar ataxia 7. ATXN8OS has MBLN1 as the target and involved in Spinocerebellar ataxia 8. 116HG upregulates many genes as the target and involved in Prader-Willi syndrome. Gomafu has DISC1 and ERBB4 as targets and involved in schizophrenia, mainly associated with behavioral abnormalities. Antisense TABLE 1. Some cancer associated LncRNAs

No.	LncRNA	Type of Cancer	References
1.	ANRIL	basal cell carcinoma, bladder cancer,	(Cunnington et al. 2010;
	(antisense non-coding RNA	melanomas, neurofibromas	Zhu et al. 2015; Stacey et al. 2009;
	in the INK4 locus) DD3/PCA3		Pasmant et al. 2011)
2.	DD3/PCA3	Prostate cancer	(Bussemakers et al. 1999;
			Durand et al. 2012; Ploussard et al. 2011)
3.	GAS5 (growth arrest-specific transcript 5)	Renal cell carcinoma (RCC)	(Qiao et al. 2013)
4.	H19	Kidney cancer	(Frevel et al. 1999)
5.	HIF-1alpha-AS1 and AS2	Kidney cancer	(Thrash-Bingham & Tartof 1999;
	-	-	Bertozzi et al. 2011)
6.	HOTAIR	Several cancer; i.e.: breast,	(Gupta et al. 2010; Kogo et al. 2011;
		colon, liver, and pancreas	Geng et al. 2011; Kim et al. 2013)
7.	HULC (highly upregulated	Hepatocellular carcinoma	(Panzitt et al. 2007)
	in liver cancer)	-	
8.	LncTCF7	Liver CSCs (Cancer Stem Cells)	(Wang et al. 2015)
9.	MALAT-1	Small cell lung cancer	(Gutschner et al. 2013)
10.	MEG3 (GTL1)	Renal cell carcinoma (RCC)	(Kawakami et al. 2006)

Uchl1 has UCHL1 as its target and involved in Parkinson's disease (PD). There are minimally eight known lncRNAs that were observed to change significantly in the brains of Huntington's disease (HD) patients: TUG1 and NEAT1 are upregulated, MEG3 and DGCR5 are downregulated, while HTTAS_v1 and BDNF-AS are transcriptionally regulated.

Another lncRNAs involved in Person with HD are HAR1F and HAR1R (Vučićević, Schrewe & Orom 2014; Pollard et al. 2006).

Herein the Table 2 some of specific long ncRNAs as hallmarks in many neurological problems and neurodegenerative diseases and disorders.

TABLE 2. Specific lncRNA in neurological problem

No.	Diseases / disorders	LncRNA	References
1.	Alzheimer's disease (AD)	beta-site amyloid precursor protein	(Luo & Chen 2016; Decourt
		cleaving enzyme-1 antisense	& Sabbagh 2011; Evin & Hince 2013;
		transcript (BACE1-AS)	Faghihi et al. 2008)
2.	Alzheimer's disease (AD)	51A	(Ciarlo et al. 2013; Ma et al. 2009)
3.	Alzheimer's disease (AD)	17A	(Wan, Su & Zhuo 2017;
			Massone et al. 2011)
4.	Alzheimer's disease (AD)	neuroblastoma differentiation marker 29 (NDM29)	(Massone et al. 2012)
5.	Alzheimer's disease (AD)	BC200 (brain cytoplasmic 200 RNA)	(Mus, Hof & Tiedge 2007)
6.	Alzheimer's disease (AD)	brain cytoplasmic (BC) RNA BCYRN1	(Mus, Hof & Tiedge 2007;
			Lukiw et al. 1992)
7.	Alzheimer's disease (AD)	NAT-Rad18	(Zlatanou et al. 2016; Parenti et al. 2007)
8.	Amyotrophic lateral sclerosis	AS C9ORF72 (chromosome 9 ORF 72)	(Renton et al. 2011; Zu et al. 2013;
	(ALS)		Lagier-Tourenne et al. 2013)
9.	Autistic spectrum disorder	MSNP1AS (moesin pseudogene 1, antisense)	(Wilkinson & Campbell 2013;
	(ASD)		Kerin et al. 2012)
10.	Glioblastoma (GBM)	There are 104 matched lncRNA-mRNA	(Han et al. 2012)
		pairs for 91 differentially expressed lncRNAs	
		In the GBM group, 654 lncRNAs were	
		downregulated and 654 were upregulated	
11.	Huntington's disease (HD)	MEG3	(Zhao et al. 2010)
12.	Huntington's disease (HD)	TUG1	(Khalil et al. 2009)
13.	Huntington's disease (HD)	NEAT1 (Nuclear enriched abundant transcript)	(Johnson 2012)
14.	Parkinson's disease (PD)	PINK1-AS (phosphatase and tensin homologue-	(Scheele et al. 2007)
		induced kinase 1)	
15.	Parkinson's disease (PD)	AS Uchl1	(Carrieri et al. 2015)
16.	Spinocerebellar Ataxia	ATXN8OS	(Chen et al. 2008)
17.	Spinocerebellar Ataxia	ATXN7L3B	(Munhoz et al. 2009)

DERMATOLOGY PERSPECTIVES

Long noncoding RNA has promising impacts and roles in dermatology problems, including melanoma, psoriasis, keratinization, and Cutaneous Squamous Cell Carcinoma (cSCC). Herein we decipher them concisely.

MELANOMA

The lncRNA SPRIGHTLY (also known as SPRY4-IT1) is upregulated in human melanoma cells. It lies within the intronic region of SPRY4 gene. SPRIGHTLY is transcribed from the first intron of SPRY4 (Sprouty 4 gene). In human melanoma cells, it is highly upregulated. In normal human melanocytes, it is ectopically expressed at low levels. It contributes to the regulation of DNA damage response, chromosome organization, cell proliferation, cell cycle, and apoptosis in melanocytes. It also regulates proliferation, motility, and apoptosis that constitute cancer hallmarks. Together with its target genes, SPRIGHTLY has an impact in melanocyte dedifferentiation and their transformation into melanomas. It has a lot of important roles in multiple regulatory pathways in melanomas. Its dysfunction in melanoma cells prohibits cell growth, differentiation, and induced apoptosis (Khaitan et al. 2011; Zhao et al. 2016; Mazar et al. 2010, 2014).

Long noncoding RNAs involved in the synthesis of melanin. LncRNA-H19 has an important role in the formation of melasma. Irradiation of melanocytes with 20 $mJ/cm^2 \ \text{UVB}$ changed expression 807 lncRNAs more than two-fold using Agilent lncRNA chip expression profile detection technology. LncRNAs involve in the UVB-induced stress response. Some lncRNAs expression alterations triggered by UVB are dependent on ROS generation. ROSmediated production of lnc-CD1D-2:1 participated in the UVB-induced melanogenesis. MAPK signaling pathway was engaged in the melanogenesis, therefore p38, ERK, and JNK phosphorylation levels were observed. The UVB-induced alterations in lncRNAs involve in the etiopathogenesis of melanoma. LncRNAUCA1 was engaged in H2O2-induced cell apoptosis, signifying relationship between ROS and IncRNAs (Kim, Lee & Lee 2010; Kim et al. 2014; Peng et al. 2014; Liu et al. 2015; Zeng et al. 2016).

Targeting a lncRNA in vivo is a potentially putative therapeutic choice, such as SAMMSON (previously known as LINC01212). SAMMSON lncRNA plays important roles in melanoma development. It is arranged by an alternative SOX factor such as SOX9, understood as a key antagonistic role to SOX10 in melanoma. It is detectable in melanocytes or non-invasive vertical growth phase melanomas, in invasive vertical growth phase melanoma, and in migratory melanoblasts (Shakhova et al. 2015; Goding 2016; Leucci et al. 2016; Hoek & Goding 2010). SAMMSON confers a growth advantage on melanoma cells. Targeting SAMMSON for degradation reduced clonogenicity, irrespective of BRAF, NRAS, or p53 status, including in cell lines exhibiting BRAF inhibitor resistance, but did not affect melanocytes, highlighting the "addiction" of melanomas to SAMMSON expression. It also reduced viability/growth of invasive melanoma cells, known to exhibit increased resistance to MAPK therapeutics. Importantly, ectopic expression of SAMMSON in melanoma cells conferred a growth advantage, indicating that SAMMSON acts in trans, an observation consistent with the lack of effect on MITF expression following SAMMSON knockdown (Shakhova et al. 2015; Goding 2016; Leucci et al. 2016; Hoek & Goding 2010).

Deciphering SAMMSON lncRNA biogenesis, we can understand how the MITF amplicon impacts melanoma proliferation. MITF (microphthalmia-associated transcription factor) is a microenvironmental hallmark of melanoma. It is required for melanoblast survival while development, melanocyte differentiation, suppresses invasion, promotes proliferation, and drives "phenotype switching" which props melanoma development (Shakhova et al. 2015; Goding 2016; Leucci et al. 2016; Hoek & Goding 2010).

The SAMMSON lncRNA gene is co-amplified with MITF in melanoma. SAMMSON-p32 complex is needed for correct mitochondrial biogenesis. Depletion of SAMMSON leads to stress connected accumulation of mitochondrial peptide precursors, mitochondrial import defects, and p53-independent apoptosis. BRAF inhibitors (BRAFi) boost dependency on mitochondrial oxidative phosphorylation and collaborate with SAMMSON inhibition (Shakhova et al. 2015; Goding 2016; Leucci et al. 2016; Hoek & Goding 2010).

PSORIASIS

There are 971 lncRNAs were statistically significant expressed in psoriasis patients, which whom 399 were underexpressed whereas 572 were overexpressed. Some of them show decreased expression in psoriasis person, such as LOC285194, Car Intergenic 10, ST7OT. Of overexpressed 572 lncRNAs, CARD14 lncRNA was significantly overexpressed. Mutations in CARD14 genes are related to susceptibility to psoriasis (Gupta et al. 2016).

KERATINIZATION

Long ncRNAs was performed by transcriptome sequencing of keratinocytes. The keratinocytes sampled were derived from palmar and forearm skin. This research had been identified 125 candidate lncRNAs which is involved in keratinization (Nomura 2016).

CUTANEOUS SQUAMOUS CELL CARCINOMA

PICSAR is lncRNA that has an important role in Cutaneous Squamous Cell Carcinoma (cSCC) progression. LncRNA PICSAR is overexpressed in cSCC cells, both in vivo and in culture. It regulates both proliferation and migration of cSCC cells and growth of cSCCs cells in vivo. It increases the activity of ERK1/2 pathway through inhibition of MAPK phosphatase DUSP6. PICSAR is a putative biomarker and futuristic therapeutic target in cSCC management (Piipponen et al. 2016).

IMMUNOLOGY PERSPECTIVE

Long noncoding RNAs (lncRNAs) have been appeared to assume imperative parts in immune cells responses and developments via various mechanisms. They have been observed to control transcriptional or post-transcriptional regulation of innate and adaptive immune responses through novel methods for blending with RNA and DNA or protein-protein interactions (Zhang & Cao 2016).

Some lncRNAs are involved in immune cell development processes, such as immune cell activation, differentiation, proliferation. They are NRON, lnc-DC, NTT, GAS5, HOTAIRM1, etc (Zhang & Cao 2016).

LncRNAs control the innate immune responses. Numerous lncRNAs that have been connected to innate immunity have been found by RNA-Seq studies and microarray, i.e.: Lethe, NEAT1, NKILA, PACER, and THRIL (Table 3), that represent the magnificent patterns of lncRNAs that are ensnared in regulating immune cells functions and immune genes expressions (Guttman et al. 2009; Carpenter & Fitzgerald 2015; Imamura & Akimitsu 2014; Li & Rana 2014).

TABLE 3	. The roles	of lncRNAs	in innate	immune responses
---------	-------------	------------	-----------	------------------

No.	lncRNA	References
1.	Lethe	(Zgheib et al. 2017; Rapicavoli et al. 2013)
2.	NEAT1	(Imamura et al. 2014; Hirose et al. 2014)
3.	NKILA (NF-KappaB interacting lncRNA)	(Huang et al. 2016)
4.	PACER (p50-associated COX-2 extragenic RNA)	(Krawczyk & Emerson 2014; Cui et al. 2014; Qian et al. 2016)
5.	THRIL (linc1992)	(Szmyrka-Kaczmarek et al. 2014; Li et al. 2014)

AUTOIMMUNE DISEASES AND LNCRNA

Autoimmune diseases are complicated and enigmatic diseases resulting from the interaction between genetics, epigenetics, and environmental factors (Wu et al. 2015). LncRNAs dysregulation regulate certain

mechanisms in autoimmune diseases, including PRINS (10p12.1) arranges G1P3 to maintain the keratinocyte hyperproliferation in psoriasis (Szegedi et al. 2012, 2010). Dysregulation of lncRNAs influences various autoimmune diseases. For further explanation, we elucidate in the Table 4 herein.

No.	Diseases	References
1.	Psoriasis Vulgaris (PV)	(Szegedi et al. 2012, 2010; Sonkoly et al. 2005; Bari et al. 2011; Chang et al. 2006; Holm et al. 2005)
2.	Systemic lupus erythematosus (SLE)	(Cope & Feldmann 2004; Chatenoud 2006; Shi et al. 2014; Giles,
3.	Rheumatoid arthritis (RA)	Nycz & Boackle 2016) (Song et al. 2014; Messemaker et al. 2016; Lu et al. 2016)

TECHNOLOGY PERSPECTIVES

The genome annotation technology is necessary to provide database management for transcriptomics data (Parikesit et al. 2014). In this respect, the gene prediction pipeline is important to annotate the missing information in the genomes (Goel, Singh & Aseri 2013). This pipeline is especially crucial in annotating the transcriptomics data that still currently lacking information. Problem arises, as the generated data will be grown exponentially, in the scale of petabytes. Thus, the data mining method for big data storage is very feasible to be applied on daily basis in order to extract for definite transcriptomics pattern (Ranganathan et al. 2011). This hunt for information could only be resolved with the complete mastery of bioinformatics science (Liew, Yan & Yang 2005). Herewith, as more sophisticated pattern recognition methods are in place, the jobs for extracting meaningful transcriptomics fingerprint will become more feasible (da Sacco, Baldassarre & Masotti 2012).

BIOINFORMATICS RESOURCES

Several websites-based bioinformatics resources are available to researchers for lncRNA research. They contain multiple repositories, databases, softwares, and other annotation tools. Bioinformatics databases that based on websites is revealed through this Table 5.

All databases that provide information about lncRNAs can identify human. Some of them include specific information towards rat (lncRNAdb, DIANAlncBase, Functional lncRNA Database, Noncode v3.0, CHIPBase), also specific towards another model organisms (lncRNAdb, CHIPBase, Functional lncRNA Database, and DIANA-lncBase). Especially, lncRNAdb and Noncode v3.0 databases include lncRNAs that express in some species, from yeasts to plants. This databases offer information about specific characterization of lncRNAs cells or tissues: lncRNAdb, lncRNome, CHIPBase, Noncode v3.0, and DIANALncBase. Only Noncode v3.0 and lncRNAdb localize lncRNAs cellular (Fritah, Niclou & Azuaje 2014).

There are different bioinformatics tools for predicting the functions and structures of RNA sequences, including some tools that concatenate other experimental data in the analysis. Moreover, remembering that the recent experimental exploratory methods are still restricted in their throughput and output, quick bioinformatics tools to recognize and characterize lncRNAs with reasonable preciseness are needed (Iwakiri, Hamada & Asai 2016).

Below we evince the available bioinformatics databases and tools which beneficial for discovering long non-coding RNAs and analyzing their secondary structures, conservation, interactions, co-expressions, and subcellular localization through Table 6.

SUMMARY

We have expounded multiperspectives of lncRNAs comprehensively based on CONDBITs perspectives, i.e.: cardiology, oncology, neurology and neuroscience, dermatology, the biology of molecular and bioinformatics, immunology, and technologies. The CONDBITs perspectives could be seen in the Table 7 below.

ACKNOWLEDGEMENT

The authors would like to thanks to the leaders of Research and CSR Institute (LPPM) of Indonesia International Institute for Life Sciences (i3L) and University of Muhammadyah Makassar for their heartfelt support toward the completion of this manuscript. We also thank Prof. Dr. Sofia Mubarika for comments on earlier versions of this manuscript.

No.	Database	Website
1.	CHIPBase	deepbase.sysu.edu.cn/chipbase
2.	DIANA-LncBase	diana.imis.athena-innovation.gr
3.	fRNAdb	www.Ncrna.org/frnadb
4.	Human Body Map lincRNAs	www.Broadinstitute.org/genome bio/human lincrnas
5.	LNCipedia	www.lncipedia.org
6.	lncRNAdb	www.lncrnadb.org
7.	lncRNAdb Expert Database	http://rnacentral.org/expert-database/lncrnadb
8.	IncRNADisease	cmbi.bjmu.edu.cn/lncrnadisease
9.	LncRNADisease database	http://www.cuilab.cn/lncrnadisease
10.	IncRNome	genome.igib.res.in/lncRNome
11.	IncRNAtor	http://lncrnator.ewha.ac.kr/index.htm
12.	Noncode v3.0	noncode.org/NONCODERv3
13.	the Functional lncRNA Database	www.valadkhanlab.org
14.	UCSC	genome.ucsc.edu

TABLE 5. The database for lncRNA research (Based on our exploration)

No.	Bioinformatics Databases/Tools	References
1.	NGS (next-generation sequencing) technologies or tiling microarrays	(Iwakiri, Hamada & Asai 2016)
2.	LAST, Tophat, STAR	(Kim et al. 2013; Kiełbasa et al. 2011; Dobin et al. 2013)
3.	BLASTX	(Gish & States 1993)
<i>4</i> .	PORTRAIT, CPC (Cording-Potential Calculator)	(Kong et al. 2007; Wang et al. 2013)
ч. 5.	RNAcode, PhyloCSF	(Washietl et al. 2011; Lin, Jungreis &
5.	Rivieode, Thylocol	Kellis 2011)
6.	QRNA, RNAz	(Rivas & Eddy 2001; Gruber et al. 2010)
7.	Expression Atlas	(Petryszak et al. 2014; Uhlén et al. 2015;
		Klijn et al. 2015)
8.	ROKU	(Kadota et al. 2006)
9.	ENCODE project	(Djebali et al. 2012)
10.	HITS-CLIP, PAR-CLIP, RAP-RNA, RIA-seq	(Licatalosi et al. 2008; Hafner et al. 2010;
		Engreitz et al. 2014; Kretz et al. 2013)
11.	IntaRNA	(Busch, Richter & Backofen 2008)
12.	CopraRNA	(Wright et al. 2013)
13.	A computational pipeline including multiple computational	(Frith, Hamada & Horton 2010; Kato et al. 2010;
	sequence analysis devices (IntaRNA, LAST, RactIP, Raccess, and TanTan)	Kiryu et al. 2011; Frith 2011)
14.	RPI-Pred	(Suresh et al. 2015)
15.	catRAPID, RPI-seq, lncPRO	(Bellucci et al. 2011; Muppirala, Honavar &
101		Dobbs 2011; Lu et al. 2013)
16.	Machine learning approaches, e.g.: support vector machine (SVM), Fisher's LDA (linear discriminant analysis), SVM (support vector machine), and RF (random forest)	(Pancaldi & Bähler 2011)
17.	Mfold, CentroidFold, RNAfold, and RNAstructure	(Sato et al. 2009; Hamada, Kiryu, et al. 2009;
17.	whold, controlation, kit hold, and kit is ucture	Zuker 2003; Lorenz et al. 2011;
		Mathews 2014b, 2014a)
18.	CentroidHomfold	(Hamada et al. 2011)
10. 19.	DMS-seq, FragSeq, MAP-seq, Mod-seq, PARS, SHAPE-seq	(Rouskin et al. 2014; Ding et al. 2014;
17.	Dhib seq, Hugber, hhu seq, hiou seq, hhub, bhhu b seq	Underwood et al. 2010; Seetin et al. 2014;
		Talkish et al. 2014; Y. Wan et al. 2014;
		Loughrey et al. 2014)
20.	RNAalifold and Centroid Alifold	(Bernhart et al. 2008; Hamada, Sato & Asai 2011;
		Hamada 2015)
21.	ProbCons	(Do et al. 2005)
22.	CentroidAlign, LARA, LocARNA, MAFFT, MXSCARNA	(Hamada, Sato, et al. 2009; Bauer, Klau &
		Reinert 2007; Will et al. 2012; Katoh & Toh 2008;
22	DETecfold	Tabei et al. 2008)
23.	PETcofold	(Seemann et al. 2011) (View et al. 2011)
24.	Raccess	(Kiryu et al. 2011) (Kiryu & Assi 2012)
25.	Rehange	(Kiryu & Asai 2012) (Uillan at al. 2006; Karan at al. 2010)
26.	MEMERIS and RNAcontext	(Hiller et al. 2006; Kazan et al. 2010) (Zhang & Zhan 2014)
27.	PLEK (predictor of long non-coding RNAs and messenger	(Zhang & Zhou 2014)
	RNAs based on an improved k-mer scheme)	

TABLE 6. The explanation on bioinformatics database

Abbreviation	Narration		
С	KCNQ1OT1 has important roles in arrhythmia and cardiac development. MIAT dysregulation has a critic on the pathogenesis of myocardial infarction (MI) and atherosclerosis. MT-LIPCAR can predict survival i with heart failure. CDKN2B-AS1 (ANRIL) can be used as a risk factor biomarker for coronary artery di MI.	in patients	
Ο	There are abundant lncRNAs associated with cancer, i.e.: breast cancer (ANRIL, BC040587, BCAR4, E DSCAM-AS1, GAS5, H19, HOTAIR, HOTAIRM1, IRAIN, LincRNA-BC4, LincRNA-BC5, Loc LSINCT5, MALAT1, MEG3, MIR31HG, PINC, PVT1, SRA1, XIST, ZNFX1-AS1), cervical cancer (I GAS5), prostate cancer (C20orf166-AS1, CBR3-AS1, CTBP1-AS, ENSG00000261777, GAS5, H19, M NEAT1, PCA3, PCAT1, PCGEM1, PRNCR1, PTENP1, RP11-267A15.1, ucRNAs, XIST). ANRIL correlated with poor prognosis and considered as a risk factor in various types of human cancer breast cancer, esophageal squamous cell carcinoma, gastric cancer, hepatocellular carcinoma, lung cancer cancer.	c554202, HOTAIR, MALAT1, rs, such as	
Ν	BACE1-AS concentrations were increased in patients with Alzheimer's disease.		
D	SAMMSON lncRNA plays important roles in melanoma development. Some of LncRNAs show of expression in psoriasis person, such as LOC285194, Car Intergenic 10, ST7OT. Of overexpressed 572 l CARD14 lncRNA was significantly overexpressed.		
В	NONCODE 2016 (www.noncode.org) contains 527,336 lncRNA transcripts from literature and public of NGS technologies or tiling microarrays to observe the fragments of the transcribed units of the sequences.		
Ι	NEAT1 has response to TLRs stimulus. Useful for formation of nuclear body paraspeckles. PRINS is over in PV. Several LncRNAs, i.e.: anti-NOS2A, Hotair, MEG9, LUST, TUG1, NEAT1 and SNHG4 were up whereas PRINS, PR antisense transcripts, mascRNA, and HOXA3as were downregulated in rho arthritis.	regulated,	
Т	Synergy-omics based technologies in lncRNAs researches in the future potentially make them as powerful b and theranostics on certain diseases and disorders.	viomarker	

TABLE 7. The CONDBITs perspectives of lncRNAs

REFERENCES

- Amaral, Paulo P. & John S. Mattick. 2008. "Noncoding RNA in Development." *Mammalian Genome* 19(7): 454-492.
- Azzouzi, Hamid El, Pieter Adrianus Doevendans & Joost Petrus Gerardus Sluijter. 2016. "Long Non-Coding RNAs in Heart Failure: An Obvious Lnc." *Annals of Translational Medicine* 4(9): 182-186.
- Bari, Lilla, Sarolta Bacsa, Eniko Sonkoly, Zsuzsanna Bata-Csörgő, Lajos Kemény, Attila Dobozy & Márta Széll. 2011.
 "Comparison of Stress-Induced PRINS Gene Expression in Normal Human Keratinocytes and HaCaT Cells." Archives of Dermatological Research 303(10): 745-752.
- Bauer, Markus, Gunnar W. Klau & Knut Reinert. 2007. "Accurate Multiple Sequence-Structure Alignment of RNA Sequences Using Combinatorial Optimization." *BMC Bioinformatics* 8(271).
- Bellucci, Matteo, Federico Agostini, Marianela Masin & Gian Gaetano Tartaglia. 2011. "Predicting Protein Associations with Long Noncoding RNAs." *Nature Methods* 8: 444-445.
- Bernhart, Stephan H, Ivo L Hofacker, Sebastian Will, Andreas R Gruber & Peter F Stadler. 2008. "RNAalifold: Improved Consensus Structure Prediction for RNAAlignments." *BMC Bioinformatics* 9: 474.
- Bertozzi, Davide, Raffaella Iurlaro, Olivier Sordet, Jessica Marinello, Nadia Zaffaroni, and Giovanni Capranico. 2011. "Characterization of Novel Antisense HIF-1α Transcripts in Human Cancers." *Cell Cycle*. 10(18): 3189-3197.
- Bhan, Arunoday, and Subhrangsu S. Mandal. 2015. "LncRNA HOTAIR: A Master Regulator of Chromatin Dynamics

and Cancer." *Biochimica et Biophysica Acta – Reviews on Cancer* 1856(1): 151-164.

- Blondeau, Jasmine Jc, Mario Deng, Isabella Syring, Sarah Schrödter, Doris Schmidt, Sven Perner, Stefan C. Müller, and Jörg Ellinger. 2015. "Identification of Novel Long Non-Coding Rnas in Clear Cell Renal Cell Carcinoma." *Clinical Epigenetics* 7: 10.
- Bokil, Nilesh J., John M. Baisden, Dorothy J. Radford & Kim M. Summers. 2010. "Molecular Genetics of Long QT Syndrome." *Molecular Genetics and Metabolism* 101(1): 1-8.
- Busch, Anke, Andreas S. Richter & Rolf Backofen. 2008. "IntaRNA: Efficient Prediction of Bacterial SRNA Targets Incorporating Target Site Accessibility and Seed Regions." *Bioinformatics* 24(24): 2849-2856.
- Bussemakers, Marion J. G., Adrie Van Bokhoven, Gerald W. Verhaegh, Frank P. Smit, Herbert F M Karthaus, Jack A. Schalken, Frans M. J. Debruyne, Ning Ru & William B. Isaacs. 1999. "DD3: A New Prostate-Specific Gene, Highly Overexpressed in Prostate Cancer." *Cancer Research*. 59(23): 5975-5979.
- Carlock, L R, D Skarecky, S L Dana & J J Wasmuth. 1985. "Deletion Mapping of Human Chromosome 5 Using Chromosome-Specific DNA Probes." *American Journal of Human Genetics* 37(5): 839-52.
- Carpenter, Susan & Katherine A Fitzgerald. 2015. "Transcription of Inflammatory Genes: Long Noncoding RNA and Beyond." Journal of Interferon & Cytokine Research : The Official Journal of the International Society for Interferon and Cytokine Research 35(2): 79-88.

- Carrieri, Claudia, Alistair R. R. Forrest, Claudio Santoro, Francesca Persichetti, Piero Carninci, Silvia Zucchelli & Stefano Gustincich. 2015. "Expression Analysis of the Long Non-Coding RNA Antisense to Uchl1 (AS Uchl1) during Dopaminergic Cells' Differentiation in Vitro and in Neurochemical Models of Parkinson's Disease." Frontiers in Cellular Neuroscience 9: 114.
- Chang, Y. T., C. T. Chou, Y. M. Shiao, M. W. Lin, C. W. Yu, C. C. Chen, C. H. & Huang, et al. 2006. "Psoriasis Vulgaris in Chinese Individuals Is Associated with PSORS1C3 and CDSN Genes." *British Journal of Dermatology* 155(4): 663-669.
- Chatenoud, Lucienne. 2006. "Immune Therapies of Autoimmune Diseases: Are We Approaching a Real Cure?" *Current Opinion in Immunology* 18(6): 710-717.
- Chen, Wei Lun, Jun Wei Lin, Hei Jen Huang, Su Min Wang, Ming Tsan Su, Guey Jen Lee-Chen, Chiung Mei Chen & Hsiu Mei Hsieh-Li. 2008. "SCA8 MRNA Expression Suggests an Antisense Regulation of KLHL1 and Correlates to SCA8 Pathology." *Brain Research* 1233: 176-184.
- Ciarlo, E., Massone, S., Penna, I., Nizzari, M., Gigoni, A., Dieci, G., Russo, C., Florio, T., Cancedda, R. & Pagano, A. 2013.
 "An Intronic NcRNA-Dependent Regulation of SORL1 Expression Affecting A Formation Is Upregulated in Post-Mortem Alzheimer's Disease Brain Samples." *Disease Models & Mechanisms* 6(2): 424-433.
- Consortium, C ARDIoGRAMplusC4D, P Deloukas, S Kanoni, C Willenborg, M Farrall, T L, Assimes, J. R. & Thompson, et al. 2013. "Large-Scale Association Analysis Identifies New Risk Loci for Coronary Artery Disease." *Nat Genet*. 45(1): 25-33.
- Cope, Andrew P. & Marc Feldmann. 2004. "Emerging Approaches for the Therapy of Autoimmune and Chronic Inflammatory Disease." *Current Opinion in Immunology* 16(6): 780-86.
- Cui, Huachun, Na Xie, Zheng Tan, Sami Banerjee, Victor John Thannickal, Edward Abraham & Gang Liu. 2014. "The Human Long Noncoding RNA Lnc-IL7R Regulates the Inflammatory Response." *European Journal of Immunology* 44(7): 2085-2095.
- Cunnington, Michael S., Mauro Santibanez Koref, Bongani M. Mayosi, John Burn, and Bernard Keavney. 2010.
 "Chromosome 9p21 SNPs Associated with Multiple Disease Phenotypes Correlate with ANRIL Expression." *PLoS Genetics* 6(4): e1000899.
- Decourt, Boris & Marwan N. Sabbagh. 2011. "BACE1 as a Potential Biomarker for Alzheimer's Disease." *Journal of Alzheimer's Disease*. 24 (Suppl 2): 53-59.
- Devaux, Yvan, Jennifer Zangrando, Blanche Schroen, Esther E. Creemers, Thierry Pedrazzini, Ching Pin Chang, Gerald W. Dorn, Thomas Thum & Stephane Heymans. 2015. "Long Noncoding RNAs in Cardiac Development and Ageing." *Nature Reviews Cardiology* 12(7): 415-425.
- Ding, Yiliang, Yin Tang, Chun Kit Kwok, Yu Zhang, Philip C. Bevilacqua & Sarah M. Assmann. 2014. "In Vivo Genome-Wide Profiling of RNA Secondary Structure Reveals Novel Regulatory Features." *Nature* 505: 696-700.
- Djebali, S, C A Davis, A Merkel, A Dobin, T Lassmann, A Mortazavi, A Tanzer, et al. 2012. "Landscape of Transcription in Human Cells." *Nature* 489(7414): 101-108.
- Do, Chuong B., Mahathi S.P. Mahabhashyam, Michael Brudno,
 & Serafim Batzoglou. 2005. "ProbCons: Probabilistic Consistency-Based Multiple Sequence Alignment." *Genome Research* 15(2): 330-340.

- Dobin, Alexander, Carrie A. Davis, Felix Schlesinger, Jorg Drenkow, Chris Zaleski, Sonali Jha, Philippe Batut, Mark Chaisson & Thomas R. Gingeras. 2013. "STAR: Ultrafast Universal RNA-Seq Aligner." *Bioinformatics* 29(1): 15-21.
- Durand, Xavier, Evanguelos Xylinas, Camelia Radulescu, Rachel Haus-Cheymol, Stephane Moutereau, Gillaume Ploussard & Aurelien Forgues, et al. 2012. "The Value of Urinary Prostate Cancer Gene 3 (PCA3) Scores in Predicting Pathological Features at Radical Prostatectomy." *BJU International*. 110(1): 43-49.
- Eis, P S, W Tam, L Sun, A Chadburn, Z Li, M F Gomez, E Lund & J E Dahlberg. 2005. "Accumulation of MiR-155 and BIC RNA in Human B Cell Lymphomas." *Proc Natl Acad Sci U S A*. 102(10): 3627-3632.
- Engreitz, Jesse M., Klara Sirokman, Patrick McDonel, Alexander A. Shishkin, Christine Surka, Pamela Russell, Sharon R. Grossman, Amy Y. Chow, Mitchell Guttman & Eric S. Lander. 2014. "RNA-RNA Interactions Enable Specific Targeting of Noncoding RNAs to Nascent Pre-MRNAs and Chromatin Sites." *Cell*. 159(1): 188-199.
- Evin, Genevieve & Christopher Hince. 2013. "BACE1 as a Therapeutic Target in Alzheimer's Disease: Rationale and Current Status." *Drugs and Aging* 30(10): 755-764.
- Faghihi, Mohammad Ali, Farzaneh Modarresi, Ahmad M. Khalil, Douglas E. Wood, Barbara G. Sahagan, Todd E. Morgan, Caleb E. Finch, Georges St. Laurent, Paul J. Kenny & Claes Wahlestedt. 2008. "Expression of a Noncoding RNA Is Elevated in Alzheimer's Disease and Drives Rapid Feed-Forward Regulation of β-Secretase." *Nature Medicine* 14(7): 723-730.
- Frevel, Mathias A E, Stephen J. Sowerby, George B. Petersen & Anthony E. Reeve. 1999. "Methylation Sequencing Analysis Refines the Region of H19 Epimutation in Wilms Tumor." *Journal of Biological Chemistry* 274(41): 29331-29340.
- Friedrichs, Frauke, Christian Zugck, Gerd Jörg Rauch, Boris Ivandic, Dieter Weichenhan, Margit Müller-Bardorff & Benjamin Meder, et al. 2009. "HBEGF, SRA1, and IK: Three Cosegregating Genes as Determinants of Cardiomyopathy." *Genome Research* 19(3): 395-403.
- Fritah, Sabrina, Simone P Niclou & Francisco Azuaje. 2014. "Databases for LncRNAs: A Comparative Evaluation of Emerging Tools." *RNA (New York, N.Y.)* 20(11): 1655-1665.
- Frith, Martin C. 2011. "A New Repeat-Masking Method Enables Specific Detection of Homologous Sequences." *Nucleic Acids Research* 39(4): e23.
- Frith, Martin C., Michiaki Hamada & Paul Horton. 2010. "Parameters for Accurate Genome Alignment." BMC Bioinformatics 11: 80-93.
- Geng, Y. J., S. L. Xie, Q. Li, J. Ma & G. Y. Wang. 2011. "Large Intervening Non-Coding RNA HOTAIR Is Associated with Hepatocellular Carcinoma Progression." *Journal of International Medical Research* 39(6): 2119-2128.
- Giles, Brendan M, Bryan T Nycz & Susan A Boackle. 2016. "GG-12 Altered Expression of Long Noncoding RNA Is Associated with a Lupus-Associated Variant in Complement Receptor 2." *Lupus Science & Medicine* 3 (Suppl 1): A33–A33.
- Gish, W & D J States. 1993. "Identification of Protein Coding Regions by Database Similarity Search." *Nat Genet* 3(3): 266-272.

- Goding, Colin R. 2016. "Targeting the LncRNA SAMMSON Reveals Metabolic Vulnerability in Melanoma." *Cancer Cell* 29 (5): 619-21.
- Goel, Neelam, Shailendra Singh & Trilok Chand Aseri. 2013. "A Comparative Analysis of Soft Computing Techniques for Gene Prediction." *Analytical Biochemistry* 438(1): 14-21.
- Grote, Phillip, Lars Wittler, David Hendrix, Frederic Koch, Sandra Währisch, Arica Beisaw & Karol Macura, et al. 2013. "The Tissue-Specific LncRNA Fendrr Is an Essential Regulator of Heart and Body Wall Development in the Mouse." *Developmental Cell* 24(2): 206-14.
- Gruber, Andreas R., Sven Findeiß, Stefan Washietl, Ivo L. Hofacker & Peter F. Stadler. 2010. "RNAZ 2.0: Improved Noncoding RNA Detection." *Pacific Symposium on Biocomputing 2010, PSB 2010.* 2010: 69-79.
- Gupta, Rajnish A., Nilay Shah, Kevin C. Wang, Jeewon Kim, Hugo M. Horlings, David J. Wong & Miao Chih Tsai, et al. 2010. "Long Non-Coding RNA HOTAIR Reprograms Chromatin State to Promote Cancer Metastasis." *Nature* 464(7291): 1071-1076.
- Gupta, Rashmi, Richard Ahn, Kevin Lai, Elizabeth Mullins, Maya Debbaneh, Michelle Dimon, Sarah Arron & Wilson Liao. 2016. "Landscape of Long Noncoding RNAs in Psoriatic and Healthy Skin." *Journal of Investigative Dermatology*. 136(3): 603-609.
- Gutschner, Tony & Sven Diederichs. 2012. "The Hallmarks of Cancer: A Long Non-Coding RNA Point of View." *RNA Biology* 9(6): 703-19.
- Gutschner, Tony, Monika Hämmerle, Moritz Eißmann, Jeff Hsu, Youngsoo Kim, Gene Hung & Alexey Revenko, et al. 2013.
 "The Noncoding RNA MALAT1 Is a Critical Regulator of the Metastasis Phenotype of Lung Cancer Cells." *Cancer Research* 73(3): 1180-1189.
- Guttman, Mitchell, Ido Amit, Manuel Garber, Courtney French, Michael F. Lin, David Feldser & Maite Huarte, et al. 2009.
 "Chromatin Signature Reveals over a Thousand Highly Conserved Large Non-Coding RNAs in Mammals." *Nature* 458: 223-227.
- Hafner, Markus, Markus Landthaler, Lukas Burger, Mohsen Khorshid, Jean Hausser, Philipp Berninger & Andrea Rothballer, et al. 2010. "Transcriptome-Wide Identification of RNA-Binding Protein and MicroRNA Target Sites by PAR-CLIP." Cell. 141(1): 129-141.
- Hajjari, Mohammadreza & Abbas Salavaty. 2015. "HOTAIR: An Oncogenic Long Non-Coding RNA in Different Cancers." *Cancer Biology & Medicine* 12(1): 1-9.
- Hamada, Michiaki. 2015. "RNA Secondary Structure Prediction from Multi-Aligned Sequences." *Methods in Molecular Biology (Clifton, N.J.)* 1269: 17-38.
- Hamada, Michiaki, Hisanori Kiryu, Kengo Sato, Toutai Mituyama & Kiyoshi Asai. 2009. "Prediction of RNA Secondary Structure Using Generalized Centroid Estimators." *Bioinformatics (Oxford, England)*. 25(4): 465-473.
- Hamada, Michiaki, Kengo Sato & Kiyoshi Asai. 2011. "Improving the Accuracy of Predicting Secondary Structure for Aligned RNA Sequences." *Nucleic Acids Research*. 39(2): 393-402.
- Hamada, Michiaki, Kengo Sato, Hisanori Kiryu, Toutai Mituyama & Kiyoshi Asai. 2009. "CentroidAlign: Fast and Accurate Aligner for Structured RNAs by Maximizing Expected Sumof-Pairs Score." *Bioinformatics* 25(24): 3236-3243.

- Hamada, Michiaki, Koichiro Yamada, Kengo Sato, Martin C. Frith & Kiyoshi Asai. 2011. "CentroidHomfold-LAST: Accurate Prediction of RNA Secondary Structure Using Automatically Collected Homologous Sequences." *Nucleic Acids Research.* 39(Suppl. 2): 100-106.
- Han, Lei, Kailiang Zhang, Zhendong Shi, Junxia Zhang, Jialin Zhu, Shanjun Zhu & Anling Zhang, et al. 2012. "LncRNA Profile of Glioblastoma Reveals the Potential Role of LncRNAs in Contributing to Glioblastoma Pathogenesis." *International Journal of Oncology* 40(6): 2004-2012.
- Hiller, Michael, Rainer Pudimat, Anke Busch & Rolf Backofen. 2006. "Using RNA Secondary Structures to Guide Sequence Motif Finding towards Single-Stranded Regions." *Nucleic Acids Research* 34(17): e117.
- Hirose, T., G. Virnicchi, A. Tanigawa, T. Naganuma, R. Li, H. Kimura & T. Yokoi, et al. 2014. "NEAT1 Long Noncoding RNA Regulates Transcription via Protein Sequestration within Subnuclear Bodies." *Molecular Biology of the Cell* 25(1): 169-183.
- Hoek, Keith S & Colin R Goding. 2010. "Cancer Stem Cells versus Phenotype-Switching in Melanoma." *Pigment Cell* & *Melanoma Research* 23(6): 746-59.
- Holm, Sofia J., Fabio Sánchez, Lina M. Carlén, Lotus Mallbris, Mona Ståhle & Kevin P. O'Brien. 2005. "HLA-Cw*0602 Associates More Strongly to Psoriasis in the Swedish Population than Variants of the Novel 6p21.3 Gene PSORS1C3." Acta Dermato-Venereologica 85(1): 2-8.
- Hua, Long, Chen-Yu Wang, Kun-Hou Yao, Jiang-Tao Chen, Jun-Jie Zhang & Wan-Li Ma. 2015. "High Expression of Long Non-Coding RNAANRIL Is Associated with Poor Prognosis in Hepatocellular Carcinoma." *International Journal of Clinical and Experimental Pathology* 8(3): 3076-3082.
- Huang, Long, Ling-Min Liao, An-Wen Liu, Jian-Bing Wu, Xiao-Ling Cheng, Jia-Xin Lin & Min Zheng. 2014.
 "Overexpression of Long Noncoding RNA HOTAIR Predicts a Poor Prognosis in Patients with Cervical Cancer." Archives of Gynecology and Obstetrics 290(4): 717-723.
- Huang, Wei, Xiuying Cui, Jianing Chen, Yuhuan Feng, Erwei Song, Jinsong Li & Yujie Liu. 2016. "Long Non-Coding RNA NKILA Inhibits Migration and Invasion of Tongue Squamous Cell Carcinoma Cells via Suppressing Epithelial-Mesenchymal Transition." Oncotarget 7(38): 62520-62532.
- Imamura, Katsutoshi & Nobuyoshi Akimitsu. 2014. "Long Non-Coding RNAs Involved in Immune Responses." Frontiers in Immunology. 5: 573-576.
- Imamura, Katsutoshi, Naoto Imamachi, Gen Akizuki, Michiko Kumakura, Atsushi Kawaguchi, Kyosuke Nagata & Akihisa Kato, et al. 2014. "Long Noncoding RNA NEAT1-Dependent SFPQ Relocation from Promoter Region to Paraspeckle Mediates IL8 Expression upon Immune Stimuli." *Molecular Cell* 53(3): 393-406.
- Ishii, Nobuaki, Kouichi Ozaki, Hiroshi Sato, Hiroya Mizuno, Susumu Saito, Atsushi Takahashi & Yoshinari Miyamoto, et al. 2006. "Identification of a Novel Non-Coding RNA, MIAT, That Confers Risk of Myocardial Infarction." *Journal* of Human Genetics 51(12): 1087-1099.
- Isin, Mustafa & Nejat Dalay. 2015. "LncRNAs and Neoplasia." *Clinica Chimica Acta* 440: 280-288.
- Iwakiri, Junichi, Michiaki Hamada & Kiyoshi Asai. 2016. "Bioinformatics Tools for LncRNA Research." *Biochimica* et Biophysica Acta 1859(1): 23-30.

- Johnson, Rory. 2012. "Long Non-Coding RNAs in Huntington's Disease Neurodegeneration." *Neurobiology of Disease*. 46(2): 245-54.
- Kadota, Koji, Jiazhen Ye, Yuji Nakai, Tohru Terada & Kentaro Shimizu. 2006. "ROKU: A Novel Method for Identification of Tissue-Specific Genes." *BMC Bioinformatics* 7: 294-302.
- Kato, Yuki, Kengo Sato, Michiaki Hamada, Yoshihide Watanabe, Kiyoshi Asai & Tatsuya Akutsu. 2010. "RactIP: Fast and Accurate Prediction of RNA-RNA Interaction Using Integer Programming." *Bioinformatics (Oxford, England)* 26(18): 460-466.
- Katoh, Kazutaka & Hiroyuki Toh. 2008. "Improved Accuracy of Multiple NcRNA Alignment by Incorporating Structural Information into a MAFFT-Based Framework." *BMC Bioinformatics* 9: 212-224.
- Kawakami, Takahiro, Tokuhiro Chano, Kahori Minami, Hidetoshi Okabe, Yusaku Okada & Keisei Okamoto. 2006. "Imprinted DLK1 Is a Putative Tumor Suppressor Gene and Inactivated by Epimutation at the Region Upstream of GTL2 in Human Renal Cell Carcinoma." *Human Molecular Genetics* 15(6): 821-30.
- Kazan, Hilal, Debashish Ray, Esther T. Chan, Timothy R. Hughes & Quaid Morris. 2010. "RNAcontext: A New Method for Learning the Sequence and Structure Binding Preferences of RNA-Binding Proteins." *PLoS Computational Biology*. 6(7): e1000832.
- Kerin, Tara, Anita Ramanathan, Kasey Rivas, Nicole Grepo, Gerhard A. Coetzee & Daniel B. Campbell. 2012. "A Noncoding RNA Antisense to Moesin at 5p14.1 in Autism." *Science Translational Medicine* 4(128): 128ra40.
- Khaitan, Divya, Marcel E. Dinger, Joseph Mazar, Joanna Crawford, Martin A. Smith, John S. Mattick & Ranjan J. Perera. 2011. "The Melanoma-Upregulated Long Noncoding RNA SPRY4-IT1 Modulates Apoptosis and Invasion." *Cancer Research* 71(11): 3852-3862.
- Khalil, Ahmad M., Mitchell Guttman, Maite Huarte, Manuel Garber, Arjun Raj, Dianali Rivea Morales & Kelly Thomas, et al. 2009. "Many Human Large Intergenic Noncoding RNAs Associate with Chromatin-Modifying Complexes and Affect Gene Expression." *Proceedings of the National Academy of Sciences* 106(28): 11667-11672.
- Kiełbasa, Szymon M., Raymond Wan, Kengo Sato, Paul Horton & Martin C. Frith. 2011. "Adaptive Seeds Tame Genomic Sequence Comparison." *Genome Research* 21(3): 487-493.
- Kim, Daehwan, Geo Pertea, Cole Trapnell, Harold Pimentel, Ryan Kelley & Steven L. Salzberg. 2013. "TopHat2: Accurate Alignment of Transcriptomes in the Presence of Insertions, Deletions and Gene Fusions." *Genome Biology* 14: R36.
- Kim, K., I. Jutooru, G. Chadalapaka, G. Johnson, J. Frank, R. Burghardt, S. Kim & S. Safe. 2013. "HOTAIR Is a Negative Prognostic Factor and Exhibits Pro-Oncogenic Activity in Pancreatic Cancer." Oncogene.
- Kim, Nan Hyung, Soo Hyun Choi, Chang Hyun Kim, Chang Hoon Lee, Tae Ryong Lee & Ai Young Lee. 2014. "Reduced MiR-675 in Exosome in H19 RNA-Related Melanogenesis via MITF as a Direct Target." *Journal of Investigative Dermatology*.
- Kim, Nan Hyung, Chang Hoon Lee & Ai Young Lee. 2010. "H19 RNA Downregulation Stimulated Melanogenesis in Melasma." *Pigment Cell and Melanoma Research*.

- Kiryu, Hisanori & Kiyoshi Asai. 2012. "Rchange: Algorithms for Computing Energy Changes of RNA Secondary Structures in Response to Base Mutations." *Bioinformatics*.
- Kiryu, Hisanori, Goro Terai, Osamu Imamura, Hiroyuki Yoneyama, Kenji Suzuki & Kiyoshi Asai. 2011. "A Detailed Investigation of Accessibilities around Target Sites of Sirnas and Mirnas." *Bioinformatics*.
- Klattenhoff, Carla A., Johanna C. Scheuermann, Lauren E. Surface, Robert K. Bradley, Paul A. Fields, Matthew L. Steinhauser & Huiming Ding, et al. 2013. "Braveheart, a Long Noncoding RNA Required for Cardiovascular Lineage Commitment." *Cell*.
- Klijn, Christiaan, Steffen Durinck, Eric W. Stawiski, Peter M. Haverty, Zhaoshi Jiang, Hanbin Liu & Jeremiah Degenhardt, et al. 2015. "A Comprehensive Transcriptional Portrait of Human Cancer Cell Lines." *Nature Biotechnology*.
- Kogo, Ryunosuke, Teppei Shimamura, Koshi Mimori, Kohichi Kawahara, Seiya Imoto, Tomoya Sudo & Fumiaki Tanaka, et al. 2011. "Long Noncoding RNA HOTAIR Regulates Polycomb-Dependent Chromatin Modification and Is Associated with Poor Prognosis in Colorectal Cancers." *Cancer Research.*
- Kong, Lei, Yong Zhang, Zhi Qiang Ye, Xiao Qiao Liu, Shu Qi Zhao, Liping Wei & Ge Gao. 2007. "CPC: Assess the Protein-Coding Potential of Transcripts Using Sequence Features and Support Vector Machine." *Nucleic Acids Research.*
- Korostowski, Lisa, Natalie Sedlak & Nora Engel. 2012. "The Kcnq1ot1 Long Non-Coding RNA Affects Chromatin Conformation and Expression of Kcnq1, but Does Not Regulate Its Imprinting in the Developing Heart." *PLoS Genetics*.
- Krawczyk, Michal & Beverly M. Emerson. 2014. "P50-Associated COX-2 Extragenic RNA (Pacer) Activates Human COX-2 Gene Expression by Occluding Repressive NF-KB P50 Complexes." *ELife*.
- Kretz, Markus, Zurab Siprashvili, Ci Chu, Dan E. Webster, Ashley Zehnder, Kun Qu, Carolyn S. & Lee, et al. 2013. "Control of Somatic Tissue Differentiation by the Long Non-Coding RNA TINCR." *Nature*.
- Kumarswamy, Regalla, Christophe Bauters, Ingo Volkmann, Fleur Maury, Jasmin Fetisch, Angelika Holzmann, Gilles Lemesle, Pascal De Groote, Florence Pinet & Thomas Thum. 2014. "Circulating Long Noncoding RNA, LIPCAR, Predicts Survival in Patients with Heart Failure." *Circulation Research*.
- Lagier-Tourenne, C., M. Baughn, F. Rigo, S. Sun, P. Liu, H.-R. Li, J. & Jiang, et al. 2013. "Targeted Degradation of Sense and Antisense C9orf72 RNA Foci as Therapy for ALS and Frontotemporal Degeneration." *Proceedings of the National Academy of Sciences*.
- Lee, Jae Hyung, Chen Gao, Guangdun Peng, Christopher Greer, Shuxun Ren, Yibin Wang & Xinshu Xiao. 2011. "Analysis of Transcriptome Complexity through RNA Sequencing in Normal and Failing Murine Hearts." *Circulation Research.*
- Leucci, Eleonora, Roberto Vendramin, Marco Spinazzi, Patrick Laurette, Mark Fiers, Jasper Wouters, Enrico Radaelli, et al. 2016. "Melanoma Addiction to the Long Non-Coding RNA SAMMSON." *Nature* 531(7595): 518-22.
- Li, Aimin, Junying Zhang & Zhongyin Zhou. 2014. "PLEK: A Tool for Predicting Long Non-Coding RNAs and Messenger

RNAs Based on an Improved k-Mer Scheme." *BMC Bioinformatics*.

- Li, Ling, Lei Zhang, Yan Zhang & Fang Zhou. 2015. "Increased Expression of LncRNA BANCR Is Associated with Clinical Progression and Poor Prognosis in Gastric Cancer." *Biomedicine & Pharmacotherapy*.
- Li, Z., T.-C. Chao, K.-Y. Chang, N. Lin, V. S. Patil, C. Shimizu, S. R. Head, Burns J. C. & Rana T. M. 2014. "The Long Noncoding RNA THRIL Regulates TNF Expression through Its Interaction with HnRNPL." *Proceedings of the National Academy of Sciences*.
- Li, Zhonghan & Tariq M. Rana. 2014. "Decoding the Noncoding: Prospective of LncRNA-Mediated Innate Immune Regulation." *RNA Biology*.
- Liao, Jiangquan, Qingyong He, Min Li, Yinfeng Chen, Yongmei Liu & Jie Wang. 2016. "LncRNA MIAT: Myocardial Infarction Associated and More." *Gene*.
- Licatalosi, Donny D., Aldo Mele, John J. Fak, Jernej Ule, Melis Kayikci, Sung Wook Chi, Tyson A. & Clark, et al. 2008. "HITS-CLIP Yields Genome-Wide Insights into Brain Alternative RNA Processing." *Nature*.
- Liew, Alan Wee-Chung, Hong Yan & Mengsu Yang. 2005. "Pattern Recognition Techniques for the Emerging Field of Bioinformatics: A Review." *Pattern Recognition* 38(11): 2055-73.
- Lin, Michael F., Irwin Jungreis & Manolis Kellis. 2011. "PhyloCSF: A Comparative Genomics Method to Distinguish Protein Coding and Non-Coding Regions." *Bioinformatics*. 27(13): 275-282.
- Liu, Youbin, Daliang Zhou, Guangnan Li, Xing Ming, Ying Feng Tu, Jinwei Tian, Huimin Lu & Bo Yu. 2015. "Long Non Coding RNA-UCA1 Contributes to Cardiomyocyte Apoptosis by Suppression of P27 Expression." *Cellular Physiology and Biochemistry* 35(5): 1986-1998.
- Lorenz, Ronny, Stephan H Bernhart, Christian Höner zu Siederdissen, Hakim Tafer, Christoph Flamm, Peter F Stadler & Ivo L Hofacker. 2011. "ViennaRNA Package 2.0." *Algorithms for Molecular Biology* 6(1): 26.
- Loughrey, David, Kyle E. Watters, Alexander H. Settle & Julius B. Lucks. 2014. "SHAPE-Seq 2.0: Systematic Optimization and Extension of High-Throughput Chemical Probing of RNA Secondary Structure with next Generation Sequencing." Nucleic Acids Research. 42(21): e165.
- Lu, Ming-Chi, Hui-Chun Yu, Chia-Li Yu, Hsien-Bin Huang, Malcolm Koo, Chien-Hsueh Tung, and Ning-Sheng Lai. 2016. "Increased Expression of Long Noncoding RNAs LOC100652951 and LOC100506036 in T Cells from Patients with Rheumatoid Arthritis Facilitates the Inflammatory Responses." *Immunologic Research* 64(2): 576-83.
- Lu, Qiongshi, Sijin Ren, Ming Lu, Yong Zhang, Dahai Zhu, Xuegong Zhang & Tingting Li. 2013. "Computational Prediction of Associations between Long Non-Coding RNAs and Proteins." *BMC Genomics* 14: 651-660.
- Lukiw, W. J., P. Handley, L. Wong & D. R. Crapper McLachlan. 1992. "BC200 RNA in Normal Human Neocortex, Non-Alzheimer Dementia (NAD), and Senile Dementia of the Alzheimer Type (AD)." *Neurochemical Research* 17(6): 591-597.
- Luo, Qiong & Yinghui Chen. 2016. "Long Noncoding RNAs and Alzheimer's Disease." *Clinical Interventions in Aging* 3(3): 131-143.

- Ma, Qiu-Lan, Douglas R Galasko, John M Ringman, Harry V Vinters, Steven D Edland, Justine Pomakian & Oliver J Ubeda et al. 2009. "Reduction of SorLA/LR11, a Sorting Protein Limiting Beta-Amyloid Production, in Alzheimer Disease Cerebrospinal Fluid." Archives of Neurology 66(4): 448-57.
- Massone, Sara, Eleonora Ciarlo, Serena Vella, Mario Nizzari, Tullio Florio, Claudio Russo, Ranieri Cancedda & Aldo Pagano. 2012. "NDM29, a RNA Polymerase III-Dependent Non Coding RNA, Promotes Amyloidogenic Processing of APP and Amyloid β Secretion." *Biochimica et Biophysica* Acta – Molecular Cell Research 1823(7): 1170-1177.
- Massone, Sara, Irene Vassallo, Gloria Fiorino, Manuele Castelnuovo, Federica Barbieri, Roberta Borghi & Massimo Tabaton et al. 2011. "17A, a Novel Non-Coding RNA, Regulates GABA B Alternative Splicing and Signaling in Response to Inflammatory Stimuli and in Alzheimer Disease." *Neurobiology of Disease* 41(2): 308-317.
- Mathews, David H. 2014a. "Using the RNAstructure Software Package to Predict Conserved RNA Structures." *Current Protocols in Bioinformatics* 46: 12.4.1-12.4.22.
- Mathews, David H. 2014b. "RNA Secondary Structure Analysis Using RNAstructure." *Current Protocols in Bioinformatics* / *Editoral Board, Andreas D. Baxevanis ... [et al.].*
- Mattick, John S & John L Rinn. 2015. "Discovery and Annotation of Long Noncoding RNAs." *Nature Structural & Molecular Biology* 22(1): 5-7.
- Mazar, Joseph, Satyabrata Sinha, Marcel E. Dinger, John S. Mattick & Ranjan J. Perera. 2010. "Protein-Coding and Non-Coding Gene Expression Analysis in Differentiating Human Keratinocytes Using a Three-Dimensional Epidermal Equivalent." *Molecular Genetics and Genomics* 284(1): 1-9.
- Mazar, Joseph, Wei Zhao, Ahmad M Khalil, Bongyong Lee, John Shelley, Subramaniam S Govindarajan & Fumiko Yamamoto et al. 2014. "The Functional Characterization of Long Noncoding RNA SPRY4-IT1 in Human Melanoma Cells." Oncotarget 5(19): 8959-8969.
- Messemaker, T. C., M. Frank-Bertoncelj, R. B. Marques, A. Adriaans, A. M. Bakker, N. Daha & S. Gay, et al. 2016. "A Novel Long Non-Coding RNA in the Rheumatoid Arthritis Risk Locus TRAF1-C5 Influences C5 MRNA Levels." *Genes and Immunity* 17(2): 85-92.
- Michalik, Katharina M., Xintian You, Yosif Manavski, Anuradha Doddaballapur, Martin Zörnig, Thomas Braun & David John et al. 2014. "Long Noncoding RNA MALAT1 Regulates Endothelial Cell Function and Vessel Growth." *Circulation Research* 114(9): 1389-1397.
- Munhoz, Renato P, Hélio A Teive, Salmo Raskin & Lineu C Werneck. 2009. "CTA/CTG Expansions at the SCA 8 Locus in Multiple System Atrophy." *Clinical Neurology* and Neurosurgery 111(2): 208-10.
- Muppirala, Usha K., Vasant G. Honavar & Drena Dobbs. 2011. "Predicting RNA-Protein Interactions Using Only Sequence Information." *BMC Bioinformatics* 12: 489-499.
- Mus, E., P. R. Hof & H. Tiedge. 2007. "Dendritic BC200 RNA in Aging and in Alzheimer's Disease." *Proceedings of the National Academy of Sciences* 104(25): 10679-10684.
- Nomura, Toshifumi. 2016. "Comprehensive Analysis of Long Non-Coding RNAs in Keratinization." Journal of Dermatological Science 84(1): e138.

- Pancaldi, Vera & Jürg Bähler. 2011. "In Silico Characterization and Prediction of Global Protein-MRNA Interactions in Yeast." *Nucleic Acids Research* 39(14): 5826-5836.
- Panzitt, Katrin, Marisa M.O. Tschernatsch, Christian Guelly, Tarek Moustafa, Martin Stradner, Heimo M. Strohmaier & Charles R. Buck et al. 2007. "Characterization of HULC, a Novel Gene With Striking Up-Regulation in Hepatocellular Carcinoma, as Noncoding RNA." *Gastroenterology* 32(1): 330-342.
- Parenti, Rosalba, Sabrina Paratore, Antonietta Torrisi & Sebastiano Cavallaro. 2007. "A Natural Antisense Transcript against Rad18, Specifically Expressed in Neurons and Upregulated during β-Amyloid-Induced Apoptosis." *European Journal* of Neuroscience 26(9): 2444-2457.
- Parikesit, Arli Aditya, Lydia Steiner, Peter F Stadler & Sonja J Prohaska. 2014. "Pitfalls of Ascertainment Biases in Genome Annotations – Computing Comparable Protein Domain Distributions in Eukarya." *Malaysian Journal of Fundamental and Applied Sciences* 10(2): 65-75.
- Pasmant, E., A. Sabbagh, M. Vidaud & I. Bieche. 2011. "ANRIL, a Long, Noncoding RNA, Is an Unexpected Major Hotspot in GWAS." *The FASEB Journal* 25(2): 444-448.
- Peng, Hsin Yi, Chih Chien Lin, Hsun Yen Wang, Ying Shih & Su Tze Chou. 2014. "The Melanogenesis Alteration Effects of Achillea Millefolium L. Essential Oil and Linalyl Acetate: Involvement of Oxidative Stress and the JNK and ERK Signaling Pathways in Melanoma Cells." *PLoS ONE*. 9(4): e95186.
- Petryszak, Robert, Tony Burdett, Benedetto Fiorelli, Nuno A Fonseca, Mar Gonzalez-Porta, Emma Hastings & Wolfgang Huber et al. 2014. "Expression Atlas Update-a Database of Gene and Transcript Expression from Microarray-and Sequencing-Based Functional Genomics Experiments." *Nucleic Acids Research* 42(Database issue): D926-D932.
- Piipponen, Minna, Liisa Nissinen, Mehdi Farshchian, Pilvi Riihilä, Atte Kivisaari, Markku Kallajoki, Juha Peltonen, Sirkku Peltonen & Veli Matti Kähäri. 2016. "Long Noncoding RNA PICSAR Promotes Growth of Cutaneous Squamous Cell Carcinoma by Regulating ERK1/2 Activity." Journal of Investigative Dermatology 136(8): 1701-1710.
- Ploussard, Guillaume, Xavier Durand, Evanguelos Xylinas, Stéphane Moutereau, Camélia Radulescu, Aurélien Forgue & Nathalie Nicolaiew et al. 2011. "Prostate Cancer Antigen 3 Score Accurately Predicts Tumour Volume and Might Help in Selecting Prostate Cancer Patients for Active Surveillance." *European Urology* 59(3): 422-429.
- Pollard, Katherine S., Sofie R. Salama, Nelle Lambert, Marie Alexandra Lambot, Sandra Coppens, Jakob S. Pedersen & Sol Katzman et al. 2006. "An RNA Gene Expressed during Cortical Development Evolved Rapidly in Humans." *Nature*. 443(7108): 167-172.
- Qian, Ming, Xinghai Yang, Zhenxi Li, Cong Jiang, Dianwen Song, Wangjun Yan & Tielong Liu, et al. 2016. "P50-Associated COX-2 Extragenic RNA (PACER) Overexpression Promotes Proliferation and Metastasis of Osteosarcoma Cells by Activating COX-2 Gene." *Tumor Biology* 37(3): 3879-3886.
- Qiao, Hui-Ping, Wei-Shi Gao, Jian-Xin Huo & Zhan-Shan Yang. 2013. "Long Non-Coding RNA GAS5 Functions as a Tumor Suppressor in Renal Cell Carcinoma." *Asian Pacific Journal* of Cancer Prevention 14(2): 1077-1082.

- Qiu, Jun-Jun, Ying-Ying Lin, Jing-Xin Ding, Wei-Wei Feng, Hong-Yan Jin & Ke-Qin Hua. 2015. "Long Non-Coding RNAANRIL Predicts Poor Prognosis and Promotes Invasion/ Metastasis in Serous Ovarian Cancer." *International Journal* of Oncology 46(6): 2497-2505.
- Ranganathan, Shoba, Christian Schönbach, Janet Kelso, Burkhard Rost, Sheila Nathan & Tin Wee Tan. 2011. "Towards Big Data Science in the Decade Ahead from Ten Years of InCoB and the 1st ISCB-Asia Joint Conference." In *BMC Bioinformatics* 12 Suppl 1:S1.
- Rapicavoli, Nicole A., Kun Qu, Jiajing Zhang, Megan Mikhail, Remi Martin Laberge & Howard Y. Chang. 2013. "A Mammalian Pseudogene LncRNA at the Interface of Inflammation and Antiinflammatory Therapeutics." *ELife*. 2016: 6205485.
- Renton, Alan E., Elisa Majounie, Adrian Waite, Javier Simón-Sánchez, Sara Rollinson, J. Raphael Gibbs, Jennifer C. & Schymick et al. 2011. "A Hexanucleotide Repeat Expansion in C9ORF72 Is the Cause of Chromosome 9p21-Linked ALS-FTD." *Neuron* 72(2): 257-268.
- Ritter, Oliver, Hannelore Haase, Hagen Dieter Schulte, Peter E. Lange & Ingo Morano. 1999. "Remodeling of the Hypertrophied Human Myocardium by Cardiac BHLH Transcription Factors." *Journal of Cellular Biochemistry* 74(4): 551-61.
- Rivas, E & S R Eddy. 2001. "Noncoding RNA Gene Detection Using Comparative Sequence Analysis." *BMC Bioinformatics* 2: 8-26.
- Rouskin, Silvi, Meghan Zubradt, Stefan Washietl, Manolis Kellis, & Jonathan S. Weissman. 2014. "Genome-Wide Probing of RNA Structure Reveals Active Unfolding of MRNA Structures in Vivo." *Nature* 505(7485): 701-5.
- Sacco, Letizia da, Antonella Baldassarre & Andrea Masotti. 2012. "Bioinformatics Tools and Novel Challenges in Long Non-Coding RNAs (LncRNAs) Functional Analysis." *International Journal of Molecular Sciences*. Molecular Diversity Preservation International. 13(1): 97-114.
- Samani, Nilesh J, Jeanette Erdmann, Alistair S Hall, Christian Hengstenberg, Massimo Mangino, Bjoern Mayer & Richard J Dixon et al. 2007. "Genomewide Association Analysis of Coronary Artery Disease." *The New England Journal of Medicine* 357(5): 443-453.
- Sato, Kengo, Michiaki Hamada, Kiyoshi Asai & Toutai Mituyama. 2009. "CentroidFold: A Web Server for RNA Secondary Structure Prediction." *Nucleic Acids Research*. 37(Web Server issue): 277-280.
- Scheele, Camilla, Natasa Petrovic, Mohammad A. Faghihi, Timo Lassmann, Katarina Fredriksson, Olav Rooyackers, Claes Wahlestedt, Liam Good & James A. Timmons. 2007. "The Human PINK1 Locus Is Regulated in Vivo by a Non-Coding Natural Antisense RNA during Modulation of Mitochondrial Function." *BMC Genomics* 8: 74-86.
- Schonrock, Nicole, Richard P. Harvey & John S. Mattick. 2012. "Long Noncoding RNAs in Cardiac Development and Pathophysiology." *Circulation Research* 111(10): 1349-1362.
- Seemann, Stefan E., Peter Menzel, Rolf Backofen & Jan Gorodkin. 2011. "The PETfold and PETcofold Web Servers for Intra- and Intermolecular Structures of Multiple RNA Sequences." *Nucleic Acids Research*. 39(Web Server issue): 107-111.

- Seetin, Matthew G., Wipapat Kladwang, John P. Bida & Rhiju Das. 2014. "Massively Parallel RNA Chemical Mapping with a Reduced Bias MAP-Seq Protocol." *Methods in Molecular Biology* 1086: 95-117.
- Shakhova, Olga, Phil Cheng, Pravin J Mishra, Daniel Zingg, Simon M Schaefer, Julien Debbache & Jessica Häusel et al. 2015. "Antagonistic Cross-Regulation between Sox9 and Sox10 Controls an Anti-Tumorigenic Program in Melanoma." Edited by Gregory S. Barsh. *PLoS Genetics* 11(1): e1004877.
- Shi, Lihua, Zhe Zhang, Angela M. Yu, Wei Wang, Zhi Wei, Ehtisham Akhter & Kelly Maurer, et al. 2014. "The SLE Transcriptome Exhibits Evidence of Chronic Endotoxin Exposure and Has Widespread Dysregulation of Non-Coding and Coding RNAs." *PLoS ONE*. 9(5): e93846.
- Song, Jinsoo, Dongkyun Kim, Jiyeon Han, Yunha Kim, Myeungsu Lee & Eun Jung Jin. 2014. "PBMC and Exosome-Derived Hotair Is a Critical Regulator and Potent Marker for Rheumatoid Arthritis." *Clinical and Experimental Medicine* 15(1): 121-126.
- Sonkoly, Eniko, Zsuzsanna Bata-Csorgo, Andor Pivarcsi, Hilda Polyanka, Anna Kenderessy-Szabo, Gergely Molnar & Karoly Szentpali et al. 2005. "Identification and Characterization of a Novel, Psoriasis Susceptibility-Related Noncoding RNA Gene, PRINS." Journal of Biological Chemistry 280(25): 24159-24167.
- Stacey, Simon N., Patrick Sulem, Gisli Masson, Sigurjon A. Gudjonsson, Gudmar Thorleifsson, Margret Jakobsdottir & Asgeir Sigurdsson et al. 2009. "New Common Variants Affecting Susceptibility to Basal Cell Carcinoma." *Nature Genetics* 41(8): 909-914.
- Sun, Miao, Shrikanth S Gadad, Dae Seok Kim & W Lee Kraus. 2015. "Discovery, Annotation, and Functional Analysis of Long Noncoding RNAs Controlling Cell-Cycle Gene Expression and Proliferation in Breast Cancer Cells." *Molecular Cell* 59(4): 698-711.
- Suresh, V., Liang Liu, Donald Adjeroh & Xiaobo Zhou. 2015. "RPI-Pred: Predicting NcRNA-Protein Interaction Using Sequence and Structural Information." *Nucleic Acids Research* 43(3): 1370-1379.
- Szegedi, Krisztina, Anikó Göblös, Sarolta Bacsa, Mária Antal, István Németh, Zsuzsanna Bata-Csörgő, Lajos Kemény, Attila Dobozy & Márta Széll. 2012. "Expression and Functional Studies on the Noncoding RNA, PRINS." International Journal of Molecular Sciences 14(1): 205-25.
- Szegedi, Krisztina, Eniko Sonkoly, Nikoletta Nagy, István Balázs Németh, Zsuzsanna Bata-Csörgo, Lajos Kemény, Attila Dobozy & Márta Széll. 2010. "The Anti-Apoptotic Protein G1P3 Is Overexpressed in Psoriasis and Regulated by the Non-Coding RNA, PRINS." *Experimental Dermatology*. 19(3): 269-278.
- Szmyrka-Kaczmarek, Magdalena, Agata Kosmaczewska, Lidia Ciszak, Aleksandra Szteblich & Piotr Wiland. 2014. "Peripheral Blood Th17/Treg Imbalance in Patients with Low-Active Systemic Lupus Erythematosus." *Postepy Higieny i Medycyny Doswiadczalnej (Online)* 68: 893-98.
- Tabei, Yasuo, Hisanori Kiryu, Taishin Kin & Kiyoshi Asai. 2008."A Fast Structural Multiple Alignment Method for Long RNA Sequences." *BMC Bioinformatics* 9: 33-49.
- Talkish, Jason, Gemma May, Yizhu Lin, John L. Woolford & C. Joel McManus. 2014. "Mod-Seq: High-Throughput

Sequencing for Chemical Probing of RNA Structure." *RNA*. 20(5): 713-720.

- Thrash-Bingham, Catherine A. & Kenneth D. Tartof. 1999. "AHIF: A Natural Antisense Transcript Overexpressed in Human Renal Cancer and during Hypoxia." *Journal of the National Cancer Institute* 91(2): 143-151.
- Uhlén, Mathias, Linn Fagerberg, Björn M Hallström, Cecilia Lindskog, Per Oksvold, Adil Mardinoglu & Åsa Sivertsson et al. 2015. "Proteomics. Tissue-Based Map of the Human Proteome." *Science (New York, N.Y.).* 347(6220): 1260419.
- Underwood, Jason G., Andrew V. Uzilov, Sol Katzman, Courtney S. Onodera, Jacob E. Mainzer, David H. Mathews, Todd M. Lowe, Sofie R. Salama & David Haussler. 2010.
 "FragSeq: Transcriptome-Wide RNA Structure Probing Using High-Throughput Sequencing." *Nature Methods*. 7(12): 995-1001.
- Vausort, Mélanie, Daniel R. Wagner & Yvan Devaux. 2014. "Long Noncoding RNAs in Patients with Acute Myocardial Infarction." *Circulation Research* 115(7): 668-77.
- Vučićević, Dubravka, Heinrich Schrewe & Ulf A Orom. 2014. "Molecular Mechanisms of Long NcRNAs in Neurological Disorders." *Frontiers in Genetics* 5: 48.
- Wan, Peixing, Wenru Su & Yehong Zhuo. 2017. "The Role of Long Noncoding RNAs in Neurodegenerative Diseases." *Molecular Neurobiology* 54(3): 2012-2021.
- Wan, Y, K Qu, Q C Zhang, R A Flynn, O Manor, Z Ouyang & J Zhang et al. 2014. "Landscape and Variation of RNA Secondary Structure across the Human Transcriptome." *Nature* 505: 706-709.
- Wang, Liguo, Hyun Jung Park, Surendra Dasari, Shengqin Wang, Jean Pierre Kocher & Wei Li. 2013. "CPAT: Coding-Potential Assessment Tool Using an Alignment-Free Logistic Regression Model." *Nucleic Acids Research* 41(6): e74.
- Wang, Yanying, Lei He, Ying Du, Pingping Zhu, Guanling Huang, Jianjun Luo & Xinlong Yan et al. 2015. "The Long Noncoding RNA LncTCF7 Promotes Self-Renewal of Human Liver Cancer Stem Cells through Activation of Wnt Signaling." Cell Stem Cell 16(4): 413-25.
- Washietl, Stefan, Sven Findei
 ß, Stephan A. M
 üller, Stefan Kalkhof, Martin Von Bergen, Ivo L. Hofacker, Peter F. Stadler & Nick Goldman. 2011. "RNAcode: Robust Discrimination of Coding and Noncoding Regions in Comparative Sequence Data." RNA. 17(4): 578-94.
- Wilkinson, Brent & Daniel B. Campbell. 2013. "Contribution of Long Noncoding RNAs to Autism Spectrum Disorder Risk." *International Review of Neurobiology* 113: 35-59.
- Will, Sebastian, Tejal Joshi, Ivo L. Hofacker, Peter F. Stadler & Rolf Backofen. 2012. "LocARNA-P: Accurate Boundary Prediction and Improved Detection of Structural RNAs." *RNA*. 18(5): 900-914.
- Wright, P. R., A. S. Richter, K. Papenfort, M. Mann, J. Vogel, W. R. Hess, R. Backofen & J. Georg. 2013. "Comparative Genomics Boosts Target Prediction for Bacterial Small RNAs." *Proceedings of the National Academy of Sciences*. 110(37): 3487-3496.
- Wu, Guo-Cui, Hai-Feng Pan, Rui-Xue Leng, De-Guang Wang, Xiang-Pei Li, Xiao-Mei Li & Dong-Qing Ye. 2015.
 "Emerging Role of Long Noncoding RNAs in Autoimmune Diseases." *Autoimmunity Reviews* 14(9): 798-805.
- Yan, Biao, Jin Yao, Jing Yu Liu, Xiu Miao Li, Xiao Qun Wang, Yu Jie Li, Zhi Fu Tao, Yu Chen Song, Qi Chen & Qin

Jiang. 2015. "LncRNA-MIAT Regulates Microvascular Dysfunction by Functioning as a Competing Endogenous RNA." *Circulation Research* 116(7): 1143-1156.

- Yang, Kai-Chien, Kathryn A Yamada, Akshar Y Patel, Veli K Topkara, Isaac George, Faisal H Cheema, Gregory A Ewald, Douglas L Mann & Jeanne M Nerbonne. 2014. "Deep RNA Sequencing Reveals Dynamic Regulation of Myocardial Noncoding RNAs in Failing Human Heart and Remodeling with Mechanical Circulatory Support." *Circulation* 129(9): 1009-1021.
- Zeng, Qinghai, Qi Wang, Xiang Chen, Kun Xia, Jintian Tang, Xiao Zhou & Yan Cheng et al. 2016. "Analysis of LncRNAs Expression in UVB-Induced Stress Responses of Melanocytes." *Journal of Dermatological Science* 81(1): 53-60.
- Zgheib, Carlos, Maggie M. Hodges, Junyi Hu, Kenneth W. Liechty & Junwang Xu. 2017. "Long Non-Coding RNA Lethe Regulates Hyperglycemia-Induced Reactive Oxygen Species Production in Macrophages." *PLoS ONE*. 12(5): e0177453.
- Zhang, Rui, Li Qiong Xia, Wen Wen Lu, Jing Zhang & Jin Shui Zhu. 2016. "LncRNAs and Cancer." Oncology Letters. 8(66): 110685-110692.
- Zhang, Yuan & Xuetao Cao. 2016. "Long Noncoding RNAs in Innate Immunity." *Cellular & Molecular Immunology* 13(2): 138-147.
- Zhao, Jing, Toshiro K. Ohsumi, Johnny T. Kung, Yuya Ogawa, Daniel J. Grau, Kavitha Sarma, Ji Joon Song, Robert E. Kingston, Mark Borowsky & Jeannie T. Lee. 2010.
 "Genome-Wide Identification of Polycomb-Associated RNAs by RIP-Seq." *Molecular Cell* 40(6): 939-953.
- Zhao, Wei, Joseph Mazar, Bongyong Lee, Junko Sawada, Jian Liang Li, John Shelley & Subramaniam Govindarajan, et al. 2016. "The Long Noncoding RNA SPRIGHTLY Regulates Cell Proliferation in Primary Human Melanocytes." *Journal* of Investigative Dermatology 136(4): 819-828.
- Zhu, Hongxue, Xuechao Li, Yarong Song, Peng Zhang, Yajun Xiao & Yifei Xing. 2015. "Long Non-Coding RNA ANRIL Is up-Regulated in Bladder Cancer and Regulates Bladder Cancer Cell Proliferation and Apoptosis through the Intrinsic Pathway." *Biochemical and Biophysical Research Communications* 467(2): 223-228.
- Zhu, Jin Gai, Ya Hui Shen, Hai Lang Liu, Ming Liu, Ya Qing Shen, Xiang Qing Kong, Gui Xian Song & Ling Mei Qian. 2014. "Long Noncoding RNAs Expression Profile of the Developing Mouse Heart." *Journal of Cellular Biochemistry* 115: 910-918.

- Zlatanou, A., S. Sabbioneda, E. S. Miller, A. Greenwalt, A. Aggathanggelou, M. M. Maurice & A. R. Lehmann et al. 2016. "USP7 Is Essential for Maintaining Rad18 Stability and DNA Damage Tolerance." *Oncogene* 35(8): 965-976.
- Zu, T., Y. Liu, M. Banez-Coronel, T. Reid, O. Pletnikova, J. Lewis & T. M. Miller et al. 2013. "RAN Proteins and RNA Foci from Antisense Transcripts in C9ORF72 ALS and Frontotemporal Dementia." *Proceedings of the National Academy of Sciences* 110(51): 4968-4977.
- Zuker, Michael. 2003. "Mfold Web Server for Nucleic Acid Folding and Hybridization Prediction." *Nucleic Acids Research* 31(13): 3406-3415.

Dito Anurogo

Faculty of Medicine University of Muhammadiyah Makassar Jl. Sultan Alauddin No. 259, Makassar 90221, Indonesia

Arli Aditya Parikesit Department of Bioinformatics School of Life Sciences, Indonesia International Institute for Life Sciences Jl. Pulomas Barat Kav 88. Jakarta Timur 13210, Indonesia

Taruna Ikrar

International School of Biomedical Sciences Pacific Health Sciences University 107 BakerField, California 93309 USA

Cellcure Center The Indonesia Army and Presidential Central Hospital (RSPAD Gatot Subroto), Jln. Abdul Rahman Saleh No. 24, Jakarta 10410, Indonesia

Corresponding author: Taruna Ikrar E-mail: taruna.ikrar@pacifichealthu.org

Tel: +62-21-3441008, +62-21-3840702 Ext 5005 Fax: +62-21-350619

Received: February 2017 Accepted for publication: February 2019

Bionanomedicine: A "Panacea" In Medicine?

Dito Anurogo^{1*}, Arli A Parikesit², Taruna Ikrar^{3,4,5*}

Faculty of Medicine, Universitas Gadjah Mada, Yogyakarta 55281, Indonesia
 Bioinformatics Program, Indonesia International Institute for Life Sciences, Jakarta 12710, Indonesia
 Biomedical Sciences, National Health University, Irvine, California 94111, USA
 Department of Neurology, Faculty of Medicine, Universitas Hasanuddin, Makassar 90245, Indonesia
 Ikrar Advanced Medicine Institute, Makassar 90142, Indonesia

*e-mail: tarunaikrar@med.unhas.ac.id

Abstract

Recent advances in nanotechnology, biotechnology, bioinformatics, and materials science have prompted novel developments in the field of nanomedicine. Enhancements in the theranostics, computational information, and management of diseases/disorders are desperately required. It may now be conceivable to accomplish checked improvements in both of these areas utilising nanomedicine. This scientific and concise review concentrates on the fundamentals and potential of nanomedicine, particularly nanoparticles and their advantages, nanoparticles for siRNA conveyance, nanopores, nanodots, nanotheragnostics, nanodrugs and targeting mechanisms, and aptamer nanomedicine. The combination of various scientific fields is quickening these improvements, and these interdisciplinary endeavours to have significant progressively outstretching influences on different fields of research. The capacities of nanomedicine are immense, and nanotechnology could give medicine a completely new standpoint.

Keywords: nanomedicine, nanotechnology, nanoparticles

Introduction

The first utilisation of the trademark frameworks in 'nanotechnology' (but preceding use of that name) was in "There's Plenty of Room at the Bottom," a speech given by physicist Richard Feynman at an American Physical Society meeting at Caltech on December 29, 1959.¹ Nanotechnology refers broadly to a field of applied science and technology whose unifying theme is the control of matter on the molecular level in scales smaller than 1 micrometer, normally 1 to 100 nanometers, and the fabrication of devices within that size range.² Nanomedicine is the design and development of theranostics tools diverged by the nanoscopic scale of its delivery vehicles and diagnostic agents.^{3,4} Briefly, Nanomedicine is an applied, practiced, and utilised nanotechnology in the field of medicine.⁵

Nanomedicine has provided some novel explanations and solutions. There are a lot of pharmaceutical companies endeavouring to advance targeted drug delivery using nanotechnology. Some of the existing drugs based on nanotechnology have the potential to revolutionise our understanding of human health and disorders. It also offers an assurance of a transformed portrait of better health care, health economics, and personalised medicine, with the eventual aim being an upgraded quality-of-life.⁶ Advances in the progression of lipid-based nanome

dicine, nanostructured drugs with effective site-targeting, nanopharmaceuticals, nano-imaging, nanoplat forms, nano-theranostics and nano-drug delivery, nano-immunochemo-therapy, and post-nano approaches [such as multistage vector (MSV) platform] will run and enhance the future development of nanomedicine, personalised medicine, and targeted therapy.^{7–10}

Nanoparticles. Nanoparticles (NPs) are particles, typically less than 200 nm in diameter, which usually comprise of lipids or polymers. NPs are capable of delivering drugs over epi-endothelial barriers and spatially limit through active-passive targeting.¹¹ Polyvalent ornament of an NP's surface with a ligand can assuage binding to a biomarker that is particularly overrepresented in targeted cells, and activate receptor-mediated endocytosis. It has extensive significance for targeted delivery. The ligands used to adjust NPs include antibodies, aptamers, engineered antibody fragments, peptides, proteins, and small molecules.^{12,13}

Some of the NPs are elucidated herein. Arginine–glycine– aspartate-grafted NPs can target avb3 integrin overexpressed by the tumour endothelium, and extravasate more conveniently. They invade the tumour through the retention effect and augment permeability.¹⁴ A nanomedicine contrived of pegylated chitosan NPs with conjugated anti-transferrin receptor antibodies are able to carry a blood–brain-barrier-impermeable caspase inhibitor to the brain.¹⁵ The arrangement of solid lipid NPs are laminated with the mucoadhesive polymer chitosan for intestinal absorption of insulin.¹⁶⁻¹⁸ Application of nanocrystalline solid dispersions, PEG-PLGA NPs, nanoparticle precipitates, particles, and liposomes can be applied for the management of pulmonary arterial hypertension.¹⁹⁻²⁰

Benefits of Nanoparticles. Benefits include the advancement of nanoparticles for screening and theranostics purposes, DNA sequencing applying nanopores, manufacture of drug delivery systems and single-virus detection, the significance and current advances in gene/drug delivery to cancer cells, the molecular imaging and diagnosis of cancer by targeted functional nanoparticles, the development and potential applications of nanoscale blueprints in medical management and diagnosis, the use of nanoparticles for stem cell tracking, differentiation, biosensing, transplantation, magnetic nanoparticle and quantum dotbased applications in tissue engineering and stem cells in humans, similar to nano-regenerative medicine.²¹

Nanoparticles for siRNA Delivery. Some requirements of nanoparticles to permit small interfering RNA (siRNA) consignment into the tumour include being very minuscule (size no bigger than 1000 nm), biocompatible, biodeg-radable, depletion of immuno stimulatory properties, and can avoid rapid hepatic/renal clearance. Some of them are lipid complex (cationic liposomes, lipoplexes, etc.), conjugated polymers (cholesterol, polymer-PEG, etc.), and cationic polymers (chitosan, atelocollagen, etc.).²²

Nanoparticles serve as conveyance vectors for siRNA and present plentiful benefits over stripped siRNA conveyance because of its capability to adjust siRNA while disseminating higher groupings of siRNA, specifically into tumour destinations. Furthermore, some of these nanoparticles can be changed with high fondness ligands to correctly target siRNA, specifically in the tumour. These nanoparticles can serve to advance controlled discharge, and when planned accurately they can give a protected and solid stage for siRNA conveyance for the management of cancer and other disorders.^{23, 24}

Nanopores. The stream of DNA via nanopores can be utilised to separate low duplicate quantities of DNA, allowing extremely fast genome sequencing. The primary exhibit of this guideline utilised a variety of round and hollow gold nanotubules with inward widths as little as 1.6 nanometres. Positive ions were rejected, and negative ions were transported through the membrane at the point when the tubules were charged positively. Interestingly, only positive ions went through when the film was adversely charged.²⁵ Recently, nanopore-based electrochemical and nucleic acids sensors can be used to detect nucleic acids selectively. It is a potentiometric

sensing blueprint from Nernst–Planck/Poisson perspective for nucleic acid hybridisation.²⁶

Nanodots. Fluorescent nanoparticles, for example, 'quantum dots',²⁷ PEBBLES (probes encapsulated by biologically localised embedding) and perfluorocarbon particles, possibly conquer these issues. 'Quantum dot' nanocrystals',²⁸ for the case, are made to a few nanometres in diameter with an almost boundless scope of pointedly characterised hues. The particles are edgy, utilising white light and can be connected to biomolecules to frame seemingly perpetual delicate probes. On a fundamental level, separate natural occasions can be checked, all the while labelling distinctive proteins or DNA sequences with nanodots of a particular colour. Nanodots are suitable platforms for advancement of photoluminescence-based sensing schemes.²⁹

Nanotheragnostic. Nanotheragnostic (theragnostic nanoparticles), or theragnostic nanomedicines, are incorporated nano particulate frameworks that analyse, convey a focus on treatment, and screen reactions to treatment.³⁰ Nanotheragnostic regimens are useful for management of cancer, inflammatory liver disease,³¹ cardiovascular diseases (i.e. atherosclerosis, thrombosis), and have a promising application in arthritis (e.g. rheumatoid arthritis), neurodegenerative diseases, age-related macular degeneration, psoriasis, atherosclerosis, and various bloodstream bacterial infections.^{32,33}

The four fundamental components that ought to be satisfied in the structure of nanotheragnostics are the biodegradable nanocarrier material (based on hybrid materials, an inorganic component, and an organic matrix), the signal emitter or imaging agent (exclusive optical, magnetic, or radioactive hallmark), the medication or remedial molecule, and changes to the later component based on passive-active delivery strategies.^{34, 35} Magnificently, theragnostic nanotools would result in a multimodality imaging procedure mixed with a multi-drug nanocarrier, in addition to supplementary treatment techniques (i.e. photodynamic treatment, hyperthermia, and photothermal treatment). Nanotheragnostics and image-guided drug delivery are relied upon to empower "precise and personalised" medicine.^{35,36}

Nanodrugs and Targeting Mechanisms. Nanodrugs in destructive tissues has uptake and aggregation. The two can happen through two systems, i.e. "uninvolved focusing on" and "dynamic focusing on". Aloof focusing on depends on both the size of the medication bearers and the cracked neovasculature of the tumour. Inactive aggregation at the tumour site is anticipated to occur through Enhanced Permeability and Retention (EPR) effect. With the more drawn out blood course time accomplished by stealth alteration (e.g. PEGyla tion), expanded gathering of NPs is conceivable through the EPR effect. EPR happens because of the expanded

vessel defectiveness and debilitated lymphatic function typically observed in tumour tissue; this allows nano-materials to enter and amass there.^{21,37,38}

Dynamic focusing of nanomaterials is being inves tigated as a strategy to allow spatial localisation by purposefully homing NPs to actively diseased regions while obliterating off-target adverse effects in healthy tissue. It is achieved by functionalization of their surface with bioactive molecules, using engineered antibodies, transferrin, folic acid, and enzymes which perceive and interplay with cancer-specific targets overexpressed on the surface of cancerous cells.³⁹

The recent bioactive molecule, QD242-encapsulated polymeric nanoparticles (NPs) functionalised with a peptide (Cys-Plec-1 targeted peptides or cys-PTP), carefully fastened to Plectin-1 (Plec-1). Plec-1 is a Biomarker of Pancreatic ductal adenocarcinoma (PDAC).⁴⁰ Active targeting to accomplish efficacious nanome dicine congeries in tumour tissue is confutable, as some experts strive to construct original and creative approaches for active tumour targeting.^{21,31} The most commonly used targeting moieties are mono-clonal antibodies or antigen binding fragments, antibody fragments, and single chain variable fragments for active targeting. The latter being favoured because of its decreased immunogenicity and high target specificity.^{21,31}

Aptamer Nanomedicine. Aptamer nanomedicine is a rising, and propitious class of therapeutics used to locate the difficulties faced by recent cancer treatments. It might address restrictiveness of different ligands for targeted treatment in oncology and profoundly perfect with combined medication treatment. Nevertheless, the strategy would require a better comprehension of drug-loading efficiency, drug-releasing mechanisms, and carrier design.^{41,42}

Micro-RNA (miRNA), small hairpin RNA (shRNA), small interfering RNA (siRNA), and antisense oligonucleotides are engineered for knocking down a specific gene (deleting a gene function) to murder definite types of cells. Conversely, plasmid DNA or mRNA are used for transfection to deliver a certain gene (enumerating a gene function) to heal a disease. Up to now, most research focuses on the development of aptamermediated miRNA, shRNA, or siRNA delivery systems for gene silencing applications. This is an emerging class of gene therapy that is particularly reassuring for cancer treatment.^{41,42}

The antinucleolin aptamer, AS1411, coupled to this liposomal design, for breast cancer cell targeting, executed cancer cells with high specificity. This aptamer-doxorubicin liposome formulation hindered breast tumour growth prompted by oestrogen, as no significant or important growth of the tumour was detected in the

group treated with the aptamer-doxorubicin liposome, while the size of the tumour in the control group raised 166%.^{21,43,44} Another example is 5-fluorouracil (5-FU) combined with AS1411 aptamer (NP-5-FU-APTAS1411), which can be used to effectively manage gastric cancer.⁴⁵

Related to drug delivery, the most effortless strategy for aptamer-based nucleic acid delivery is to connect the therapeutic nucleic acid directly to the aptamer. This is famous as an aptamer-therapeutic nucleic acid chimaera. The experts have created functional DNA nano structures to convey the chemotherapy medication to resistant cancer cells. These nanostructures comprise of two components, a DNA aptamer and a double-stranded DNA (dsDNA). Recently, nucleic acid–based nano devices have prompted energising molecular biotech nologies to the top of the line biological imaging.^{42, 46, 47}

The chimaeras Chi-29b and GL21.T-let are supple mentary examples of direct conjugation of the aptamer to a therapeutic nucleic acid. Chi-29b consists of an antimucin 1 (MUC1) aptamer and miRNA miR-29b for ovarian cancer treatment.^{21,42,48} It becomes illuminating that the critical steps for clinical translation of nanotherapeutics need further inter national and interdisciplinary efforts, where the entire stakeholder community is involved from bench to bedside. The period of nanomedicine is ready to develop and mature in the following couple of decades; integrating elements of personalised and precision medicine. It will influence the therapeutic world in an effective and everlasting way.

Transcriptomics Tools for Nanomedicine. The design of nanobiomedicine-based drugs could only be feasible with the certain incorporation of solid assistant tools.⁴⁹ Bioinformatics, as the interdisciplinary field of biology and computer science, is playing a cardinal role in designing nanobiomedicine-based drugs.50,51 Due to the rising importance of the transcriptomics approach, bioinformatics is adjusted to cope with this development as well.⁵² The Vienna RNA Package is one of the tools that could be utilised to design siRNA.⁵³ The theoretical basis for siRNA design is a solid comprehension of chemical kinetics and thermodynamics, especially the modelling of transition states between compounds.54 The Vienna RNA Package also provides tools for secondary structure prediction, multiple sequence alignments, and others. However, the rising importance of transcriptomics is still strongly correlated with the recent advances in proteomics. The important role of Transcription factor proteins, such as Dicer and Argonout, for regulating non-coding (NC)RNA is still considered by the scientific community as important.⁵⁵ Comprehension of Protein Domain annotation would eventually shed light to the narration of the transcriptomics mechanistic insights.⁵⁶ Thus, the dynamism of nucleic acids has already been unveiled with the DNA-biped nanomodeling.⁵⁷ These theoretical bases are important as the cornerstone for nanobiomedicine-based drug development.

The application of transcriptomics-based bioinformatics in drug design is already in sight. Pharmaceutical research has provided the clinical application for cancer, HIV/ AIDS, hepatitis, and others.⁵⁸ However, due to the incomplete understanding of nano-based modelling of drug-target interaction, only a handful of products are available on the market.⁵⁸ The different nature of molecules in nano-scale size should be considered when constructing a solid computational model. Thus, a new field that incorporates bioinformatics and nanomedicine has already born. Nanoinformatics is the intersection between bioinformatics and nanobiotechnology.⁵⁹ The advancements in nanomaterials have made it possible to scale them into the realm of nanobiomedicine.⁶⁰ However, real applications of nanoinformatics remain to be seen. These nano-based computations need strong computational power as provided in the computer clusters and supercomputers.⁶¹

Proteomics-based Computation for nanobiome dicinebased Drug Design. The growing field of transcriptomics still needs advancement in proteomics. Most of the drugs in the market still target protein receptors and enzymes for knock-down of the disease. Three important methods for the computation of drug design, namely Molecular Docking, Molecular Dynamics, and ADMET are constructing their models based upon protein-ligand interactions.⁶²⁻⁶⁴ Molecular docking method has successfully simplified the labourous High Throughput Screening (HTS) process that is necessary to identify the most feasible lead compound. Meanwhile, molecular dynamics has given vivid illustrations towards the mechanistic insights of molecular interactions. ADMET computation has simplified the research of drug metabolism as well. The commonly used drug types are natural products, semi-synthetic, and synthetic molecules.^{65,66} Some groundbreaking drug candidates are peptide and nucleotidebased molecules.^{67,68} The comprehension of the molecular mechanism on a sub-atomic level with those methods will always be an important contribution to the advancement of modern drug design.

Future of Bionanomedicine: Intersection of Big Data and Automatisation of Laboratory protocols. On one side, the growing data and tools of sophistication of GenBank will enable researchers to compute the best information to the scientific community. On the other side, increasing automatisation of laboratory protocols will release the researcher from the laborious hours of bench work. In the end, the researcher could be more focused on the novelty of their idea, and less on the laborious techniques. Nanobiomedicine is the interface between basic science and applied science, and also between computational and wet laboratory methods. This multidisciplinary effort could be a major trend in the scientific community.

Acknowledgement

Special thanks to Mr Vicente Rey-Valenzuela, PhD. Plant Pathologist at Cenibanano - Augura, Colombia, for his help in getting relevant journals and references.

Conflicts of Interest Statement

The Authors declare that there is no conflict of interest regarding the publication of this paper.

References

- Feynman R. There is plenty of room at the bottom: an invitation to enter a new field of physics. Reprinted in: Crandall BC, Lewis J (eds) Nanotech nology: Research And Perspectives., Cambridge, MA: The MIT Press; 1992. p.347-363.
- Sanna V, Pala N, Sechi M. Targeted therapy using nanotechnology: focus on cancer. *Int J Nanomed.* 2014;9:467-83.
- Kunjachan S, Ehling J, Storm G, Kiessling F, Lam mers T. Noninvasive Imaging of Nanomedicines and Nanotheranostics: Principles, Progress, and Prospects. *Chem Rev.* 2015;115:10907-37
- 4. Jagtap P, Sritharan V, Gupta S. Nanotheranostic ap proaches for management of bloodstream bacterial infections. *Nanomedicine*. 2017;13:329-41.
- 5. Dai Z (Ed.). 2016. Advances in Nanotheranostics II: *Cancer Theranostic Nanomedicine*. Singapore: Springer.
- Schwartz S. Unmet needs in developing nano particles for precision medicine. *Nanomedicine*. 2017;12:271-4
- Carmen C, Valentina G, Mariana CC, Keng-Shiang H, Florin I, Yu-Mei L, *et al.* Nanostructured Approaches for the Targeted Delivery of Antibiotics in Difficult Infections. *Curr Org Chem.* 2017;21:45-52.
- Hoop M, Mushtaq F, Hurter C, Chen XZ, Nelson BJ, Pané S. A smart multifunctional drug delivery nano platform for targeting cancer cells. *Nanoscale*. 2016;8:12723-8.
- Kateb B, Chiu K, Black KL, Yamamoto V, Khalsa B, Ljubimova JY, *et al.* Nanoplatforms for constructing new approaches to cancer treatment, imaging, and drug delivery: what should be the policy? *Neuroimage*. 2011;54 Suppl 1:S106-24.
- Venuta A, Wolfram J, Shen H, Ferrari M. Post-nano strategies for drug delivery: multistage porous silicon microvectors. J Mater Chem B. 2017;5:207-19.
- 11. Da Róz AL, Ferreira M, de Lima Leite F, Oliveira ON. 2017. Nanostructures. Cambridge, MA: Elsevier.
- 12. Moradi-Kalbolandi S, Habibi-Anbouhi M, Golkar M, Behdani M, Rezaei G, Ghazizadeh L, *et al.* Development of a novel engineered antibody targeting human CD123. *Anal Biochem.* 2016;511:27-30.
- Chen Y, Xianyu Y, Jiang X. Surface Modification of Gold Nanoparticles with Small Molecules for Biochemical Analysis. Acc Chem Res. 2017;50:310-9
- Schaufler V, Czichos-Medda H, Hirschfeld-Warnecken V, Neubauer S, Rechenmacher F, Medda R, *et al.* Selective binding and lateral clustering of α5β1 and αvβ3 integrins:

Unravelling the spatial requirements for cell spreading and focal adhesion assembly. *Cell Adhes Migration*. 2016.

- 15. Liu G, Li K, Luo Q, Wang H, Zhang Z. PEGylated chitosan protected silver nanoparticles as water-borne coating for leather with antibacterial property. *J Colloid Interface Sci.* 2017;490:642-51.
- 16. Sandri G, Motta S, Bonferoni MC, Brocca P, Rossi S, Ferrari F, et al. Chitosan-coupled solid lipid nanoparticles: Tuning nanostructure and muco adhesion. European J of Pharmaceut Biopharm. 2017;110:13-8.
- Shitrit Y, Bianco-Peled H. Acrylated chitosan for mucoadhesive drug delivery systems. *Int J Pharm.* 2017;517:247-55.
- Wang J, Kong M, Zhou Z, Yan D, Yu X, Cheng X, *et al.* Mechanism of surface charge triggered intestinal epithelial tight junction opening upon chitosan nanoparticles for insulin oral delivery. *Carbohydr Polym.* 2017;157:596-602.
- Shete G, Modi SR, Bansal AK. Effect of Mannitol on Nucleation and Crystal Growth of Amorphous Flavonoids: Implications on the Formation of Nanocrystalline Solid Dispersion. *J Pharm Sci.* 2015;104:3789-97.
- 20. Xiao H, Fei-Fei Y, Xiao-Lan W, Guang-Yin Y, Chun-Yu L, Ying Z, et al. Curcumin Acetate Nanocrystals for Sustained Pulmonary Delivery: Preparation, Characterization and In Vivo Evaluation. J Biomed Nanotechnol. 2017;13:99-109.
- 21. Igarashi E. 2015. Nanomedicines and Nanopro ducts: Applications, Disposition, and Toxicology in the Human Body. CRC Press. Taylor & Francis Group. USA.
- 22. Wan Y, Moyle PM, Gn PZ, Toth I. Design and evaluation of a stearylated multi component peptide-siRNA nanocomplex for efficient cellular siRNA delivery. *Nanomedicine*. 2017;12:281-93.
- 23. Corbet C, Ragelle H, Pourcelle V, Vanvarenberg K, Marchand-Brynaert J, Préat V, *et al.* Delivery of siRNA targeting tumor metabolism using non-covalent PEGylated chitosan nanoparticles: Identifi cation of an optimal combination of ligand structure, linker and grafting method. *J Control Release.* 2016;223:53-63.
- 24. Yan Y, Zhou K, Xiong H, Miller JB, Motea EA, Boothman DA, et al. Aerosol delivery of stabilized polyester-siRNA nanoparticles to silence gene expression in orthotopic lung tumors. *Biomaterials*. 2017;118:84-93.
- 25. Edel JB, Albrecht T. 2013. Engineered Nanopores for Bioanalytical Applications. Waltham, MA: Elsevier.
- Makra I, Brajnovits A, Jágerszki G, Fürjes P, Gyurcsányi R. Potentiometric sensing of nucleic acids using chemically modified nanopores. *Nanoscale*. 2017;9:739-47.
- 27. Prando G. Qubits in a row. Nature Nanotechnology. *Phys Rev Appl.* 2016;6:054013.
- Credi A (Ed.). 2017. Photoactive Semiconductor Nanocrystal Quantum Dots: *Fundamentals and Applications*. Springer. Switzerland. ISBN 978-3-319-51192-4.
- 29. Rodrigues SSM, Riberio DSM, Soares JX, Passos MLC, Saraiva MLMFS, Santos JLM. Application of nanocrystalline CdTe quantum dots in chemical analysis: Implementation of chemo-sensing schemes based on analyte-triggered photoluminescence modulation. *Coord Chem Rev.* 2017;330:127-43.
- Devasena T. Diagnostic and Therapeutic Nanomaterials. In: *Therapeutic and Diagnostic Nanomaterials*. Singapore: Springer; 2017. p. 1-13.
- 31. Bartneck M, Tacke F. Targeted Modulation of Macrophage Functionality by Nanotheranostics in Inflammatory Liver Disease and Cancer. In: *The Immune Response to*

Implanted Materials and Devices. Switzerland: Springer International Publishing.

- 32. Evangelopoulos M, Tasciotti E. Bioinspired approaches for cancer nanothera nostics. *Nanomedicine*. 2017;12:5-7.
- Jagtap P, Sritharan V, Gupta S. Nanotheranostic approaches for management of bloodstream bacterial infections. Nanomedicine: Nanotechnology. *Bio Med.* 2017;13:329-41.
- 34. Arias JL. Drug Targeting by Magnetically Respon sive Colloids. New York: Nova Science Publishers Inc; 2010.
- Jabr-Milane LS, LE van Vlerken, S Yadav, MM Amiji. Multifunctional nanocarriers to overcome tumor drug resistance. *Cancer Treat Rev.* 2008;34:592-602.
- Fang C, M Zhang. Nanoparticle-based theragnostics: Integrating diagnostic and thera peutic potentials in nanomedicine. *J Control Release*. 2010;146:2-5.
- Shi J, Kantoff PW, Wooster R, Farokhzad OC. Cancer nanomedicine: progress, challenges and opportunities. *Nat Rev Cancer*. 2017;17:20-37.
- Nakamura Y, Mochida A, Choyke PL, Kobayashi H.. Nanodrug Delivery: Is the Enhanced Permeability and Retention Effect Sufficient for Curing Cancer? *Bioconjugate Chem.* 2016;27:2225-38.
- Xu X, Ho W, Zhang X, Bertrand N, Farokhzad O. Cancer nanomedicine: from targeted delivery to combination therapy. *Trends Mol Med.* 2015;21:223-32.
- 40. Sanna V, Nurra S, Pala N, Marceddu S, Pathania D, Neamati N, *et al.* Targeted Nanoparticles for the Delivery of Novel Bioactive Molecules to Pancreatic Cancer Cells. *J Med Chem.* 2016;59:5209-20.
- 41. Godsey ME, Suryaprakash S, Leong KW. Materials Innovation for Co-delivery of Diverse Therapeutic Cargos. *RSC Adv.* 2013;3:24794-811.
- 42. Lao YH, Phua KKL, Leong KW. Aptamer Nanomedicine for Cancer Therapeutics: Barriers and Potential for Translation. ACS Nano. 2015;9:2235-54.
- Karagkiozaki V, Logothetidis S (Eds). Horizons in Clinical Nanomedicine. 2014. USA: CRC Press. Taylor & Francis Group; 2015. p. 2235-54.
- 44. Charoenphol P, Bermudez H. Aptamer-Targeted DNA Nanostructures for Thera peutic Delivery. *Mol Pharmaceut*. 2014;11:1721-5.
- 45. Behrooz AB, Nabavizadeh F, Adiban J, Ardestani MS, Vahabpour R, Aghasadeghi MR, *et al.* Smart bomb AS1411 aptamer-functionalized/PAMAM dendrimer nanocarriers for targeted drug delivery in the treatment of gastric cancer. *Clin Exp Pharmacol Physiol.* 2017;44:41-51.
- 46. Liu J, Wei T, Zhao J, Huang Y, Deng H, Kumar A, *et al.* Multifunctional aptamer-based nanoparticles for targeted drug delivery to circumvent cancer resistance. *Biomaterials*. 2016;91:44-56.
- Chakraborty K, Veetil AT, Jaffrey SR, Krishnan Y. Nucleic Acid–Based Nanodevices in Biological Imaging. *Annu Rev Biochem.* 2016;85:349-73.
- 48. Muluhngwi P, Richardson K, Napier J, Rouchka EC, Mott JL, Klinge CM. Regulation of miR-29b-1/a transcription and identification of target mRNAs in CHO-K1 cells. *Mol Cell Endocrinol*. 2017;444:38-47.
- 49. Yu M, Wu J, Shi J, Farokhzad OC. Nanotechnology for protein delivery: Overview and perspec tives. J Control Release. 2016;240:24-37.
- 50. D'Mello SR, Das SK, Das NG. Polymeric nanoparticles for small-molecule drugs. in Y. Pathak and D. Thassu, (Eds.) *Drug Delivery Nanoparticles Formulation and Characterization.* New York: Informa Healthcare; 2009. p. 16-34.

- 51. Schönbach C, Nakai K, Tan TW, Ranganathan S. 2010;11. InCoB2010-9th International Conference on Bioinformatics at Tokyo, Japan, September 26-28, 2010. BMC Bioinformatics. Suppl 7 (SUPPL. 7):S1.
- 52. Dong Z, Chen Y. Transcrip tomics: advances and approaches. *Sci China Life Sci.* 2013;56:960-7.
- 53. Gruber AR, Bernhart SH, Lorenz R. The viennaRNA web services. In: RNA *Bioinformatics*. 2015:307-26.
- 54. Hofacker IL, Stadler PF. Memory efficient folding algorithms for circular RNA secondary structures. *Bioinformatics.* 2006;22:1172-6.
- 55. Parikesit AA, Steiner L, Stadler PF, Prohaska SJ. Pitfalls of Ascertainment Biases in Genome Annotations— Computing Comparable Protein Domain Distributions in Eukarya. *Malaysian J Fundam Appl Sci.* 2014;10:65-75.
- Parikesit AA, Stadler PF, Prohaska SJ. Evolution and Quantitative Compa rison of Genome-Wide Protein Domain Distributions. *Genes (Basel)*. 2011;2:912-24.
- Ben-Ari I, Boushaba K, Matzavinos A, Roitershtein A. Stochastic Analysis of the Motion of DNA Nanomechanical Bipeds. *Bull Math Biol.* 2011;73:1932-51.
- 58. Burnett JC, Rossi JJ. RNA-based therapeutics: current progress and future prospects. *Chem Biol*. 2012;19:60-71.
- 59. González-Nilo F, Pérez-Acle T, Guínez-Molinos S, Geraldo DA, Sandoval C, Yévenes A, *et al.* Nanoinformatics: an emerging area of infor mation technology at the intersection of bioinfor matics, computational chemistry and nanobio technology. *Biol Res.* 2011;44:43-51.
- 60. Maojo V, Fritts M, Martin-Sanchez F, De la Iglesia D, Cachau RE, Garcia-Remesal M, *et al.* Nanoinformatics:

developing new computing applications for nanomedicine. *Computing*. 2012;94:521-39.

- 61. Akbar Z, Handoko LT. GRID architecture through a public cluster. In: 2008 International Conference on Computer and Communication Engineering. *IEEE*. 2008:1016-8.
- Kitchen DB, Decornez H, Furr JR, Bajorath J. Docking and scoring in virtual screening for drug discovery: methods and applications. *Nat Rev Drug Discov*. 2004;3:935-49.
- Karplus M. Molecular dynamics of biological macromolecules: a brief history and perspective. *Biopolymers*. 2003;68:350-8.
- 64. van de Waterbeemd H, Gifford E. ADMET in silico modelling: towards prediction paradise? *Nat Rev Drug Discov*. 2003;2:192-204.
- 65. Parikesit AA, Ardiansah B, Handayani DM, Tambunan USF, Kerami D. Virtual screening of Indonesian flavonoid as neuraminidase inhibitor of influenza a subtype H5N1. *IOP Conf Ser Mater Sci Eng.* 2016;107:012053.
- 66. Kampmann T, Yennamalli R, Campbell P, *et al.* In silico screening of small molecule libraries using the dengue virus envelope E protein has identified compounds with antiviral activity against multiple flaviviruses. *Antiviral Res.* 2009;84:234-41.
- 67. Soltero R. Oral Protein and Peptide Drug Delivery. In: Wang B, Siahaan TJ, Soltero R, eds. *Drug Delivery: Principles and Application*. John Wiley & Sons, Inc; 2005. p.189-200.
- 68. Julander JG, Bantia S, Taubenheim BR, *et al.* BCX4430, a novel nucleo side analog, effectively treats yellow fever in a Hamster model. *Antimicrob Agents Ch.* 2014;58:6607-14.



The Neuropharmacogenomical Perspectives of Bipolar Disorders

Dito Anurogo

¹S2 Biomedical Sciences, Faculty of Medicine, Universitas Gadjah Mada (FK UGM), Yogyakarta, Indonesia ²Indonesian Literacy Fellowship (ILF), UKM Jurnal Paradigma, FAM, IYHPS, HIMMPAS, ILC, HMP ³Health consultant in detik.com

ABSTRACT

Bipolar disorder (BD), also known as manic-depressive illness, is a brain disorder causing unusual shifts in mood, energy, activity levels, and the ability to carry out daily tasks, caused by multifactorial and enigmatic etiologies. The main objective of this overview is to review recent findings and critically evaluate BD based on neurogenomics and pharmacogenomics perspectives, through searching appropriate online database sources and relevant bibliographies. Recent studies and references explain genome-wide significant loci for bipolar disorder (polygenetics), potential biomarkers (apoptosis and neurotrophic factors, immuno-inflammatory factors, neurotrophins, BDNF, IGF-1, VEGF, etc.), dysregulation of immuno-inflammatory mechanisms, the role of neuroplasticity in the pathophysiology and treatment of BD, genetic effect of lithium response in BD. Stem cells, omics technologies, and optogenetics is considered to be effective strategies to overcome BD.

Keywords: Biomarkers, bipolar disorder (BD), neurogenomics, neuropharmacogenomics, neuroplasticity, optogenetics, pharmacogenomics.

ABSTRAK

Bipolar disorder (BD), dikenal pula sebagai *manic-depressive illness*, adalah gangguan otak dengan etiologi enigmatik dan multifaktorial yang menyebabkan perubahan *mood*, energi, tingkat aktivitas, serta kemampuan untuk melakukan tugas sehari-hari. *Review* ini menelusuri penemuan-penelitian terkini dan mengevaluasi BD secara kritis berdasarkan perspektif *neurogenomics* dan *pharmacogenomics*, melalui pencarian database *online* dan bibliografi yang relevan. Pelbagai riset-referensi termutakhir menjelaskan *genome-wide significant loci* (poligenetik), *biomarker* potensial (faktor apoptosis dan neurotrofik, faktor imun-inflamasi, neurotrofin, BDNF, IGF-1, VEGF, dll), disregulasi mekanisme imunoinflamatori, peran neuroplastisitas, efek genetik respon lithium pada BD. Teknologi sel punca, teknologi berbasis *–omics*, dan *optogenetics* yang mengungkap aspek-aspek neurofarmakogenomik berdasarkan riset berkesinambungan dipertimbangkan menjadi strategi efektif untuk mengatasi BD. **Dito Anurogo. Perspektif Neurofarmakogenomik Kelainan Bipolar.**

Kata kunci: Biomarkers, bipolar disorder (BD), neurogenomics, neuropharmacogenomics, neuroplasticity, optogenetics, pharmacogenomics.

INTRODUCTION

Bipolar Disorder (BD) is a complex neuropsychiatric disorder affecting 1-4% of the population worldwide, with a lifetime prevalence of 2.8 to 6.5% and a genetic diversity (heritability) of 59-93%. It is characterized by a cycle of recurrent depressive episodes, manic-hypomanic episodes, and interspersed with intervals of remission.1,2,3 Lithium (Li) is the mainstay in BD management. Even so, only about 30% BD patients indicate a good response in long-term cohort studies.4 Multifactorial causes and uncertainty in research findings have made BD unable to be resolved until now.

OBJECTIVE AND METHODS

The main objective of this scientific review

Alamat Korespondensi email: dito.anurogo@ugm.ac.id

was to find out various researches and new approaches in the management of BD, based on neurogenomics and pharmacogenomics perspectives. Literature for this overview was identified by searching database sources (PubMed, Medline, PsycINFO, Web of Knowledge Content, Medscape, etc.), Cochrane Libraries, and recent bibliographies.

Pharmacogenomics Perspective

Pharmacogenomic approach focuses on identifying genetic predictors of treatment response to Li and mood stabilizers. Candidategene approaches have so far focused on genes codifying for elements of biological pathways shown to be target of lithium, such as proteins of the intracellular second messenger cascade mediated by inositol, Wnt and neurotrophins pathways and the GSK-3 β protein.5,6

Li response in BD can be determined using GRANITE (Genetic Regulatory Analysis of Networks Investigational Tool Environment), a genomic tool that provides visualization of complex data sets and produces interactive networks. By measuring a large data set of mRNAs and miRNAs, the tools finds that the Let-7 miRNA family is consistently and preferentially downregulated by Li in the BD responder group. The dynamic networks created by GRANITE will lead to a more effective and reliable tool for clinical use in predicting BD patients' response to medications.⁷

TINJAUAN PUSTAKA

Neurogenomics Perspective

Neurogenomics is the study of the genes of the nervous system. In a broad scope, neurogenomics is defined as the study of how the genome serves as a whole, which contributes to the evolution, development, structure, and function of the nervous system. Neurogenomics has applications in basic research, in pharmaceutical industry and in the management of neurological disorders.8

Brain abnormalities found in BD patients include enlargement of the lateral ventricles and abnormal white substance, particularly in prefrontal cortex. Structural imaging studies have also found volume deficits in the hippocampus in child and adolescent BD patients and larger volumes of amygdala in adults. N-acetylaspartate level as a marker of neuronal integrity decreased in the dorsolateral prefrontal cortex, anterior cingulate, and hippocampus in BD patients.^{9,10}

Preliminary studies of PET (positron emission tomography) reported a reduction in 5-hydroxytryptamine (5-HT1A) receptor binding potential in raphe and hippocampusamygdala in the depressives, especially in bipolar depressives and unipolar depressives with bipolar relatives. One of the factors that contribute to the reduction of 5-HT1A receptor binding in depression is the increased cortisol secretion, since the expression of postsynaptic 5-HT1A receptor mRNA is under tonic inhibition by corticosteroid receptor stimulation in several brain regions.¹¹

Recent GWAS (genome-wide association studies) on BD populations have identified a number of genes with strong statistical association to susceptibility to BD. One of them is ankyrin 3 (ANK3), a gene that encodes multiple isoforms of ankyrin G protein, and alpha 1C subunit of L-type voltage-gated calcium channel (CACNA1C). XBP1 genes also play a role in the pathogenesis of BD.¹²⁻¹⁴GWAS have identified new genome-wide significant risk loci in the chromosome 4 gene (NDST3). The examination of SNP, rs11098403, showed a consistent effect regardless of diagnosis (schizophrenia or BD).^{15,16} To determine the genome-wide significant loci, then please refer to table.17

Table. The genome-wide significant loci in BD.16

Locus	Implicated Gene(s) and Symbol(s)	
Genome-wide significant in bipolar disorder		
10q21.2	Ankyrin 3 (ANK3)	
12p13.3	Calcium channel, voltage-dependent, L-type, alpha 1C subunit (CACNA1C)	
11q14.1	Teneurin transmembrane protein 4 (TENM4, formerly known as ODZ4)	
19p12	Neurocan (NCAN)	
6q25.2	Spectrin repeat containing, nuclear envelope 1 (SYNE1)	
3p22.2	Tetratricopeptide repeat and ankyrin repeat containing 1 (TRANK1)	
5p15.31	Adenylate cyclase 2 (ADCY2)	
6q16.1	MicroRNA 2113 (MIR2113); POU class 3 homeobox 2 (POU3F2; formerly known as OTF 7)	
10q24.33	Arsenite methyltransferase (AS3MT)	
Genome-wide significant in bipolar disorder + schizophrenia (combined)		
2q32.1	Zinc finger protein 804A (ZNF804A)	
3p21.1	Inter-alpha-trypsin inhibitor heavy chain 3 (ITIH3); Inter-alpha-trypsin inhibitor heavy chain 4 (ITIH4);	
16p11.2	Mitogen-activated protein kinase 3 (MAPK3)	
Genome-wide significant in bipolar disorder + unipolar depression (combined)		

Calcium Signaling Abnormalities

Ca⁺ channel signaling genes have a role in BD. Ca⁺ channel controls the movement of calcium between cells. There are certain genetic changes that increase the flow of Ca leading to the brain, thus producing excitement.¹⁸ Calcium ions serve an important role in regulating the synthesis and the release of neurotransmitters, neuronal excitability, and long-term neuroplasticity. Numerous studies have successfully demonstrated the presence of intracellular Ca²⁺ in peripheral cells of BD patients.¹⁹

Inflammatory Hypothesis

studies Numerous have confirmed dysregulation of immuno-inflammatory mechanism in BD. Autoimmune thyroiditis was often found to be associated with BD.²⁰ The role of praecox stressors has been postulated to explain the dysfunction of brain prefrontal-subcortical region in BD.²¹ Neurodevelopmental model of BD has revealed that immune system changes due to multifactorial causes, such as decreased vitamin D, hypoferremia and iron deficiency, contribute to brain development abnormalities.22

The relationship between M2 receptor,



inflammation, and cognition can lead to an understanding that a change in inflammatory pathways may cause cognitive deficits associated with BD.²³

Biomarker Panel

In BD patients, biomarker panel is found to be unique and distinctive such as the presence of endothelial inflammation. In the first year of BD, the oxidant status rises. In patients with chronic BD, the potentiated antioxidant system also increases.24

Abnormalities in neurotrophins and other trophic factors have important implications in the etiology of BD. The role of neurotrophins is important to be understood as the basis for the development of new therapies.^{25,26} Recent studies also reveal that the involvement of brain-derived neurotrophic factor (BDNF), insulin-like growth factor (IGF-1), vascular endothelial growth factor (VEGF), etc. shows typical patterns in various different stages of BD. In the manic episode of BD, the serum levels of fibroblast growth factor-2 (FGF-2), NGF and IGF-1 are found to be increased, while in the mixed episode of BD, the plasma levels of BDNF are found to be decreased. BDNF serum potentially serves as a BD biomarker. BDNF-encoding genes are located on the short arm of chromosome 11 in the region where some BD linkage studies have found evidence of gene susceptibility. This clearly indicates the potential of various biomarkers for identifying BD subgroups and developing effective management.²⁷⁻³⁰

Inositol hexaphosphate (IP6, inositol hexakisphosphate, phytic acid) is a naturallyoccuring derivative of phosphorylated myoinositol. Myo-inositol has been proven to be able to control mood symptoms and have a good tolerability for BD. The efficacy and tolerability of IP6 as adjunctive lithium therapy is being studied.^{31,32}

The Roles of Cytokines

The dysregulation of cytokines also serves as one of the neurodegenerative aspects, especially in patients with long-term BD.³³ BD is closely related to genetic polymorphisms of cytokines.³⁴ Cytokine level varies according to clinical symptoms. The presence of elevated level of interleukin 6 (IL-6) is a result of the activation of monocytes. Interestingly, the IL-6 alleles have different distributions among





adults with BD, control, and offspring (with and without mood disorders).35 IL-1, one of cytokines, and its receptors are an example of immunological marker whose levels significantly increase in BD. IL-1 is found in postmortem frontal cortex.³⁶Cytokines can act as a mediator between immune abnormalities and central nervous system development.³⁷ In fact, cytokines play a significant role in all stages of neurodevelopment process. Cytokines managed to become a "bridge" between altered immune system, neurotransmission dysfunction, and impaired neurodevelopment. All these aspects contribute to the onset of BD.³⁸

The levels of monocytes and monocyte chemoattractant protein 1 (MCP-1) are also increased. MCP-1 is a cytokine that plays a role in innate immunity process, also known as CCL2. The increased level of serum CCL2 supports the hypothesis of Th1 hyperactivation.⁴⁹ In manic phase, the level of CCL11 rises. Moreover, the level of cortisol in patients with bipolar depression is found to be elevated. Decrease in PUFA (polyunsaturated fatty acids) in brain membranes is a result of hyperactivation of arachidonic acid cascade. The level of plasma cortisol decreases in mania.^{39,40}

Neuroplasticity

The manifestation of neuroplasticity in mature central nervous system is characterized by changes in the function of dendrites, synaptic remodeling, long-term potentiation (LTP), axonal sprouting, neurite extension, synaptogenesis and neurogenesis.41,42 The sustainability of neuroplasticity is determined by multifactorial causes. Protein Kinase C (PKC) plays an important role in the regulation of synaptic plasticity and various forms of learning and memory. GSK-3 plays an important role in regulating neuroplasticity and cellular resilience. The effects of Lithium and VPA on GSK-3 have an important role in the regulation of various processes, such as synaptic plasticity, cell survival in the mature central nervous system (mature CNS). BDNF serves as a mediator of various neuroplastic changes during mood episode.

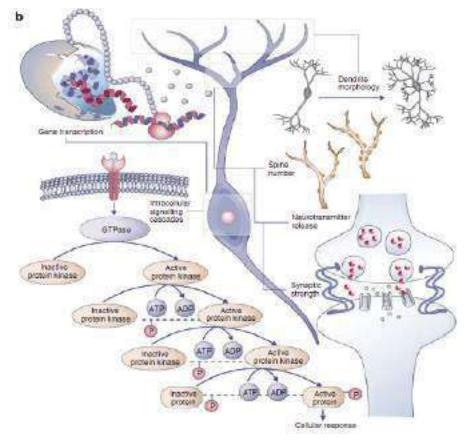


Figure. Biological mechanisms underlying neuroplasticity.45

Glia function abnormalities are clearly proven to impair the structural plasticity and overall pathophysiology of mood disorders. Abnormalities in the regulation of signal transduction cascades and neuroplasticity may underlie the pathophysiology of BD. It is clear that all these processes are involved in the pathophysiology and management of BD.⁴³⁻⁴⁵

Stem Cells

Along with the technological advancement, iPSC (induced pluripotent stem cells) studies are introduced to address various problems of BD. iPSCs and cell-derived neuronal-related studies are useful in understanding the actions of drugs and pathophysiology of BD.⁴⁶

In the future, approaches based on gene therapy, stem cells, omics technologies, optogenetics^{47,48} to analyze and reveal various aspects of BD are predicted to generate

effective strategies in dealing with BD.47-49

SUMMARY

Bipolar Disorder (BD), also known as manic-depressive illness, is a complex neuropsychiatric disorder affecting 1-4% of the population worldwide, with a lifetime prevalence of 2.8 to 6.5% and 59-93% genetic diversity (heritability). Recent researches on neuropharmacogenomical perspectives of bipolar disorders has been discussed. The future and continuing studies to conquer bipolar disorders should be done based on comprehensive and multidisciplinary paradigm.

ACKNOWLEDGEMENT: --

- 1. Adjunct Prof. Dr. Taruna Ikrar, M.D., M.Pharm., Ph.D. from Department of Anatomy and Neurobiology, University of California, Irvine, USA and Brain Circulation Institute of Indonesia (BCII), Surya University, Indonesia for helpful and critical proof-reading and revising this manuscript.
- 2. Vicente Rey-Valenzuela, Ph.D., plant pathologist at Cenibanano Augura, Colombia for supporting me with relevant references.

TINJAUAN PUSTAKA



REFERENCES:

- 1. McGuffin P, Rijsdijk F, Andrew M, Sham P, Katz R, Cardno A, et al. The heritability of bipolar affective disorder and the genetic relationship to unipolar depression. Arch Gen Psychiatry. 2003;60(5):497-502.
- 2. Garnham J, Munro A, Slaney C, Macdougall M, Passmore M, Duffy A, et al. Prophylactic treatment response in bipolar disorder: Results of a naturalistic observation study. J Affect Disord. 2007; 104: 185–90.
- 3. Coryell W. Maintenance treatment in bipolar disorder: A reassessment of lithium as the first choice. Bipolar Disord. 2009; 11: 77–83.
- 4. Squassina A, Manchia M, Zompo MD. Pharmacogenomics of mood stabilizers in the treatment of bipolar disorder. Human Genomics and Proteomics 2010;2010:159761. doi:10.4061/2010/159761.
- 5. Severino G, Squassina A, Costa M, Pisanu C, Calza S, Alda M, et al. Pharmacogenomics of bipolar disorder. Pharmacogenomics. 2013;14(6):655-74. doi: 10.2217/ pgs.13.51.
- 6. Hunsberger JG, Chibane FL, Elkahloun AG, Henderson R, Singh R, Lawson J, et al. Novel integrative genomic tool for interrogating lithium response in bipolar disorder. Transl Psychiatry 2015;5:504. doi: 10.1038/tp.2014.139.
- 7. Jain KK. Applied neurogenomics. Pharmacogenomics. 2001;2:143-53.
- 8. Newberg AR, Catapano LA, Zarate CA, Manji HK. Neurobiology of bipolar disorder. Expert Rev Neurother. 2008, 8:93–110.
- 9. Brambilla P, Hatch JP, Soares JC: Limbic changes identified by imaging in bipolar patients. Curr Psychiatry Rep. 2008; 10:505–9.
- 10. Drevets WC, Frank E, Price JC, Kupfer DJ, Holt D, Greer PJ, et al. PET imaging of serotonin 1A receptor binding in depression. Biol Psychiatry 1999;46:1375-87.
- 11. Leussis MP, Madison JM, Petryshen TL. Ankyrin 3: Genetic association with bipolar disorder and relevance to disease pathophysiology. Biology of Mood & Anxiety Disorders 2012;2:18.
- 12. Ferreira MA, O'Donovan MC, Meng YA, Jones IR, Ruderfer DM, Jones L, et al. Collaborative genome-wide association analysis supports a role for ANK3 and CACNA1C in bipolar disorder. Nature Genetics 2008;40(9): 1056–8. doi: 10.1038/ng.209.
- 13. Kakiuchi C, Iwamoto K, Ishiwata M, Bundo M, Kasahara T, Kusumi I, et al. Impaired feedback regulation of XBP1 as a genetic risk factor for bipolar disorder. Nature Gen. 2003; 35(2): 171–5
- 14. Lencz T, Guha S, Liu C, Rosenfeld J, Mukherjee S, DeRosse P, et al. Genome-wide association study implicates NDST3 in schizophrenia and bipolar disorder. Nat Commun. 2013;4:2739. doi: 10.1038/ncomms3739.
- 15. Harrison PJ. Molecular neurobiological clues to the pathogenesis of bipolar disorder. Curr Opin Neurobiol 2016;36:1-6.
- 16. Jain KK. Applied neurogenomics. Springer, New York: Humana Press; 2015.
- 17. Li P, Andreopoulos S, Warsh J. Signal transduction abnormalities in bipolar affective disorder. In: Reith MEA, editor. Cerebral signal transduction. Totowa: Humana Press; 2000. p. 283-312.
- 18. Dubovsky SL, Murphy J, Thomas M, Rademacher J.. Abnormal intracellular calcium ion concentration in platelets and lymphocytes of bipolar patients. Am J Psychiatr. 1992;149:118-20.
- 19. Vonk R, van der Schot AC, Kahn RS, Nolen WA, Drexhage HA. Is autoimmune thyroiditis part of the genetic vulnerability (or an endophenotype) for bipolar disorder? Biol Psychiatr. 2007; 62: 135–40.
- 20. Roybal DJ, Singh MK, Cosgrove VE, Howe M, Kelley R, Barnea-Goraly N, et al. Biological evidence for a neurodevelopmental model of pediatric bipolar disorder. Isr J Psychiatr Relat Sci. 2012; 49: 28–43.
- 21. Anderson G, Berk M, Dodd S, Bechter K, Altamura AC, Dell'osso B, et al. Immunoinflammatory, oxidative and nitrosative stress, and neuroprogressive pathways in the etiology, course and treatment of schizophrenia. Prog Neuropsychopharmacol Biol Psychiatr. 2013; 42: 1–4. doi: 10.1016/j.pnpbp.2012.10.008.
- 22. Berk M, Kapczinski F, Andreazza AC, Dean OM, Giorlando F, Maes M, et al. Pathways underlying neuroprogression in bipolar disorder: Focus on inflammation, oxidative stress and neurotrophic factors. Neurosci Behav Rev. 2011; 35: 804–17. doi: 10.1016/j.neubiorev.2010.10.001.
- 23. Altamura AC, Buoli M, Pozzoli S. Role of immunological factors in the pathophysiology and diagnosis of bipolar disorder: Comparison with schizophrenia. Psychiatr Clin Neurosci. 2014; 68: 21–36.
- 24. Wu R, Fan J, Zhao J, Calabrese JR, Gao K. The relationship between neurotrophins and bipolar disorder. Expert Rev Neurother. 2014;14(1):51-65.
- 25. Scola G, Andreazza AC. The role of neurotrophins in bipolar disorder. Progr Neuro-Psychopharmacol Biol Psychiatr. 2015;56(2):122-8.
- 26. Green E, Craddock N. Brain-derived neurotrophic factor as a potential risk locus for bipolar disorder: Evidence, limitations, and implications. Curr Psychiatr Rep. 2003;5(6):469-76.
- 27. Kapczinski F, Frey BN, Kauer-Sant'Anna M, Grassi-Oliveira R. Brain-derived neurotrophic factor and neuroplasticity in bipolar disorder. Expert Rev Neurother. 2008;8(7):1101-13.
- 28. Liu X, Zhang T, He S, Hong B, Chen Z, Peng D, et al. Elevated serum levels of FGF-2, NGF and IGF-1 in patients with manic episode of bipolar disorder. Psychiatr Res. 2014;(218)1–2:54–60. doi: 10.1016/j.psychres.2014.03.042.
- 29. Kim YK, Na KS, Hwang JA, Yoon HK, Lee HJ, Hahn SW, et al. High insulin-like growth factor-1 in patients with bipolar I disorder: A trait marker? J Affective Disord. 2013;151(2):738–43. doi: 10.1016/j.jad.2013.07.041.
- 30. Shi Y, Azab AN, Thompson MN, Greenberg ML. Inositol phosphates and phosphoinositides in health and disease. Biology of Inositols and Phosphoinositides. Springer US; 2006. p. 265-92.
- 31. Harwood AJ. Lithium and bipolar mood disorder: The inositol-depletion hypothesis revisited. Mol Psychiatr. 2005; 10(1): 117-26.
- 32. Altamura AC, Buoli M, Serati M. Duration of illness and duration of untreated illness in relation to drug response in psychiatric disorders. Neuropsychiatry 2011; 1: 81–90.
- 33. Altamura AC, Mundo E, Cattaneo E, Pozzoli S, Dell'osso B, Gennarelli M, et al. The MCP-1 gene (SCYA2) and mood disorders: Preliminary results of a case-control association study. Neuroimmunomodulation 2010; 17: 126–31. doi: 10.1159/000258696.
- 34. Padmos RC, Hillegers MH, Knijff EM, Vonk R, Bouvy A, Staal FJ, et al. A discriminating messenger RNA signature for bipolar disorder formed an aberrant expression of inflammatory genes in monocytes. Arch Gen Psychiatry 2008; 65: 395–407. doi: 10.1001/archpsyc.65.4.395.



- 35. Rao JS, Harry GJ, Rapoport SI, Kim HW. Increased excitotoxicity and neuroinflammatory markers in postmortem frontal cortex from bipolar disorder patients. Mol Psychiatry 2010; 15: 384–92.
- 36. Altamura AC, Pozzoli S, Fiorentini A, Dell'Osso B. Neurodevelopment and inflammatory patterns in schizophrenia in relation to pathophysiology. Prog Neuropsychopharmacol Biol. Psychiatry 2013; 42: 63–70.
- 37. Jain KK. A handbook of biomarkers. New York: Springer; 2010.
- 38. Balanzá-Martínez V, Fries GR, Colpo GD, Silveira PP, Portella AK, Tabarés-Seisdedos R, et al. Therapeutic use of omega-3 fatty acids in bipolar disorder. Expert Rev Neurother. 2011;11(7):1029–47. doi: 10.1586/ern.11.42.
- 39. Chiu CC, Huang SY, Su KP, Lu ML, Huang MC, Chen CC, et al. Polyunsaturated fatty acid deficit in patients with bipolar mania. Eur Neuropsychopharmacol. 13.2 (2003): 99-103.
- 40. Duman RS. Synaptic plasticity and mood disorders. Mol Psychiatry 2002;7(Suppl. 1):29-34.
- 41. Kuhlman SJ, Olivas ND, Tring E, Ikrar T, Xu X, Trachtenberg JT. A disinhibitory microcircuit initiates critical-period plasticity in the visual cortex. Nature 2013;501:543–6.
- 42. Manji HK, Quiroz JA, Gould TD. Cellular resilience and neuroplasticity in mood disorders. Psychiatric Times 2003: 55-9.
- 43. Grande I, Fries GR, Kunz M, Kapczinski F. The role of BDNF as a mediator of neuroplasticity in bipolar disorder. Psychiatry Investig. 2010; 7(4): 243–50. doi: 10.4306/ pi.2010.7.4.243
- 44. Schloesser RJ, Huang J, Klein PS, Manji HK. Cellular plasticity cascades in the pathophysiology and treatment of bipolar disorder. Neuropsychopharmacol Rev. 2008;33:110–33.
- 45. Wang JL, Shamah SM, Sun AX, Waldman ID, Haggarty SJ, Perlis RH. Label-free, live optical imaging of reprogrammed bipolar disorder patient-derived cells reveals a functional correlate of lithium responsiveness. Transl Psychiatry 2014; 4:428.
- 46. Anurogo D, Ikrar T. International seminary on ethics, medical law, and neuroscience in psychiatry: "Building good perception about future". Surabaya: Medical Faculty of Airlangga University; 2015.
- 47. Anurogo D, Ikrar T. Treatment of epilepsy: Background and future directions. Progr Communication in Sciences 2014;1(1):27-41.
- 48. Drexhage RC, Hoogenboezem TH, Versnel MA, Berghout A, Nolen WA, Drexhage HA. The activation of monocyte and T cell networks in patients with bipolar disorder. Brain Behav. Immun. 2011; 25: 1206–13.

 $See \ discussions, stats, and author \ profiles \ for \ this \ publication \ at: \ https://www.researchgate.net/publication/268252532$

Treatment of Epilepsy: Background and Future Directions

Article · October 2014

CITATION 1	READS 631		
2 authors:			
dr Dito Surya University 14 PUBLICATIONS 7 CITATIONS SEE PROFILE	Taruna Ikrar Pacific Health Sciences University, California, United State 83 PUBLICATIONS 569 CITATIONS SEE PROFILE		
Some of the authors of this publication are also working on these related projects: Neurosciencs View project			



Advanced Medicine as a current solution for degenerative disorders View project



Treatment of Epilepsy: Background and Future Directions

Dito Anurogo † and Taruna Ikrar $^{\dagger \ddagger}$

[†]Brain Circulation Institute of Indonesia (BCII), Surya University, Indonesia [‡]School of Medicine, University of California, Irvine, USA

Abstract—Epilepsy is a mystery even though it affects an estimated 50 million people worldwide. Its management is enigmatic and as such, is not curative, but rather aims to attain freedom from seizures without side-effects. However, an approach for the selection of the most effective drugs and doses for individual patients is lacking. Almost all of the antiepileptic drugs in current use are associated with adverse reactions, some of which are severe and life-threatening. A more comprehensive treatment strategy requires improved research on epilepsy. This is the key to developing a treatment plan focused on the individual needs of each patient. Pharmacogenetics can offer a novel line of attack in the treatment of epilepsy. The potential advantages of gene therapy in the management of epilepsy are manifold. It encompasses the principle of testing as to how genetic variation among individuals affects variation in drug response, efficacy, and potential adverse drug events. Pharmacogenomics is the investigation of relationships between patient genotype and responses to drug treatment. It holds the promise of selecting the right drug at the right dose for the right person. A conceptual framework that outlines the pharmacogenetic and pharmacogenomic aspects of epilepsy presented here. Future directions for research and the application of these technologies to the clinical practice of individualising treatment for epilepsy are also discussed. A combination of research strategies and prudent policies from government may lead to a better understanding of treatment effects and futuristic but realistic management in epilepsy.

Keywords—Epilepsy, etiology, neurogenetics, pharmacogenomics, pharmacogenetics.

I. INTRODUCTION

EPILEPSY is one of the oldest known brain disorders. The word "epilepsy" is derived from a Greek word meaning, "a condition of being overcome, seized, or attacked." It was mentioned more than 2,000 years ago and references to it can be found in ancient papyri and Vedic texts, the Bible, and the Koran [1][2]. Decades ago, the 'falling sickness' was believed to be caused by a demon or angel, and epilepsy became known as a 'demonic possession' or 'sacred disease' [3].

Russia's greatest novelist, Fyodor Mihailovich Dostoevsky (1821-1881), probably suffered from temporal lobe epilepsy (most likely left mesiotemporal) and partial epilepsy coexisting with idiopathic generalized epilepsy (petit-mal – grand-mal), with complex-partial and secondary generalized seizures, with a relatively benign course [4].

A. Definition

There are some definitions in epilepsy phrases based on International League Against Epilepsy (ILAE) commission. The terminology includes: "epileptic disorder", "epilepsies", "epileptic seizure", and "epileptic syndrome".

Epilepsy is a brain disorder in which a person has repeated seizures (convulsions) over time. Seizures are episodes of disturbed brain activity that cause changes in attention or behavior [5]. Epileptic disorder is a chronic neurologic condition characterized by recurrent epileptic seizures. Epilepsies are those conditions involving chronic recurrent epileptic seizures that can be considered epileptic disorders. Epileptic seizure is manifestation(s) of epileptic (excessive and/or hypersynchronous), usually self-limited activity of neurons in the brain [4]. An epileptic seizure can be defined clinically as an intermittent, stereotyped, disturbance of consciousness, behavior, emotion, motor function, or sensation that on clinical grounds is believed to result from cortical neuronal discharge [6]. Epileptic syndrome is an epileptic disorder characterized by a cluster of signs and symptoms customarily occurring together, including type of seizure, etiology, anatomy, precipitating factors, age of onset, severity, chronicity, diurnal and circadian cycling, and, sometimes, prognosis [7].

Therefore, epilepsy can be defined as a condition in which seizures recur, usually spontaneously. Two major types of epilepsy are recognized, i.e.; epilepsy with focal and epilepsy with generalized seizures.

B. Classification

Epilepsy is an extremely extraordinary-heterogeneous disease with various syndromes and subtypes. The classification at **TABLE I** shows the wide variety of epilepsy [8].

TABLE II shows the classification of seizures. It makes use of both clinical and EEG information. Brain inflammation might contribute to the onset and perpetuation of seizures in a variety of epilepsies [9].

Corresponding author: Taruna Ikrar (e-mail: taruna.ikrar@surya.ac.id). This paper was submitted on August 04, 2014; revised on September 29, 2014; and accepted on October 23, 2014.

Seizures may also result from nonepileptic causes, as in cardiogenic seizures or psychogenic nonepileptic seizures. The cause of epileptic seizures is unknown in just under 70% of cases, whereas some neurologic etiology is identified in approximately 30% of patients [10].

TABLE I ILAE CLASSIFICATION OF EPILEPTIC SEIZURES [8]

I. Partial (focal) seizures

- A. Simple partial seizures (consciousness not impaired)
 - With motor signs (including jacksonian, versive, and postural)
 With sensory symptoms (including visual, somato sensory,
 - auditory, olfactory, gustatory, and vertiginous)With psychic symptoms (including dysphasia, dysmensic, hallucinatory, and affective changes)
 - With autonomic symptoms (including epigastric sensation, pallor, flushing, pupillary changes)
- B. Complex partial seizures (consciousness impaired)
 - 1. Simple partial onset followed by impaired consciousness
 - 2. With impairment of consciousness at onset
 - 3. With automatisms
- C. Partial seizuers evolving to secondarily generalized seizures
- II. Generalized seizures of nonfocal origin (convulsive or nonconvulsive)
 A. Absence seizures
 - 1. With impaired consciousness only
 - 2. With one or more of the following: atonic components, tonic components, automatisms, autonomic components
 - B. Myoclonic seizures, myoclonic jerks (single or multiple)
 - C. Tonic-clonic seizures (may include clonic-tonic-clonic seizures)
 - D. Tonic seizures
 - E. Atonic seizures

Atonic seizures

III. Unclassified epileptic seizures

ILAE: International League against Epilepsy

TABLE II ILAE CLASSIFICATION OF SEIZURES [6]

Partial seizures (seizures beginning locally)
Simple (consciousness not impaired)
With motor symptoms
With somatosensory or special sensory symptoms
With autonomic symptoms
With psychic symptoms
Complex (with impairment of consciousness):
Beginning as simple partial seizures (progressing to complex seizure)
Impairment of consciousness at onset
Partial seizures becoming secondarily generalized
Generalized seizures:
Absence seizures
Typical (petit mal)
Atypical
Absence with special features
Myoclonic absence
Eyelid myoclonia
Myoclonic seizures
Myoclonic
Myoclonic atonic
Myoclonic tonic
Clonic seizures
Tonic seizures
Tonic-clonic seizures (in any combination)

Examples of the application of the five-axis syndrome-oriented system would appear as follows: [11]

28

- Axis 1 (ictal semiology): generalized tonic-clonic seizure
- Axis 2 (underlying mechanism of seizure types): generalized tonic-clonic seizures
- Axis 3 (epilepsy syndrome): epilepsy with generalized tonic-clonic seizures on awakening
- Axis 4 (etiology): genetic causes
- Axis 5 (impairment): based upon the revised International Classification of Functioning, Disability and Health rating (<u>http://www.who.int/icidh</u>).

TABLE III THE ETIOLOGY OF EPILEPTIC SEIZURES [11],[14]

	D .4	
Age Group	Pot	ential Causes
Newborns	1.	Brain malformations
	2.	Lack of oxygen during birth
	3.	Low levels of blood sugar, blood calcium, blood,
		magnesium, or other electrolyte disturbances
	4.	Inborn errors of metabolism
	5.	Intracranial hemorrhage
	6.	Maternal drug use
	7.	Infection
Neonatal	1.	Perinatal injury
Incollatal	1. 2.	Hypoxia
	2. 3.	Hypoglycemia
	3. 4.	Hypocalcemia
	4. 5.	Pyridoxine deficiency
	6.	Intraventricular hemorrhage
	7.	Intraparenchymal hemorrhage
	8.	Subdural hemorrhage
Children	1.	Perinatal injury
	2.	Developmental malformation
	3.	Febrile seizures
	4.	Stroke
	5.	Vascular malformations
	6.	Head injury
	7.	Infections
	8.	Brain tumors
	9.	Amino acid disorders
	10.	Urea cycle disorders
		Gray matter storage diseases
Infants		
		Fever (febrile seizures)
and		Infections
Children		Brain tumor (rarely)
	4.	Mesial temporal (Ammon's horn) sclerosis [14]
Children	1.	Congenital conditions (Down syndrome, Angelman
and		syndrome, tuberous sclerosis and neurofibromatosis
Adults	2.	Genetic factors
	3.	Head trauma
	4.	Progressive brain diseases (rare)
Middle years	1.	Neoplasm (high risk)
Adults/Elderly	1.	Trauma
2	2.	Tumor
	3.	Substance abuse or drug withdrawal
	4.	Drug reactions (stimulants, antihistamines, tricyclics,
		phenothiazines, butyrophenones, certain antibiotics,
		aminophylline)
	5.	CNS infections
	<i>6</i> .	Stroke
	0. 7.	Intracranial hemorrhage
	7. 8.	Vascular malformations
	o. 9.	Systemic/metabolic derangements
		Alzheimer disease
		Dementia (high risk for > 65 years)
		Cerebrovascular disease (high risk for > 65 years)
	12.	Cerebrovascular disease (ingli fisk 101 > 0.5 years)

Using the five-tiered patient-oriented classification, the above patient according to the 2001 ILAE proposal would be classified as follows: [12]

- Dimension 1 (epileptogenic zone): generalized (epilepsy with generalized tonic-clonic seizures on awakening)
- Dimension 2 (semiologic seizure classification): generalized tonic-clonic seizure
- Dimension 3 (etiology): unknown
- Dimension 4 (seizure frequency): persistent (one per year)
- Dimension 5 (related medical information): seizures triggered upon awakening

Etiology may be divided into epilepsies due to genetic and acquired causes and those due to a combination of both, which contribute to the predisposition of recurrent seizures.¹¹ Although many cases may be multifactorial, clinicians should decide the most appropriate predisposition or risk factor in order to establish diagnosis and determine the right treatment.

C. Etiology

The etiology of epileptic seizures differs across the lifespan and depends upon the age of seizure onset. The most common causes of epilepsy for each age group have been reported by the Epilepsy Foundation of America (2008) [13] and are listed in **TABLE III** [11],[14].

Mesial temporal (Ammon's horn) sclerosis is the most common single lesion to be found post mortem in the brains of chronic epileptics who die a natural death. Evidence shows that it usually arises in infancy, often as a result of a prolonged febrile convulsion, and that it then becomes a potent epileptogenic lesion [14].

The causes and prognoses of epilepsies in children are varied and, therefore, each child with epilepsy needs an individualized, multiaxial assessment of their epilepsy syndrome, and any additional morbidities [15].

D. Epidemiology

Epilepsy is a chronic disorder, or group of neurological disorders, in which the indispensable feature is recurrence of seizures that are caused by abnormal electrical discharges from the brain; typically unprovoked and usually unpredictable. Absence epilepsy involves seizures that cause a sudden loss of awareness. It is characterized by the periodic occurrence of spontaneous seizures and affecting about 0.5%-1% of the world's population [16],[17], approximately 1 in 130 people [18], or at least 50 million people worldwide [19]. It often starts in childhood or adolescence and appears to be a major cause of morbidity in elderly [20].

E. Incidence

The incidence of epilepsy is particularly high in Latin America and in several African countries. The overall incidence of epilepsy is generally taken to be about 50 cases per 100000 persons per year (range 40 to 70 per 100000/year) [21] in developed countries, higher incidence figures are generally found from studies in developing countries [22].

In developing countries, a range of 100 to 190 per 100000 per year has been given [21]. The incidence of epilepsy is high in childhood, decreases in young people and rises again in the elderly [23]. Epilepsy has a lifetime cumulative incidence approaching 1 in 25, thus representing one of the most common serious neurological disorders [18].

F. Prevalence

The overall prevalence of active epilepsy in 5550 persons aged 55-95 years in the Netherlands from 1991 to 1993 was 0.8%-0.9%. It increased with age from 0.7% for those aged 55-64 years to 1.2% for those aged 85-94 years. The increase with age was detected among men and women both [20]. Another report, its prevalence is usually regarded as between 5 and 10 cases per 1000 persons. The lifetime prevalence of seizures is between 2% and 5% [22]. In children with epilepsy, the prevalence of refractory epilepsy is variably reported as 9%-24% [24].

G. Prognosis

Prognostic factors may include demographic features, disease-specific indicators (i.e., seizure frequency, etiology of epilepsy) or comorbidity. The study of the prognosis of epilepsy is confounded by the diversity of underlying diagnoses [25].

Overall, between 70% and 80% of people developing epilepsy will go into long-term remission, usually within the first 5 years. Over two-thirds of patients enter long-term remission, and subsequent relapse is uncommon [22]. Generally, the 1-year remission rate is between 65% and 80% [26]. The prognosis is largely determined by the background etiology [22].

H. Recurrence

The recurrence of epilepsy is multifactorial. A wide variety of prognostic factors will influence the recurrence rates of epilepsy, such as: age, sex, seizures, etiology, history, and medication.

Factors	Explanation	References
Age	Onset below 10 years or 16 years or over 65 years has been correlated with recurrence.	[27],[28],[29],[30]
Sex	Sex does not correlate with prognosis for early recurrence.	[31],[32]
Seizures	Partial seizures are associated with poorer outcome for recurrence. Nocturnal seizures and mixed seizure types have also shown higher recurrence rates.	[33],[34],[35]
Etiology	Congenital neurological deficits, head injury, remotes causes of epilepsy (i.e. tumours) predict higher rates of recurrence. Abnormal neurological examination has been correlated to recurrence.	[36],[37],[38],[39]
History	A family history of seizure disorders increases the risk of recurrence. The presence of an EEG abnormality is a risk factor for recurrence.	[40],[41]
Medication	A threefold increased risk of seizure recurrence in the untreated group by 2 years.	[30],[41],[42]

TABLE IV

I. Remission

Remission of epilepsy is the seizure-free period experienced by a patient who has had one or more seizures. It is usually defined as being of 1-5 years' duration. Terminal remission is when the remission continues to the end of follow-up [42].

Several studies have shown that up to a quarter of children with early intractability (within the first 2 years of follow-up have a remission of at least 1 year at 5 years [43],[44]. The probability of being in a remission lasting for five years or more was 61% at 10 years and as high as 70% at 20years [6].

J. Screening

The screening for epilepsy was taken from the World Health Organization (WHO) research protocol, i.e., (1) Have you ever lost consciousness? (2) Have you ever had episodes where you lost contact with your surroundings? (3) Have you ever had any shaking of your arms and legs which you could not control? [45]

Episodic memory impairment is a key feature of temporal lobe epilepsy (TLE). TLE is the most common form of focal epilepsy. Cognitive impairment is a major concern for patients as well as clinicians [46].

The EEG has great potential for investigating the presence or severity of epilepsy (epileptogenicity) and its development (epileptogenesis) in vivo and in vitro, owing to the capacity to utilize both macroelectrodes and microelectrodes, and to record normal and abnormal neuronal firing with excellent time resolution [47],[48]. Andrade-Valença et al., investigated the possibility of noninvasive detection of interictal high-frequency oscillations (HFOs) via scalp EEG recordings for more-precise delineation of the seizure-onset zone (SOZ) in patients with focal epilepsy [47]. Recording of HFOs with scalp electrodes was previously thought to be virtually impossible [48]. Investigation of HFOs is of great importance, since these oscillations can reveal fundamental mechanisms of epileptogenesis and epileptogenicity, and also have possible clinical value [49].

K. Prevention

There are a lot of ways to prevent epilepsy. Reduction in the incidence of stroke should be accompanied by a decline in head trauma mostly because of road traffic accidents may decrease the incidence of epilepsy. To prevent epilepsy in early life, we should reduce perinatal morbidity and improve genetic understanding of genetic disorders that is associated with epilepsy. A continuing counseling concerning provocative and underlying factors of epilepsy (such as: alcohol, drug abuse, etc) must be given to patients and their families [6]. Chronic epilepsy is very difficult to control and may best be prevented by more effective treatment at the onset of the disorder [50].

Suicide in epilepsy may occur during interictal dysphoric episodes with or without psychotic features or in a state of postictal depression. It can be prevented by psychopharmacologic treatment [51]. Sudden unexpected death in epilepsy is found to be associated with frequent generalized tonic-clonic seizures and greater ictal maximal heart rate, especially during nocturnal attacks. Thus, supervision at night is associated with a lower risk of occurrence [52].

L. Biomarker

Recent research has showed that tetranectin could be a candidate biological marker for epilepsy psy [53].

Tetranectin (TN) is a plasminogen kringle 4 binding protein and regulates fibrinolysis and proteolytic processes via binding to plasminogen [54],[55]. In brain tissue, TN is present in most neurons and myelinated fibers of the white matter in both the cerebrum and cerebellum and is located in cytoplasm. It is not expressed in glial cells [56],[57]. The concentration of TN in serum is approximately 10 mg/l [58]. The serum-TN concentrations of patients suffering from first-episode seizures were 3.77 mg/l to 9.03 mg/l. It is hypothesized that patients with lower serum-TN concentrations would progress to drug-refractory epilepsy [53].

Cerebrospinal fluid-tetranectin (CSF-TN) levels increased in epileptic patients while serum-TN levels decreased. Lower serum-CSF levels might be correlated with drug-resistance in epilepsy [53].

TABLE V DIFFERENTIAL DIAGNOSIS OF EPILEPSY [6]

_				
1.	Syncope:			
	1.1. Reflex syncope:			
	a) Postural			
	b) Psychogenic			
	c) Carotid sinus syncope			
	d) Micturition syncope			
	e) Valsalva			
	1.2. Cardiac syncope:			
	a) Dysrhythmias (heart block, tachycardias, etc)			
	b) Valvular disease (especially aortic stenosis)			
	c) Cardiomyopathies			
	d) Shunts			
	1.3. Perfusion failure:			
	a) Hypovolaemia			
b) Syndrome of autonomic failure				
2.	Psychogenic attacks:			
	2.1. Pseudoseizures			
	2.2. Panic attacks			
	2.3. Hyperventilation			
	2.4. Night terrors			
	2.5. Breath holding			
3.	Transient ischaemic attacks (TIA)			
4.	Migraine			
5.	Narcolepsy			
6.	Hypoglycaemia			

M. Differential Diagnosis

Epilepsy must be differentiated from other diseases and disorders. Syncope and pseudoseizures are most common fallibilities or pitfalls in the diagnosis of epilepsy. Both are common in young adults [6].

Seizure diagnosis is essentially clinical with no single, simple diagnostic test. Even in experienced hands the diagnosis is often incorrect, with psychogenic non-epileptic attack disorder and convulsive syncope all too commonly misdiagnosed and mistreated as epilepsy [59].

Multiple diagnosis and multi-aspects that should be considered carefully before diagnosing epilepsy could be seen in **TABLE V**.

II. PATHOPHYSIOLOGY OF EPILEPSY: EPILEPTOGENESIS

Epileptogenesis is the process whereby, after an acute brain insult, pathological and pathophysiological alterations gradually occur in certain brain regions, leading to the expression of epilepsy [60]. The epileptogenic zone is the region from which the seizure discharges arise.

The epileptogenic zone refers to the region of cerebral cortex where localization-related epileptic seizures originate. Specific lesions such as mesial temporal sclerosis or foreign tissue lesions are referred to as anatomic or structural lesions. These focal anatomic lesions produce a surrounding primary epileptogenic zone, which in turn may produce distant epileptogenic zones, a condition referred to as secondary epileptogenesis [11].

There is some evidence in humans that epileptogenic foci in the mesial temporal regions may arise from epileptogenic neocortex surrounding distant primary structural lesions. This concept is still controversial because it has not been adequately demonstrated. FDA-approved anti-epileptic drugs (AEDs), such as levetiracetam have been tested using the kindling model without demonstrating efficacy in other more conventional models such as maximal electroshock and phenylenetetrazol models [61].

Temporal lobe structures, notably the hippocampus, the amygdala, and the piriform cortex are most susceptible to seizurogenic and epileptogenesis-triggering brain insults; accordingly, temporal lobe epilepsy (TLE) is the most common form of epilepsy [62].

Six steps lead from focal epileptogenesis to clinical epilepsy: (1) the generation of enhanced physiological responses, (2) paroxysmal depolarizing shift (PDS), which in turn lead to interictal spike appearance in EEG, (3) focus spread to perifocal neurones, (4) the utilisation or breakdown of control mechanisms with brain circuits that limit the propagation of seizure discharges via preferred routes of spread; (5) the appearance of secondary foci in regions synaptically linked to the primary focus, and (6) the emergence of clinical seizures [63]. Correlation between mechanisms of epileptogenesis and mechanisms of action of antiepileptic drugs (AEDs) can be seen in detail in **TABLE VI** [64]

Quinolinic acid is an endogenous ligand of the N-methyl-D-aspartate (NMDA) receptor which is elevated in the brain of some epileptic patients. A decrease in quinolinphosphoribosyltranspherase in the frontal and temporal cortex in epileptic human tissue, may lead to quinolinic acid accumulation with the corresponding amplification of some excitatory synapses, thus predisposing to epileptogenesis [65]-[67].

	TABLE VI						
	Mechanisms of epileptogenesis	Mechanisms of actions of AEDs					
GABA	 Reduced GABA in microgyric cortex Reduced benzodiazepine receptor binding in medial thalamic nucleus (mesial temporal lobe epilepsy) Reduced benzodiazepine receptor density in CA1 region (hippocampal sclerosis) Reduced GABA levels and GAD activity (epileptic foci) Auto-antibodies to GAD (Stiff-man syndrome) 	 Increased functional pool of GABA (vigabatrin, tiagabine) Enhanced GABA-ergic inhibition (benzodiazepines) GABA agonistic effects (progabide) (Weaker) GABA-ergic properties (phenobarbital, gabapentin, topiramate, valproate, zonisamide) 					
Glu	 Upregulation of hippocampal ionotropic glutamate receptors (temporal lobe epilepsy) Anti-gluR3 antibodies (Rasmussen encephalitis) Increased plasma glutamate levels (absence seizures) 	 Inhibition of glutamate release (<i>lamotrigine</i>) Block of glycine site at NMDA receptor (<i>felbamate</i>) 					
Na ⁺	 Mutation voltage-gated Na⁺ channel (generalized epilepsy with febrile seizures) 	 Reduction of voltage-gated Na⁺ currents (carbamazepine, felbamate, lamotrigine, oxcarbazepine, phenytoin, topiramate, valproate, zonisamide) 					
K+	Mutation voltage-gated K ⁺ channel (<i>benign familial</i> <i>neonatal convulsions</i>)	 Reduction of T-type Ca²⁺ currents (<i>ethosuximide</i>, 					
Ca ²⁺	• Reduced ACh-mediated Ca flux (<i>nocturnal frontal lobe</i> <i>epilepsy</i>)	valproate)					
	→ Increased membrane excitability	\rightarrow Decreased membrane excitability					

Increases in postsynaptic glutamate receptors and decreases in gamma-aminobutyric acid (GABA) (A) receptors in microgyric cortex could promote epileptogenesis [68]. Changes in metabotropic glutamate receptor function may also play a key role in epileptogenesis [69]. Excessive glutamate release can underlie the resulting brain damage [70]. Thus, excessive glutamatergic activity is important in the induction of neuronal pathology that can lead to hyperexcitability and epilepsy.

Glutamate excitotoxicity is due to overstimulation of glutamate receptors producing excessive neuronal depolarization, which is accompanied by an overwhelming increase in free intracellular calcium, entering via glutamate channels and voltage gated calcium channels, as well as released from intracellular stores; the calcium-dependent signaling pathways that are subsequently activated lead to neuronal dysfunction and pathological alterations in morphology or death [70],[71].

Noradrenaline was increased in midbrain and brainstem whereas decreased levels of dopamine have been found in the nucleus caudatus [72] in the epileptic foci of epilepsy patients [73].

There are two mechanisms of interictal-ictal transition. A. Nonsynaptic mechanisms, i.e., (1) Alterations in the ionic

microenvironment, e.g., increased extracellular K^+ , decreased extracellular Ca^{2+} (2) Decreases in size of extracellular space (3) Failure of ion transport : Na⁺–K⁺ pump or Cl–K⁺ co-transport (4) Presynaptic terminal bursting, (5) Ephaptic interactions. What is this? B. Synaptic mechanisms, i.e., (1) Depression of GABA-ergic inhibition (2) NMDA receptor activation, voltage-dependent epilepsy (3) Frequency potentiation of epilepsy (4) Actions of modulators [74].

A. The role of amygdala and cytokine

The amygdala play a prominent role in the pathogenesis and the symptomatology of epilepsy. The basolateral nucleus of the amygdala (BLA) plays the most important role in the initiation and spread of seizures. It appears to be most susceptible to seizure generation [1],[76].

Magnetic resonance imaging has revealed that a common pathology of the amygdala in TLE is atrophy (reduced volume associated with neuronal loss), which can range from 10% to 57% volume reduction [77]. A correlation of amygdala atrophy with the chronicity of epilepsy has been found in some studies [78]. More severe amygdala atrophy may be associated with a history of prolonged febrile convulsions [79]. In many cases, amygdala damage is co-present with damage in other brain regions and particularly the hippocampus [80].

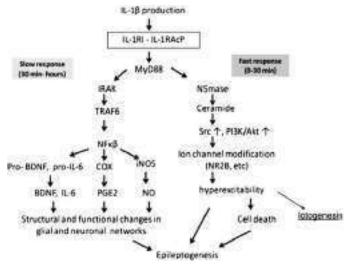


Figure 1 IL-1beta signaling in epilepsy

Elevated NMDA receptor activation may contribute to hippocampal hyperexcitability in epileptic patients. Hyperexpression of Glu6 (kainate) produces permanent change in hippocampal excitability which in turn may provoke epileptogenesis.

Most recently, experimental and clinical findings support a crucial role of inflammatory processes in the brain contributing to the etiopathogenesis of seizures and to the establishment of a chronic epileptic focus [83]. Prototypical inflammatory cytokines, such as IL-1beta, TNF-alpha and IL-6 have been shown to be overexpressed in experimental models of seizures in brain areas of seizure generation and propagation, prominently by glia and to a lesser extent by neurons. Cytokine

receptors are also up regulated, and the related intracellular signaling is activated in both cell populations highlighting autocrine and paracrine actions of cytokines in the brain [84].

Alterations in distinct astrocyte membrane channels, receptors, transporters and phenotypic changes in activated microglial cells have been described in chronic epileptic tissue and they are possibly associated with the epileptic state characterized by recurrent spontaneous seizures [85]-[87].

Several reports show increased cytokines in serum and CSF in patients with epilepsy. For example, recent tonic-clonic induce higher seizures IL-6 levels and lower IL-1Ra-to-IL-1alpha ratio [88]. The analysis of human brain specimens from drug-refractory epileptic patients showed strong activation of the IL-1beta/IL-1R1 system in brain resident cells, such as in glia and neurons [89]. The finding that ongoing inflammatory events occur during epileptogenesis suggests that the activation of the IL-1beta system observed in human chronic epileptic tissue may precede the onset of epilepsy possibly playing an etiopathogenetic role [90].

Figure 1 shows IL-1beta signalling in epilepsy [85]. This is the cascade of events that explain the activation of IL-1beta following a precipitating event (eg. a primary brain insult), accounting for the role of IL-1beta in epileptogenesis and ictogenesis [85],[90].

III. TREATMENT AND MANAGEMENT

There are several ways one can treat epilepsy, such as treatment with medications, surgery, stem cell, and gene therapy. In treating patients with epilepsy disorders, one is frequently faced with the decision of how long drug therapy should be continued. Permanent remissions of seizure of epilepsy are frequent in children and rare in adults. After a patient has remained seizure free on therapy for one and a half to three years, the drugs may gradually be withdrawn. The electroencephalogram is of some help in the decision about when drugs can safely be discontinued, but there is no dependable way to predict which patients will remain symptom free after medication is eliminated.

A. Pharmacologic Therapy

In the past two decades, nine new antiepileptic drugs have been marketed, making the choice of initial therapy complex. Antiepileptic drugs (AEDs) are classified as being either broad-spectrum or narrow-spectrum drugs with regard to efficacy against different seizure types and epilepsy syndromes. Broad-spectrum antiepileptic drugs are particularly useful because they are reasonable initial choices in most adult patients, regardless of the type of seizure or syndrome. These drugs include valproate, lamotrigine, topiramate, levetiracetam, and zonisamide. In contrast, narrow-spectrum drugs, which include carbamazepine, phenytoin, gabapentin, tiagabine, oxcarbazepine and pregabalin, should be restricted to patients who have localization-related (focal) epilepsy with partial and secondarily generalized seizures [91]. These drugs are less effective than broad-spectrum agents in the idiopathic generalized epilepsy syndromes and they may even exacerbate some seizure types in these patients [92]. About half of patients in whom epilepsy is newly diagnosed become seizure-free while receiving the first antiepileptic drug. Failure of the first antiepileptic drug for reasons other than tolerability increases the likelihood of nonresponse to other drugs, but nearly two thirds of patients become seizure-free after receiving the second or third drug [93]. Further detailed explanation of AEDs could be seen in **TABLE VII**.

TABLE VII	ANTIEPILEPTIC DRUG	s (AEDs)
-----------	--------------------	----------

Antiepileptic Drugs (AEDs)	Indications	Side Effects and Explanation	References
Carbamazepine Partial complex seizures, GTC, mixed SZ p types. S		Diplopia, dizziness, leucopenia, rash, SIADH. Efficacy as measured by seizure recurrence showed remacemide to be inferior to carbamazepine. Significant deterioration was seen on measures of information processing speed and attention after treatment with carbamazepine [95]. Efficacy as measured by seizure recurrence showed remacemide to be inferior to carbamazepine [96]. Significant deterioration was seen on measures of information processing speed and attention after treatment with carbamazepine [96].	[94], [95],[96]
Clobazam	broad spectrum antiepileptic, monotherapy for partial and selected epilepsies in childhood. intractable seizures [99] refractory epilepsy in children [100]	 without much side effects [97]; drowsiness The cognitive and behavioural effects of clobazam appear to be similar to those of standard monotherapy [98]. Mood changes recorded included irritability, depression, and disinhibition [99]. Once started, clobazam should be tailed off with caution [99]. Severe behavior disorder in children like: aggressive agitation, self injurious behavior, insomnia, and incessant motor activity occurring between 10 and 55 days after initiation of drug therapy [100] A useful additional drug added to conventional anticonvulsant regimes [101]. A useful treatment for epilepsy as intermittent or short-term add-on therapy, but it should also be tried as long-term therapy in some situations, especially as add-on therapy for patients with refractory epilepsy, as add-on or monotherapy for patients with anxiety, or in some women in association with oral contraceptives [102]. 	[97].[98], [99],[100], [101],[102]
Clonazepam	Partial and generalized SZ (including absence and myoclonus). Lennox– Gastaut syndrome, neonatal SZ, infantile spasms and status epilepticus. (Adults and children)	Sedation (common and may be severe), cognitive effects, drowsiness, ataxia, personality and behavioural changes, hyperactivity, restlessness, aggressiveness, psychotic reaction, seizure exacerbations, hypersalivation, tone changes, leucopenia, withdrawal symptoms. Useful action especially in children. A broad spectrum of activity against the various types of epilepsy [104]. Hypersalivation and excessive bronchial secretion may be a problem in children and infants [104]. Although the mechanism of action of clonazepam has not yet been established, some investigators have been suggested that it involves enhancement of anti-anxiety effects, anticonvulsant effects on subclinical epilepsy, increase in 5-HT/monoamine synthesis or decrease in 5-HT receptor sensitivity mediated through the GABA system, and regulate in GABA activity [105]. Although reading epilepsy is usually refractory to anticonvulsant therapy, treatment with clonazepam resulted in complete control of the involuntary movements precipitated by reading [106]. Inhibition of seizure activity seems to be achieved already at low plasma levels of clonazepam. Plasma concentrations of clonazepam were determined 23 nmol/L, range = 11-41 nmol/L [107].	[103], [104],[105], [106],[107]
Ethosuximide Absence, childhood absence epilepsy		Nausea, vomiting, rash, blood dyscrasias, increase frequency of grand mal seizures in mixed SZ types if used alone. The addition of ethosuximide to valproate can be helpful to those with myoclonic absences, where this combination appears more beneficial than either valproate or ethosuximide alone and in eyelid myoclonia with absences [108]. Ethosuximide and valproic acid are more effective than lamotrigine in the treatment of childhood absence epilepsy. Ethosuximide is associated with fewer adverse attentional effects [109]. Although ethosuximide, lamotrigine and valproate are commonly used to treat people with absence seizures we have insufficient evidence to show which drugs are best for treating seizures in children and adolescents with absence epilepsy [110].	[94],[108], [109],[110]
Gabapentin	Partial or secondarily generalized epilepsy. Adults and children (over age of 6 years)	Drowsiness, dizziness, seizure exacerbation, ataxia, headache, tremor, diplopia, nausea, vomiting, rhinitis.	[103]
Lamotrigine	Partial and generalized epilepsy. Also in Lennox–Gastaut syndrome and other	Rash (sometimes severe), headache, blood dyscrasia, ataxia, asthenia, diplopia, nausea, vomiting, dizziness, somnolence, insomnia, depression, psychosis,	[103],[108]

	generalized epilepsy syndromes. Adults and children over 2 years of age.	tremor, hypersensitivity reactions. Lamotrigine can be effective therapy for juvenile myoclonic epilepsy and eyelid myoclonia with absences when used alone and, in conjunction with other antiepileptic drugs (AED) (usually valproate) for early myoclonic encephalopathy, myoclonic-astatic epilepsy and particularly, epilepsy with myoclonic absences [108].	
Levetiracetam	Partial seizures with or without secondarily generalized seizures. Adults only.	Somnolence, asthenia, infection, dizziness, headache, irritability, aggression, behavioural and mood changes	[103]
Oxcarbazepine	Partial and secondarily generalized seizures. Adults and children	Somnolence, headache, dizziness, diplopia, ataxia, rash, hyponatraemia, weight gain, alopecia, nausea, gastrointestinal disturbance.	[103]
Phenobarbital	Anticonvulsant, sedative, hypnotic	Sedation, paradoxical excitement, hyperactivity, rash.	[94]
Phenytoin	Tonic-clonic SZs, psychomotor SZs, status epilepticus, prevention and treatment of SZs post-neurosurgery.	Nystagmus, ataxia, rash, gingival, hypertrophy, impaired cognition.	[94]
Pregabalin	Partial seizures with or without secondary generalization. Adults only	Somnolence, dizziness, ataxia, asthenia, weight gain, blurred vision, diplopia, tremor.	[103]
Primidone	Monotherapy or adjunctive in GTC, psychomotor SZs	Sedation, dizziness, ataxia, rash, paradoxical excitement.	[94]
Tiagabine	Partial and secondarily generalized seizures. Patients \geq 12 years of age only	Dizziness, tiredness, nervousness, tremor, diarrhoea, nausea, headache, confusion, psychosis, flu-like symptoms, ataxia, depression, word-finding difficulties, encephalopathy, non-convulsive status epilepticus.	[103]
Topiramate	Partial and secondarily generalized seizures. Also for Lennox–Gastaut syndrome. Idiopathic generalized epilepsy. Adults and children over 2 years of age.	Dizziness, ataxia, headache, paraesthesia, tremor, somnolence, cognitive dysfunction, confusion, agitation, amnesia, depression, emotional lability, nausea, diarrhoea, diplopia, weight loss.	[103]
Valproate acid	Absence (petit mal), atypical absence, GTC, adjunctive for multiple SZ types.	Nausea, vomiting, tremor, thrombocytopenia, hepatic dysfunction, hair loss, weight gain. The treatment of first choice for benign myoclonic epilepsy in infants, myoclonic astatic epilepsy, epilepsy with myoclonic absences, eyelid myoclonia with absences, juvenile myoclonic epilepsy and progressive myoclonus epilepsy [98]. The risk of abortion was greater with use of valproate (8%) than with other drugs (from 1% with phenobarbital to 6% with lamotrigine). Doses of valproate below 700 mg/day were associated with a malformation rate in a similar range as that of carbamazepine 400–1000 mg/day, phenobarbital less than 150 mg/day, and lamotrigine of 300 mg/day or higher. The risk of major malformations increases with the prescribed dose of valproate, in general with greater risks at doses above 600–1500 mg/day [111].	[94],[98]
Vigabatrin	Partial and secondarily generalized epilepsy. West syndrome	Mood change, depression, psychosis, aggression, confusion, weight gain, insomnia, changes in muscle tone in children, tremor, diplopia, severe visual field constriction.	[103]
Zonisamide	Refractory partial epilepsy and generalized epilepsy (all types). Lennox– Gastaut syndrome. West syndrome. Progressive myoclonic epilepsy.	Somnolence, ataxia, dizziness, fatigue, nausea, vomiting, irritability, anorexia, impaired concentration, mental slowing, itching, diplopia, insomnia, abdominal pain, depression, skin rashes, hypersensitivity. Significant risk of renal calculi. Weight loss, oligohidrosis and risk of heat stroke. Zonisamide added to clonazepam and valproate or a barbiturate, can reduce the cascade of myoclonia in progressive myoclonus epilepsies for at least 2 years, but relapse may occur thereafter [108].	[103],[108

GTC: generalized tonic clonic, SZ: seizure

B. Ketogenic Diet

The ketogenic diet was created by Wilder in 1921 at the Mayo Clinic in Rochester, Minnesota for children with refractory epilepsy. It restricted carbohydrates, protein, calories, and fluids while significantly increasing fat intake to comprise approximately 90% of calories. Within several years it became widely used for adults, as well as children [112]. The ketogenic diet, which is high fat and extremely low in carbohydrates, can help control seizures in some patients [113].

There are four different ketogenic diets available to choose from: the traditional 'classic' ketogenic diet, the medium-chain triglyceride (MCT) diet, the modified Atkins diet (MAD) and the low glycemic index treatment (LGIT). These alternative diets are better choices for many patients with epilepsy who are concerned about the difficulty in changing their lifestyle to adopt a ketogenic diet, including adolescents, adults, busy families with multiple children, and patients with very high baseline carbohydrate intake (or fat aversion). The details of each diets could be seen in **TABLE VIII**.

THE FOUR MAJOR KETOGENIC DIETS [114]						
Component	Component Classic ketogenic (4:1) MCT Modified Atkins					
Carbohydrate (%)	8 (3%)	50 (20%)	10 (5%)	40 (27%)		
Fat (g, % calories)	100 (90%)	78 (70%)	70 (70%)	60 (45%)		
Protein (g, %)	17 (7%)	25 (10%)	60 (25%)	40 (28%)		
MCT: medium chain triglyseride; LGIT: low glycemic index treatment				tment		

TABLE VIII COMPARISON OF HE FOUR MAJOR KETOGENIC DIETS [11

Adenosine may play a role in the ketogenic diet's antiseizure effects [115]. Norepinephrine plays a key role in the ketogenic diet's anticonvulsant mechanism [116],[117].

A ketogenic diet can decrease morphological signs of mitochondrial damage and protect against conditions wherein mitochondrial DNA damage occurs [118]. Moreover, ketogenic diets also may exert a neuroprotective effect through antioxidant mechanisms mediated via the nuclear factor E2-related transcription factor [119].

Recently, the ketogenic diet is extensively indicated for: [120]-[124]

- 1. absence epilepsy
- 2. Alzheimer's disease
- 3. amyotrophic lateral sclerosis (ALS)
- 4. autism
- 5. brain tumors
- 6. children receiving only formula
- 7. children with Lennox-Gastaut syndrome
- 8. Dravet syndrome
- 9. hypothalamic hamartoma

- 10. hypoxic-ischemic encephalopathy
- 11. infantile spasms
- 12. migraine
- 13. myoclonic-astatic epilepsy
- 14. Parkinson disease
- 15. refractory status epilepticus
- 16. Rett syndrome
- 17. Sturge–Weber syndrome
- 18. traumatic brain injury
- 19. tuberous sclerosis complex

Providing the ketogenic diet within 7-10 days as a formula through a nasogastric tube to a patient in an intensive care unit (ICU) with status epilepticus is a very feasible option [125].

The clinicians and physicians should be aware of the side effects of giving the ketogenic diets. **TABLE IX** shows side effects and solution of the ketogenic diets: [126]-[128]

TABLE IX

	Side effects		Solution
۶	hypercholesterolemia	~	alternative diets (MAD, LGIT)
۶	mineral deficiencies	\checkmark	avoiding a fasting protocol
۶	acidosis	\checkmark	supplements (calcium, selenium, zinc, and
≻	constipation		vitamin D)
۶	weight loss	~	oral citrates (children with the ketogenic diet)

C. Neurogenetics

Neurogenetics is synthesis between neurology and genetics studies and researches. The comprehensive understanding of epilepsy neurogenetics is the key to study, learn, and develop epilepsy pharmacogenetics and pharmacogenomics. **TABLE X** shows an example of the study of epilepsy neurogenetics.

TABLE X THE STUDY OF EPILEPSY NEUROGENETICS

Diseases/Disorders	The Gene Symbols	Sum	References
Generalized myoclonic epilepsy, febrile seizures, absences	ALDH7A1, BRD2, CACNA1A, CACNA1H, CACNB4, CASR, CHRNA2, CHRNA4, CHRNB2, CLCN2, CSTB, EFHC1, EPM2A, GABRA1, GABRB3, GABRD, GABRG2, GPR98, GRIN2A, GRIN2B, KCNMA1, KCNQ2, KCNQ3, KCTD7, MBD5, ME2, NHLRC1, PCDH19, PRICKLE1, PRICKLE2, SCARB2, SCN1A, SCN1B, SCN2A, SCN9A, SLC2A1, TBC1D24.	37	[129],[130]
Syndromic epilepsy	ARFGEF2, ARHGEF9, A2BP1, ASPA, ATP1A2, ATP2A2, ATP6V0A2, CACNA1A, CCDC88C, CLCNKA, CLCNKB, COH1, DLGAP2, GFAP, GLI3, GLRA1, GLRB, GPHN, KCNA1, KCNJ1, KCNJ10, KIAA1279, LAMA2, LBR, LGI1, MLC1, MLL2, NF1, NIPBL, PANK2, PI12, PIGV, PLA2G6, RAI1, SCN8A, SETBP1, SHH, SLC4A10, SLC6A5, SMC1A, SMC3, SYNGAP1, TBX1, TSC1, TSC2, VPS13A, ZEB2.	47	[131]
Epileptic encephalopathies	ARHGEF9, ARX, CDKL5, CNTNAP2, FOXG1, GABRG2, GRIN2A, GRIN2B, MAPK10, MECP2, NRXN1, PCDH19, PNKP, RNASEH2A, RNASEH2B, RNASEH2C, SAMHD1, SCN1A, SCN1B, SCN2A, SCN9A, SLC2A1, SLC25A22, SLC9A6, SPTAN1, STXBP1, TCF4, TREX1, UBE3A, ZEB2	30 genes	[132]
Epilepsy with mental retardation	ARHGEF9, ARX, ATP6AP2, ATRX, CASK, CDKL5, CUL4B, CXORF5, DCX, FGD1, GPC3, GRIA3, HSD17B10, JARID1C, OPHN1, PAK3, PHF6, PLP1, PQBP1, RAB39B, SLC9A6, SMC1A, SMS, SRPX2, SYP	25 genes	[133]
Joubert syndrome (brain malformations)	AHI1, ARL13B, CC2D2A, CEP290, CXORF5, INPP5E, NPHP1, RPGRIP1L, TMEM67, TMEM216	10 genes	[46],[130],[134]

IV. THE FUTURE OF EPILEPSY BASED ON PHARMACOGENETICS AND PHARMACOGENOMICS APPROACH

A. Pharmacogenetics

Pharmacogenetics is the study of how an individual's genetics affects his or her response to drugs, combining traditional pharmaceutical sciences, such as biochemistry, with annotated knowledge of genes, proteins and single-nucleotide polymorphisms (SNPs) [136].

Pharmacogenetics aims to: [137]

- 1. Identify genetic variants that could explain variable response to AEDs (including drug resistance) and could potentially be used for treatment optimization in individual patients, resulting in a more targeted, more efficacious and less harmful treatment.
- 2. Aid development of new, more efficacious AEDs. As such, it could have important implications for the conduct of new AED trials.
- 3. Describe variation, either genetically or biochemically in a handful of proteins and genes.
- 4. Deliver a range of tests that could guide the clinician in his choice of treatment.

Ideally, pharmacogenetic studies should be conducted prospectively, i.e., patients should be genotyped before or at the time they start a specific drug, and then have their response studied over time and correlated to their genotype. Such studies are obviously more difficult to conduct than retrospective studies [138].

Moreover, recently several pharmaceutical companies have attempted to identify genetic variants that predict response to the drug ('efficacy pharmacogenetics') and genetic variants associated with toxicity ('safety pharmacogenetics') [139].

The potential advantages of epilepsy pharmacogenetics offer a revolutionary approach to clinical practice and the management of epilepsy. It can be used and developed as a tool during new drug trials and in the clinical setting as an effective treatment of epilepsy and as a guide to new AED development [136].

B. Pharmacogenomics

Pharmacogenomics is a more broad term that encompasses the influence of the wide range of tools of gene-based molecular science on pharmacology, including the strategy using the genetic association approach with new ways to design drugs and vaccines and also the goal of identifying genes that influence clinical response to drug treatment. Pharmacogenomic research has rapidly incorporated advances in biochemistry, molecular biology, cell biology, and genomics [140],[141].

Pharmacogenomic studies should consider non-genetic factors that can interact in influencing the phenotype. Pharmacogenomics will aid in understanding how genetics influence disease development, drug response, and contribute to discovery of new treatments [142].

Recent developments in genetic technology (including GWAS, Genome-wide association study) may facilitate the development of the best treatment for epilepsy. The effective crosscentre infrastructure of multinational collaboration will support and reinforce the developing platform and framework of epilepsy pharmacogenomics [143].

The roles of pharmacogenomics in clinical trials are: identification of variations in a large number of genes that affect drug action, stratification of patients in clinical trials according to genotype, reduction of the total number of patients required for clinical trials, reduction in drug development time by demonstrating efficacy in specific populations, prediction of drug-drug interactions, prediction of optimal doses of the drug in different patient populations, prediction of adverse reactions or therapeutic failures based on the genotype of the patient.¹⁴⁴ Moreover, steps in the application of pharmacogenomics in clinical trials are: [144]

- 1. Identification of the mechanism of action of drug
- 2. Identification of the target for drug action
- 3. Identification of the candidate gene
- 4. Clinical trials for relationship between candidate gene variants and efficacy/safety sequence
- 5. Controlled clinical trials on populations stratified by genotyping sequence

A conceptual framework that outlines the pharmacogenetic and pharmacogenomic aspects of epilepsy is proposed and summarized in **TABLE XI**.

Pharmacogenetics implies the study of a single gene whereas pharmacogenomics implies the study of many genes or entire genomes. Moreover, pharmacogenomics covers levels above that of DNA, such as mRNA or proteins, and thus relates more to drug development than does pharmacogenetics [156].

The main candidate gene categories in epilepsy pharmacogenetics are: genes affecting pharmacokinetics, e.g., drug transporter and drug-metabolizing enzyme-encoding genes, genes influencing pharmacodynamics, e.g., drug target-encoding genes, genetic factors relating to the epilepsy itself, and others, e.g., genes encoding immune factors implicated in idiosyncratic drug reactions [157].

Established genetic associations in epilepsy pharmacogenetics include cytochrome P450(CYP)2C9 alleles. doses and levels of the AED phenytoin. A functional polymorphisms in the voltage-gated neuronal sodium channel gene SCN1A, doses of phenytoin and carbamazepine, the human leukocyte antigen (HLA)-B*1502 allele and Stevens-Johnson syndrome on carbamazepine [158].

New technologies for comprehensive genomic analysis have already been applied. Therefore, a combination of research strategies may lead to a better understanding of treatment effects and management in epilepsy.

Anti Epileptic Drugs (AED)			Main Target [136],[151]
Carbamazepine	azepine MDR1, MRP2 Epoxidation (CYP3A4>CYP1A2, CYP2C8), hydrolysis (mEH); glucuronidation (UGT2B7); inhibition of voltage-dependent sodium conductance; action on monoamine, acetylcholine, and NMDA receptors		VG Na ⁺ channels
Felbamate	MDR1	60% hydroxylation (CYP3A4, CYP2E1OCYP2C19); conjugation; 40% unchanged renal excretion; inhibition of NMDA receptor (glycine recognition site) and sodium-channel conductance	NMDA receptors
Gabapentin	MDR1, LNAA	> 95% unchanged renal excretion; elevates GABA concentrations in the occipital cortex of epileptic patients [152].	Binds to the alpha-2-delta subunit of the L-type VG calcium channel [153]
Lamotrigine	MDR1	Glucuronidation (UGT1A4); inhibition of voltage-dependent sodium conductance; block voltage-sensitive calcium channels; selectively target neurons that synthesizes glutamate and aspartate [154].	VG Na ⁺ channels
Pregabalin	LNAA	98% unchanged renal excretion; binds to alpha-2-delta subunit of the voltage-gated calcium channel, reduces release of glutamate and other excitatory neurotransmitters	VG Ca2 ⁺ channel alpha-2-delta-subunit
Phenobarbital	MDR1	8–34% hydroxylation (CYP2C9, CYP2C19OCYP2E1); glucuronidation; N-glucosidation; epoxidation, hydrolysis (mEH); enhances activity of GABA-A receptor; depresses glutamate excitability, and affects sodium, potassium and calcium conductance	GABA _A receptor
Phenytoin	MDR1, MRP2	Hydroxylation (~90% CYP2C9, ~10% CYP2C19), hydrolysis (mEH), or GSH and GST; glucuronidation; inhibition of voltage-dependent sodium channels	VG Na ⁺ channels
Topiramate	MDR1	80% unchanged renal excretion; 20% hydroxylation (CYP2C19) and glucuronidation; inhibition of voltage-gated sodium channels; potentiation of GABA-mediated inhibition at the GABA-A receptor; reduction of AMPA receptor activity; inhibition of high-voltage calcium channels; carbonic anhydrase activity	VG Na $^+$ channels
Valproate (sodium valproate)	MRP	beta-oxidation; glucuronidation; CYP2A6, CYP2C9, CYP2C19; effects on GABA and glutaminergic activity, calcium (T) conductance and potassium conductance; decreases brain concentrations of the excitatory amino acid aspartate without influencing those of glutamate or GABA; elevates brain GABA levels and potentiates GABA responses [155].	Blockade of neuronal sodium channels in a voltage-and frequency-dependent manner [150].

TABLE XI EPILEPSY PHARMACOGENETICS AND PHARMACOGENOMICS

S-transferase; NMDA, N-methyl-D-aspartate; AMPA, aminohydroxymethylisozole propionic acid. GABA, gamma-aminobutyric acid. VG, voltage gated.

C. Future therapeutic directions

Clinical trials to develop new therapies of epilepsy diseases in the next few years will be very expensive. The development of medicine may make testing these new therapies more economical by allowing the selection of patients who are most likely to respond to a given treatment. Controlled clinical trials are required to use a comparator group, and trial designs range from using true placebo treatments to using comparisons or add on therapies as compared to the control groups receiving the current standard of care. Improving the ability to identify subsets of patients who are more likely to respond biologically to a given agent would allow a more robust comparison between a treatment and a control group, expose less patients inappropriately to a test treatment, as well as increase the efficiency and reduce the costs of clinical trials. Drugs with apparently equivalent efficacy in an entire population may show particular benefits in different subsets of these populations.

1) Stem Cell Therapy

Stem cell-based epileptic therapies have the potential to repair and even correct the defects related to brain human diseases. Although stem cell applications have moved forward in the clinical setting, progress is slow, and ethical challenges have yet to be definitively addressed. The goal of developing pluripotent cells that can transmute to organ-specific maturity

at our direction and possibly cure many brain human diseases has yet to be attained [159].

With recent advances, however, gene correction involving stem cells is becoming closer. Although techniques for correcting genetic abnormalities have been available in the laboratory for years, the tools for manipulating the genome tend to leave traces of unwanted genetic material within the cell or within the genes themselves.

2) Gene Therapy

Gene therapy is a novel form of drug delivery that enlists the synthetic machinery of the patient's cells to produce a therapeutic agent. Using the body to treat its own disease overcomes the need to manufacture highly purified proteins. It also eliminates the need for repeated parenteral administration of proteins or drugs and reduces the difficulties of complying with exogenous-drug regimens. Applications of gene therapy are not limited to rare inherited diseases, but extend potentially to common acquired disorders, including epilepsy, brain disorder, cancer, heart disease, and the acquired immunodeficiency syndrome [160].

Gene therapy is likely to have broad implications for the future practice of medicine. An important aspect of gene-delivery systems is the ability to regulate the expression of the introduced gene. With the vectors that are now approved

for gene therapy, cells express the genes continuously. As a result, the production of the therapeutic protein cannot be modulated. In diseases such as epilepsy regulation of the new gene is critical . In most other diseases, gene regulation is desirable; indeed, constitutive expression of the introduced gene may be detrimental or even life-threatening. To overcome this problem, yeast-gene or bacterial-gene regulatory systems have been adapted for use in mammalian cells. These inducible systems appear advantageous because they affect the expression of introduced, but not resident genes. There is no toxicity and the gene-inducing agent can be administered

orally.

In principle, these new regulatory systems allow genes to be turned on and off and the level of the therapeutic protein varied over time. The complex goal of regulating genes through the use of endogenous biologic signals is also being pursued, but will take time to reach the epileptic therapy. One preclinical trial belonging to gene therapy, involves use allatostatin receptor (AlstR)/ligand system to regulate inhibitory neuron to make synchrony of brain functions by electrophysiology, laser scanning photostimulation, and voltage-sensitive dye imaging methods. The AlstR approach represents an important advancement for genetic manipulation of neuronal activity that can be valuable for many basic applications. The AlstR system can also be potentially used in translational applications, in seizure control and epilepsy treatment as a molecular anticonvulsant with few side effects [161].

V. SUMMARY

Epilepsy affects millions of peoples in the world. The disorder requires the participation of all parties, from families, physicians, researchers, and of course the government. A combination of research strategies and prudent policies from government may lead to a better understanding of treatment effects and realistic management of epilepsy.

DISCLOSURE

The authors report no conflicts of interest in this work.

ACKNOWLEDGMENT

The Author would like to thank Drs. Stephen C. Bondy and Andrew San Antonio for their critical reading of the manuscript and helpful revision comments.

REFERENCES

- [1] Pestronk A. The first neurology book written in English (1650) by Robert Pemell. De Morbis Capitis. Arch Neurol 1989;46:215-20. <u>CrossRef</u>
- [2] Nathan BN. The medical aphorisms of Muhammad the Prophet of Islam: a translation. Am J Chin Med 1991;19:79-81. <u>CrossRef</u>
- [3] Temkin O. The Falling Sickness: A History of Epilepsy from the Greeks to the Beginning of Modern Neurology. Baltimore: The Johns Hopkins University. 1945:8.
- [4] Rossetti AO, Bogousslavsky J. Dostoevsky and Epilepsy: An Attempt to Look Through the Frame. In: Bogousslavsky J, Boller F (eds): Neurological Disorders in Famous Artists. Front Neurol Neurosci. Basel, Karger, 2005, vol 19, pp 65–75. <u>CrossRef</u>

[5] ILAE Commission Report (Blume-Chair WT, Lüders HO, Mizrahi E, Tassinari C, van Emde Boas W, Engel J). Glossary of Descriptive Terminology for Ictal Semiology: Report of the ILAE Task Force on Classification and Terminology. Epilepsia 2001;42(9):1212-1218.

38

- [6] Chadwick D. Epilepsy. Journal of Neurology, Neurosurgery, and Psychiatry 1994;57:264-277. <u>CrossRef</u>
- [7] Senanayake N. Classification of Epilepsies and Epileptic Syndromes Using the 1989 International League Against Epilepsy Classification: A Hospital-Based Study of 1250 Patients in a Developing Country. J Epilepsy 1995;8:33-40. <u>CrossRef</u>
- [8] Commission on Classification and Terminology of the International League Against Epilepsy. Proposal for revised clinical and electroencephalographic classification of epileptic seizures. Epilepsia.1981;22:489-501. <u>CrossRef</u>
- [9] Vezzani A, French J, Bartfai T, Baram TZ. The role of inflammation in epilepsy. Nat Rev Neurol. 2011;7:31–40. <u>CrossRef</u>
- [10] Hauser AW, Hesdorffer DC. Epilepsy: Frequency, causes and consequences. Landover, MD: Epilepsy Foundation of America Publications.1990.
- [11] Tatum IV WO, Kaplan PW, Jallon P. Epilepsy A to Z: A Concise Encyclopedia. Second Edition. Demos Medical Publishing. New York. 2009.
- [12] Engel J Jr. A proposed diagnostic scheme for people with epileptic seizures and with epilepsy: report of the ILAE Task Force on Classification and Terminology. Epilepsia 2001;42:796-803. CrossRef
- [13] Epilepsy Foundation of America. 2008. Cited from: http://www.epilepsyfoundation.org/about/statistics.cfm
- [14] Murray A, Falconer. Mesial Temporal (Ammon's Horn) Sclerosis as A Common Cause of Epilepsy.The Lancet. Sep 1974;304(7883):767-770. <u>CrossRef</u>
- [15] Raspall-Chaure M, Neville BG, Scott RC. The medical management of the epilepsies in children: conceptual and practical considerations. Lancet Neurol 2008;7:57-69. <u>CrossRef</u>
- [16] Baraister M. In: The Genetics of Neurological Disorders, second ed. Oxf. Monogr. Med. Genet., No. 18 Oxford University Press. New York. 1990. pp. 96-113.
- [17] Posner EB, Mohamed KK, Marson AG. Ethosuximide, sodium valproate or lamotrigine for absence seizures in children and adolescents. Cochrane Database of Systematic Reviews 2005, Issue 4. Art. No.: CD003032. <u>CrossRef</u>
- [18] Kwan P, Brodie MJ. Refractory epilepsy: mechanisms and solutions. Expert Rev Neurother 2006;6:397–406. <u>CrossRef</u>
- [19] Forsgren L, Beghi E, Oun A, Sillanpaa M. The epidemiology of epilepsy in Europe–a systematic review. Eur J Neurol 2005;12:245–253. <u>CrossRef</u>
- [20] Duncan JS, Sander JW, Sisodiya SM, Walker MC. Adult epilepsy. Lancet 2006;367:1087–1100. <u>CrossRef</u>
- [21] De la Court A, Breteler MMB, Meinardi H, Hauser A, Hofman A. Prevalence of Epilepsy in the Elderly. Epilepsia, 1996;37(2):141-147. <u>CrossRef</u>
- [22] Sander JW, Shorvon SD. Epidemiology of the epilepsies. Journal of Neurology, Neurosurgery and Psychiatry 1996;61:433-443. CrossRef
- [23] Bell GS, Sander JW. The epidemiology of epilepsy: the size of the problem. Seizure 2001;10:306-316. <u>CrossRef</u>
- [24] Arts WF, Brouwer OF, Peters AC, et al. Course and prognosis of childhood epilepsy: 5-year follow-up of the Dutch study of epilepsy in childhood. Brain 2004;127:1774-84. <u>CrossRef</u>
- [25] Sander JW, Hart YM, Johnson AL, Shorvon SD. National General Practice Study of Epilepsy: newly diagnosed epileptic seizures in a general population. Lancet 1990;336:1267-1271. <u>CrossRef</u>
- [26] Macdonald B. The prognosis of epilepsy. Seizure 2001;10:347-358. CrossRef
- [27] Sander JW, Sillanpaa M. Natural history and prognosis. In: Epilepsy: A Comprehensive Textbook (Eds J. Engel and T.A. Pedley). Philadelphia, Lippincott-Raven Publishers, 1997:pp.69-86.

- [28] Hopkins A, Garman A, Clarke C. The first seizure in adult life: value of clinical features, electroencephalogram, and computerized tomography scanning in prediction of recurrence. Lancet 1988;721-726. <u>CrossRef</u>
- [29] Hart YM, Sander JWAS, Johnson AL, Shorvon SD. National general practice study of epilepsy: recurrence after a first seizure. Lancet 1990;336:1271-1274. <u>CrossRef</u>
- [30] Beghi E, Tognoni G. Prognosis of epilepsy in newly referred patients: a multicenter prospective study. Collaborative group for the study of epilepsy. Epilepsia 1988;29:236-243. <u>CrossRef</u>
- [31] Musicco M, Beghi E, Solari A, Viani F, FIRST Group. Treatment of first tonic-clonic seizure does not improve the prognosis of epilepsy. Neurology 1997;49:991-998. <u>CrossRef</u>
- [32] Hauser WA, Anderson VE, Loewenson RB, McRoberts SM. Seizure recurrence after a first unprovoked seizure. NEJM 1982;307:522-528. CrossRef
- [33] Annegers JF, Shirts SB, Hauser WA, Kurland LT. Risk of recurrence after an initial unprovoked seizure. Epilepsia 1986;27:43-50. <u>CrossRef</u>
- [34] Goodridge DM, Shorvon SD. Epileptic seizures in a population of 6000.
 II: Treatment and prognosis. British Medical Journal: Clinical Research Edition 1983;287:645-647. CrossRef
- [35] Camfield PR, Camfield CS, Smith EC, Tibbles JA. Newly treated childhood epilepsy: a prospective study of recurrences and side effects. Neurology 1985;35:722-753. <u>CrossRef</u>
- [36] Shinnar S, Berg AT, Moshe SL, et.al. Risk of seizure recurrence following a first unprovoked seizure in childhood: a prospective study. Pediatrics 1990;85:1076-1085.
- [37] Camfield PR, Camfield CS, Dooley JM, Tibbles JA, Fung T, Garner B. Epilepsy after a first unprovoked seizure in childhood. Neurology 1985;35:1657-1660. CrossRef
- [38] Jennett BW, Lewin W. Traumatic epilepsy after closed head injuries. Journal of Neurology, Neurosurgery and Psychiatry 1960;23:295-301. <u>CrossRef</u>
- [39] Annegers JF, Grabow JD, Groover RV, Laws ER Jr, Elveback LR, Kurland LT. Seizures after head trauma: a population study. Neurology 1980;30:683-689. <u>CrossRef</u>
- [40] Berg AT, Shinnar S. The risk of seizure recurrence following a first unprovoked seizure: a quantitative review. Neurology 1991;41:965-972. <u>CrossRef</u>
- [41] Cleland PG, Mosquera I, Steward WP, Foster JB. Prognosis of isolated seizures in adult life. British Medical Journal 1981;283:1364. <u>CrossRef</u>
- [42] First seizure trial group. Randomized clinical trial on the efficacy of antiepileptic drugs in reducing the risk of relapse after a first unprovoked tonic-clonic seizure (FIRST Group). Neurology 1993;43:478-483. CrossRef
- [43] Berg AT, Shinnar S, Levy SR, Testa FM, Smith-Rapaport S, Beckerman B. Early development of intractable epilepsy in children: a prospective study. Neurology 2001;56:1445-52. <u>CrossRef</u>
- [44] Huttenlocher PR, Hapke RJ. A follow-up study of intractable seizures in childhood. Ann Neurol 1990;28:699-705. <u>CrossRef</u>
- [45] Macdonald B. The prognosis of epilepsy. Seizure 2001;10:347-358. CrossRef
- [46] Bell B, Lin JJ, Seidenberg M, Hermann B. The neurobiology of cognitive disorders in temporal lobe epilepsy. Nat Rev Neurol.2011;7:154–164. <u>CrossRef</u>
- [47] Andrade-Valença LP, Dubeau F, Mari F, Zelmann R, Gotman J. Interictal scalp fast oscillations as a marker of the seizure onset zone. Neurology 2011;77:524–531. <u>CrossRef</u>
- [48] Cendes F, Engel J Jr. Extending applications for high-frequency oscillations: the ripple effect. Neurology 2011;77:518–519. <u>CrossRef</u>
- [49] Cendes F. Nat Rev Neurol.2012;8:70-71. CrossRef
- [50] Reynolds EH, Elwes RDC, Shorvon SD. Why Does Epilepsy Become Intractable? The Lancet. Oct 1983;322(8356):952-954. <u>CrossRef</u>
- [51] Blumer D, Montouris G, Davies K, Wyler A, Phillips B, Hermann B. Suicide in epilepsy: psychopathology, pathogenesis, and prevention. Epilepsy & Behavior June 2002;3(3):232–241. <u>CrossRef</u>

- [52] Philippe R, Alexandra M, Philippe K. Sudden unexpected death in epilepsy: from mechanisms to prevention. Current Opinion in Neurology. Apr 2006;19(2):194-199. <u>CrossRef</u>
- [53] World Health Organization. Research protocol for measuring the prevalence of neurological disorders in developing countries. Geneva: World Health Organization, Neurosciences Program, 1981.
- [54] Wang L, Pan Y, Chen D, Xiao Z, Xi Z, Xiao F, Wang X. Tetranectin is a potential biomarker in cerebrospinal fluid and serum of patients with epilepsy. Clinica Chimica Acta 2010;411:581–583. <u>CrossRef</u>
- [55] Clemmensen I, Petersen LC, Kluft C. Purification and characterization of a novel, oligomeric, plasminogen kringle 4 binding protein from human plasma: tetranectin. Eur J Biochem 1986;156:327–33. <u>CrossRef</u>
- [56] Holtet TL, Graversen JH, Clemmensen I, Thogersen HC, Etzerodt M. Tetranectin, a trimeric plasminogen-binding C-type lectin. Protein Sci 1997;6:1511–5. <u>CrossRef</u>
- [57] Christensen L, Clemmensen I. Tetranectin immunoreactivity in normal human tissues. An immunohistochemical study of exocrine epithelia and mesenchyme. Histochemistry 1989;92:29–35. <u>CrossRef</u>
- [58] Stoevring B, Jaliashvili I, Thougaard AV, et al. Tetranectin in cerebrospinal fluid: biochemical characterisation and evidence of intrathecal synthesis or selective uptake into CSF. Clin Chim Acta 2005;359:65–71. <u>CrossRef</u>
- [59] Christensen L, Johansen N, Jensen BA, Clemmensen I. Immunohistochemical localization of a novel, human plasma protein, tetranectin, in human endocrine tissues. Histochemistry 1987;87:195–9. CrossRef
- [60] Chadwick D, Smith D. The misdiagnosis of epilepsy. Br Med J 2002; 234:495–6. <u>CrossRef</u>
- [61] De Smedt T, Vonek K, Raedt R, et al. Rapid kindling in preclinical antiepilepsy drug development. The effect of levetiracetam. Epilepsy Res Suppl 2005;67:109-116. <u>CrossRef</u>
- [62] Aroniadou-Anderjaskaa V, Fritsch B, Qashub F, Bragaa MFM. Pathology and pathophysiology of the amygdala in epileptogenesis and epilepsy. Epilepsy Research 2008;78: 102—116. <u>CrossRef</u>
- [63] Engel J. Seizures and Epilepsy. F.A. Davis, Philadelphia.1989.
- [64] Delgado-Escueta AV, Horan MP. Neurobiology. General principles related to epilepsy. In: Glaser GH, Penry JK, Woodbury DM (ed.) Antiepileptic drugs. Mechanisms of action, New York: Raven Press, 1980, pp.85-126.
- [65] Feldblum S, Rougier A, Loiseau H, Cohadon F, Morselli PL, Lloyd KG. Quinolinic-phosphoribosyl transferase activity is decreased in epileptic human tissue. Epilepsia 1988;29:523-9. <u>CrossRef</u>
- [66] Van Gelder NM, Sherwin AL, Rasmussen T. Amino acid content of epileptogenic human brain: focal vs. surrounding regions. Brain Res 1972;40:385-93. <u>CrossRef</u>
- [67] Ure JA, Perassolo M. Update on the pathophysiology of the epilepsies. Journal of the Neurological Sciences 2000;177:1–17. <u>CrossRef</u>
- [68] Jacobs KM, Kharazia VN, Prince DA. Mechanisms underlying epileptogenesis in cortical malformations. Epilepsy Res 1999;36:165-188. <u>CrossRef</u>
- [69] Chapman AG. Glutamate receptors in epilepsy. Prog Brain Res 1998;116:371-383. CrossRef
- [70] Yi JH, Hazell AS, Excitotoxic mechanisms and the role of astrocytic glutamate transporters in traumatic brain injury. Neurochem Int 2006;48:394—403. <u>CrossRef</u>
- [71] DeLorenzo RJ, Sun DA, Deshpande LS. Erratum to "Cellular mechanisms underlying acquired epilepsy: the calcium hypothesis of the induction and maintenance of epilepsy" [Pharmacol. Ther. 105(3) (2005) 229—266]. Pharmacol Ther 2006;111:288—325. CrossRef
- [72] McNamara JO, Huang YZ, Leonard AS. Molecular signaling mechanisms underlying epileptogenesis. Sci. STKE 2006,re12.
- [73] Hara M, Sasa M, Kawabata A, Serikawa T, Yamada T. et al. Decreased dopamine and increased norepinephrine levels in the spontaneously epileptic rat, a double mutant rat. Epilepsia 1993;34:433-440. <u>CrossRef</u>
- [74] Mori A, Hiramatsu M, Namba S, Nishimoto A, Ohmoto T, et al. Decreased dopamine level in the epileptic focus. Res Commun Chem Path Pharmacol 1987;56:157-164.

- [75] Engelborghs S, D'Hooge R, De Deyn PP. Pathophysiology of epilepsy. Acta Neurol Belg 2000;100:201-213.
- [76] White LE, Price JL. The functional anatomy of limbic status epilepticus in the rat. I. Patterns of 14C-2-deoxyglucose uptake and Fos immunocytochemistry. J. Neurosci. 1993;13:4787—4809.
- [77] White LE, Price JL. The functional anatomy of limbic status epilepticus in the rat. II. The effects of focal deactivation. J. Neurosci. 1993;13:4810—4830.
- [78] Pitkanen A, Tuunanen J, Kalviainen R, Partanen K, Salmenpera T. Amygdala damage in experimental and human temporal lobe epilepsy. Epilepsy Res. 1998;32:233—253. <u>CrossRef</u>
- [79] Bernasconi N, Natsume J, Bernasconi A. Progression in temporal lobe epilepsy: differential atrophy in mesial temporal structures.Neurology 2005;65:223—228. <u>CrossRef</u>
- [80] Salmenpera T, Kalviainen R, Partanen K, Pitkanen A. Hippocampal and amygdaloid damage in partial epilepsy: a cross-sectional MRI study of 241 patients. Epilepsy Res 2001;46:69—82. <u>CrossRef</u>
- [81] Guerreiro C, Cendes F, Li LM, Jones-Gotman M, Andermann F, Dubeau F, Piazzini A, Feindel W. Clinical patterns of patients with temporal lobe epilepsy and pure amygdalar atrophy. Epilepsia 1999;40:453—461. CrossRef
- [82] Comair Y, Tocco G, Najm I, Kaakaji R, Luders H, Baudry M. Changes in hippocampal glutamate/AMPA receptors in epileptic human hippocampus. Soc Neurosci Abstr 1994;20:1452.
- [83] Telfeian AE, During M, Federoff HJ, Mirchandani G, Williamson A. Long term changes in hippocampal excitability following overexpression of GluR6. Soc Neurosci Abstr 1994;20:1667.
- [84] Vezzani A, Granata T. Brain inflammation in epilepsy: experimental and clinical evidence. Epilepsia 2005;46:1724–1743. <u>CrossRef</u>
- [85] Vezzani A, Balosso S, Ravizza T. The role of cytokines in the pathophysiology of epilepsy. Brain, Behavior, and Immunity 2008;22:797–803. <u>CrossRef</u>
- [86] Seifert G, Schilling K, Steinhauser C. Astrocyte dysfunction in neurological disorders: a molecular analysis. Nat Neurosci 2006;7:194– 206. <u>CrossRef</u>
- [87] Boer K, Spliet WG, van Rijen PC, Redeker S, Troost D, Aronica E. Evidence of activated microglia in focal cortical dysplasia. J Neuroimmunol 2006;173:188–195. <u>CrossRef</u>
- [88] Ravizza T, Gagliardi B, Noe F, Boer K, Aronica E, Vezzani A. Innate and adaptive immunity during epileptogenesis and spontaneous seizures: evidence from experimental models and human temporal lobe epilepsy. Neurobiol Dis 2008;29:142–160. <u>CrossRef</u>
- [89] Peltola J, Palmio J, Korhonen L, Suhonen J, Miettinen A, Hurme M, Lindholm D, Keranen T. Interleukin-6 and interleukin-1 receptor antagonist in cerebrospinal fluid from patients with recent tonic-clonic seizures. Epilepsy Res 2000;41:205–211. CrossRef
- [90] Ravizza T, Boer K, Redeker S, Spliet WG, van Rijen PC, Troost D, Vezzani A, Aronica E. The IL-1beta system in epilepsy-associated malformations of cortical development. Neurobiol Dis 2006;24:128–143. <u>CrossRef</u>
- [91] Vezzani A, Baram TZ. New roles for interleukin-1beta in the mechanism of epilepsy. Epilepsy Curr 2007;7:45–50. <u>CrossRef</u>
- [92] French JA, Kanner AM, Bautista J, et al. Efficacy and tolerability of the new antiepileptic drugs. I. Treatment of new onset epilepsy: report of the Therapeutics and Technology Assessment Subcommittee and Quality Standards Subcommittee of the American Academy of Neurology and the American Epilepsy Society. Neurology 2004;62:1252-1260. CrossRef
- [93] Perucca E, Gram L, Avanzini G, Dulac O. Antiepileptic drugs as a cause of worsening seizures. Epilepsia 1998;39:5-17. <u>CrossRef</u>
- [94] Kwan P, Brodie MJ. Early identification of refractory epilepsy. N Engl J Med 2000;342:314-319. <u>CrossRef</u>
- [95] Winkler SR, Luer MS. Antiepileptic Drug Review: Part 1. Surg Neurol 1998;49:449-52. CrossRef
- [96] Wesnes KA, Edgar C, Dean AD, Wroe SJ. The cognitive and psychomotor effects of remacemide and carbamazepine in newly

diagnosed epilepsy. Epilepsy Behav.2009 Mar;14(3):522-8. Epub 2008 Dec 25. CrossRef

40

- [97] Wesnes KA, Edgar C, Dean AD, Wroe SJ. The cognitive and psychomotor effects of remacemide and carbamazepine in newly diagnosed epilepsy. Epilepsy Behav. 2009 Mar;14(3):522-8. Epub 2008 Dec 25. <u>CrossRef</u>
- [98] Anandam R. Clobazam in epilepsy. Indian J Pediatr. 2000 Jan;67(1 Suppl):S88-91.
- [99] Bawden HN, Camfield CS, Camfield PR, Cunningham C, Darwish H, Dooley JM, et.al. The cognitive and behavioural effects of clobazam and standard monotherapy are comparable. Canadian Study Group for Childhood Epilepsy. Epilepsy Res. 1999 Feb;33(2-3):133-43. <u>CrossRef</u>
- [100] Allen JW, Oxley J, Robertson MM. Clobazam as adjunctive treatment in refractory epilepsy. BMJ 1983;286:1246-7. <u>CrossRef</u>
- [101] Sheth RD, Goulden KJ, Ronen GM. Aggression in children treated with clobazam for epilepsy. Clin Neuropharm 1994;17(4):332-337. <u>CrossRef</u>
- [102] Scott DF, Moffett A. The long-term effect of clobazam as adjunctive therapy in epilepsy. Acta Neurologica Scandinavica. 1988;77(6):498– 502. <u>CrossRef</u>
- [103] Remy C. Clobazam in the treatment of epilepsy: a review of the literature. Epilepsia. 1994;35 Suppl 5:S88-91. <u>CrossRef</u>
- [104] Shorvon SD. Handbook of Epilepsy Treatment Forms, Causes and Therapy in Children and Adults. 2nd edition. Blackwell Publishing Ltd. USA. 2005;Chapter 3:p.114-196. <u>CrossRef</u>
- [105] Pinder RM, Brogden RN, Speight TM, Avery GS. Clonazepam: a review of its pharmacological properties and therapeutic efficacy in epilepsy. Drugs 1976;12(5):321-361. <u>CrossRef</u>
- [106] Morishita S. Clonazepam as a therapeutic adjunct to improve the management of depression: a brief review. Hum. Psychopharmacol. Clin. Exp. 2009;24:191–198. <u>CrossRef</u>
- [107] Hall JH, Marshall PC. Clonazepam therapy in reading epilepsy. Neurology May 1,1980;30(5):550. <u>CrossRef</u>
- [108] Dahlin MG, Amark PE, Nergårdh AR. Reduction of seizures with low-dose clonazepam in children with epilepsy.Pediatr Neurol 2003;28(1):48-52. <u>CrossRef</u>
- [109] Wallace SJ.Myoclonus and epilepsy in childhood: A review of treatment with valproate, ethosuximide, lamotrigine and zonisamide. Epilepsy Research 1998;29(2):147-154. <u>CrossRef</u>
- [110] Glauser TA, Cnaan A, Shinnar S, Hirtz DG, Dlugos D, Masur D. Ethosuximide, Valproic Acid, and Lamotrigine in Childhood Absence Epilepsy. N Engl J Med 2010;362:790-9. <u>CrossRef</u>
- [111] Tomson T, Battino D. Teratogenic effects of antiepileptic drugs. Lancet Neurol July 16,2012:1-11. <u>CrossRef</u>
- [112] Wilder RM. The effect of ketonemia on the course of epilepsy. Mayo Clin Bulletin 1921; 2:307–308.
- [113] Rudderham M, Laff R, Devinsky O.Nutrition and Epilepsy. In: Devinsky O, Schachter S, Pacia S.(Eds) Complementary and Alternative Therapies for Epilepsy. Demos Medical Publishing. New York.2005.Chapter 19,page 191.
- [114] Kossoff EH, Hartman AL. Ketogenic diets: new advances for metabolism-based therapies. Curr Opin Neurol 2012;25:173–178. CrossRef
- [115] Masino SA, Li T, Theofilas P, et al. A ketogenic diet suppresses seizures in mice through adenosine A1 receptors. J Clin Invest 2011;121:2679– 2683. <u>CrossRef</u>
- [116] Szot P, Weinshenker D, Rho JM, et al. Norepinephrine is required for the anticonvulsant effect of the ketogenic diet. Brain Res Dev Brain Res 2001;129:211–214. <u>CrossRef</u>
- [117] Martillotti J, Weinshenker D, Liles LC, Eagles DA. A ketogenic diet and knockout of the norepinephrine transporter both reduce seizure severity in mice. Epilepsy Res 2006; 68:207–211. <u>CrossRef</u>
- [118] Ahola-Erkkila S, Carroll CJ, Peltola-Mjosund K, et al. Ketogenic diet slows down mitochondrial myopathy progression in mice. Hum Mol Genet 2010;19:1974–1984. <u>CrossRef</u>

- [119] Milder JB, Liang LP, Patel M. Acute oxidative stress and systemic Nrf2 activation by the ketogenic diet. Neurobiol Dis 2010;40:238–244. CrossRef
- [120] Kossoff EH, Zupec-Kania BA, Amark PE, et al. Optimal clinical management of children receiving the ketogenic diet: recommendations of the International Ketogenic Diet Study Group. Epilepsia 2009; 50:304– 317. <u>CrossRef</u>
- [121] Groomes LB, Pyzik PL, Turner Z, et al. Do patients with absence epilepsy respond to ketogenic diets? J Child Neurol 2011; 26:1601–1605. <u>CrossRef</u>
- [122] Kossoff EH, Bosarge JL, Comi AM. A Pilot Study of the Modified Atkins Diet for Sturge-Weber Syndrome. Epilepsy Res 2010; 92:240–243. CrossRef
- [123] Chapman KE, Kim DY, Rho JM, et al. Ketogenic diet in the treatment of seizures associated with hypothalamic hamartomas. Epilepsy Res 2011;94:218–221. <u>CrossRef</u>
- [124] Baranano KW, Hartman AL. The ketogenic diet: uses in epilepsy and other neurologic illnesses. Curr Treat Options Neurol 2008; 10:410–419. CrossRef
- [125] Nabbout R, Mazzuca M, Hubert P, et al. Efficacy of ketogenic diet in severe refractory status epilepticus initiating fever induced refractory epileptic encephalopathy in school age children (FIRES). Epilepsia 2010;51:2033–2037. CrossRef
- [126] Bergqvist AG, Schall JI, Gallagher PR, et al. Fasting versus gradual initiation of the ketogenic diet: a prospective, randomized clinical trial of efficacy. Epilepsia 2005;46:1810–1819. <u>CrossRef</u>
- [127] Bergqvist AG, Schall JI, Stallings VA. Vitamin D status in children with intractable epilepsy, and impact of the ketogenic diet. Epilepsia 2007;48:66–71. <u>CrossRef</u>
- [128] McNally MA, Pyzik PL, Rubenstein JE, et al. Empiric use of oral potassium citrate reduces symptomatic kidney stone incidence with the ketogenic diet. Pediatrics 2009; 124:e300–e304. <u>CrossRef</u>
- [129] Cossette P. Channelopathies and juvenile myoclonic epilepsy. Epilepsia 2010;51(1):30–32. <u>CrossRef</u>
- [130] Garofalo S, Cornacchione M, Di Costanzo A. From Genetics to Genomics of Epilepsy. Hindawi Publishing Corporation Neurology Research International Volume 2012, Article ID 876234, 18 pages. <u>CrossRef</u>
- [131] Beghi E, "The concept of the epilepsy syndrome: how useful is it in clinical practice?" Epilepsia 2009;50(5):4–10. <u>CrossRef</u>
- [132] Nicita F, De Liso P, Danti FR, et al. The genetics of monogenic idiopathic epilepsies and epileptic encephalopathies. Seizure.2012;21(1):3–11. CrossRef
- [133] Xiang B, Zhu H, Shen Y, et al., "Genome-wide oligonucleotide array comparative genomic hybridization for etiological diagnosis of mental retardation: a multicenter experience of 1499 clinical cases," Journal of Molecular Diagnostics 2010;12(2):204–212. CrossRef
- [134] Prince E, Ring H. Causes of learning disability and epilepsy: a review. Current Opinion in Neurology 2011;24(2):154–158. <u>CrossRef</u>
- [135] Vogel F. Moderne probleme der humangenetik. Ergeb Inn Med Kinderheilkd 1959;12:52–125. <u>CrossRef</u>
- [136] Depondt C. The potential of pharmacogenetics in the treatment of epilepsy. Eur J Paed Neurol 2006;10:57–65. CrossRef
- [137] Szoeke CEI, Newton M, Wood JM, Goldstein D, Berkovic SF, OBrien TJ, Sheffield LJ. Update on pharmacogenetics in epilepsy: a brief review.Lancet Neurol 2006;5:189–96. <u>CrossRef</u>
- [138] Roses AD. Pharmacogenetics and the practice of medicine. Nature 2000;405:857–865. <u>CrossRef</u>
- [139] Roses AD. Pharmacogenetics and drug development, the path to safer and more effective drugs. Nature Rev Genet 2004;5(9):645-656. <u>CrossRef</u>
- [140] Rusnak JM, Kisabeth RM, Herbert DP, McNeil DM, Pharmacogenomics: a clinician's primer on emerging technologies for improved patient care. Mayo Clin Proc.2001;76:299–309. <u>CrossRef</u>
- [141] Evans WE, McLeod HL. Pharmacogenomics, drug disposition, drug targets, and side effects. N Engl J Med.2003;348:538–549. CrossRef
- [142] Evans WE, Relling MV. Moving towards individualized medicine with pharmacogenomics. Nature 2004;429(6990):464-468. <u>CrossRef</u>

- [143] Cavalleri GL, McCormack M, Alhusaini S, Chaila E, Delanty N. Pharmacogenomics and epilepsy: the road ahead. Pharmacogenomics 2011;12(10):1429–1447. <u>CrossRef</u>
- [144] Anurogo D. Pharmacogenetic and Pharmacogenomic: The Art of Bipolar Disorder Management. First Bipolar National Conference, 9-10 March 2012, Sheraton Hotel, Surabaya.
- [145] Loscher W, Potschka H. Role of multidrug transporters in pharmacoresistance to antiepileptic drugs. J Pharmacol Exp Ther 2002;301(1):7–14. <u>CrossRef</u>
- [146] Jezyk N, Li C, Stewart BH, et al. Transport of pregabalin in rat intestine and Caco-2 monolayers. Pharm Res 1999;16:519–26. <u>CrossRef</u>
- [147] Shorvon SD. The treatment of epilepsy. Oxford: Blackwell Publishers; 2004. <u>CrossRef</u>
- [148] Patsalos PN, Froscher W, Pisani F, van Rijn CM. The importance of drug interactions in epilepsy therapy. Epilepsia 2002;43(4):365–85. CrossRef
- [149] Staines AG, Coughtrie MW, Burchell B. N-glucuronidation of carbamazepine in human tissues is mediated by UGT2B7. J Pharmacol Exp Ther 2004;311(3):1131–7. <u>CrossRef</u>
- [150] Sills GJ, Brodie MJ. Update on the mechanisms of action of antiepileptic drugs. Epileptic Disord 2001;3:165-72.
- [151] Kwan P, Sills GJ, Brodie MJ. The mechanisms of action of commonly used antiepileptic drugs. Pharmacol Ther 2001;90:21–34. <u>CrossRef</u>
- [152] Petroff OAC, Rothman DL, Behar KL et al. The effect of gabapentin on brain gamma-aminobutyric acid in patients with epilepsy. Ann Neurol 1996;39:95-9. <u>CrossRef</u>
- [153] Gee NS, Brown JP, Dissanayake VUK, et al. The novel anticonvulsant drug, gabapentin (Neurontin), binds to the alpha-2-delta subunit of a calcium channel. J Biol Chem 1996;271:5768-76. <u>CrossRef</u>
- [154] Stefani A, Spadoni F, Bernardi G. Voltage-activated calcium channels: targets of antiepileptic drug therapy? Epilepsia 1997;38:959-65. CrossRef
- [155] Löscher W. Valproate: a reappraisal of its pharmacodynamic properties and mechanisms of action. Prog Neurobiol 1999;58:31-59. <u>CrossRef</u>
- [156] Goldstein DB, Tate SK, Sisodiya SM. Pharmacogenetics Goes Genomic. Nature Reviews Genetics. Dec 2003;4:937-947. <u>CrossRef</u>
- [157] Kirk RJ, Hung JL, Horner SR, Perez JT. Implications of Pharmacogenomics for Drug Development. Exp Biol Med 2008;233:1484–1497 <u>CrossRef</u>
- [158] Depondt C, Shorvon SD. Genetic association studies in epilepsy pharmacogenomics: lesson learnt and potential applications. Pharmacogenomics (2006);7(5):731-745. CrossRef
- [159] Chu K, Kim K, Jung, el at. Human neural stem cell transplantation reduces spontaneous recurrent seizures following pilocarpine-induced status epilepticus in adult rats. Brain Research 2004; 1023; 213–221. <u>CrossRef</u>
- [160] Noè F, Pool A, Nissinen J, et al. Neuropeptide Y gene therapy decreases chronic spontaneous seizures in a rat model of temporal lobe epilepsy. Brain 2008; 131: 1506-1515. <u>CrossRef</u>
- [161] Ikrar T, Shi Y, Velasquez T, Goulding M, Xu X. Cell-type specific regulation of cortical excitability through the allatostatin receptor system. Front Neural Circuits. 2012;6: 1-12. <u>CrossRef</u>





Having satisfactorily completed the course of study is herewith and henceforth recognized as

ADVANCED HUMAN CAPITAL MANAGEMENT (AHCM)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of Our Participants as Advanced Human Capital Management.

September 12th, 2021





DIRECTOR



IEEEL INSTITUTE Indonesia Excellent Education For Excellent Life

Certificate Number : AHCM-012092021





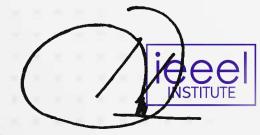
Having satisfactorily completed the course of study is herewith and henceforth recognized as

ADVANCED PROFESSIONAL HANDWRITING ANALYST (APHA)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of Our Participants as Advanced Professional Handwriting Analyst.

September 15th, 2021





DR. HENDY TANNADY

DIRECTOR



IEEEL INSTITUTE Indonesia Excellent Education For Excellent Life

Certificate Number : APHA-002092021





Having satisfactorily completed the course of study is herewith and henceforth recognized as

BASIC HUMAN RESOURCE BUSINESS PARTNER (BHRBP)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of Our Participants as Basic Human Resource Business Partner.

August 15th, 2021



Certificate Number : BHRBP-002082021

ee

DR. HENDY TANNADY

DIRECTOR

BHRBP



IEEEL INSTITUTE

Hereby With This Certificate We Are Proud To Entitle



Having satisfactorily completed the course of study is herewith and henceforth recognized as

BASIC HUMAN RESOURCE MANAGEMENT (BHRM)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of Our Participants as Basic Human Resource Management.

August 15th, 2021





DR. HENDY TANNADY

DIRECTOR

Certificate Number : BHRM-002082021





No. 02/ECETM3-STMI/VIII/2021

THIS CERTIFICATE IS PROUDLY PRESENTED TO :

Dito Anurogo, C.ECETM

Has Successfully completed online training on :

Certified Early Childhood Education Teacher Mastery

Which was held on August 15th, 2021, From 06.30 PM – 08.30 PM



Headmaster of STMI

Jakarta, August 15th, 2021

Revi Hervita Suryani Nasution, M.Pd,

TRAINER





IEEEL INSTITUTE

Hereby With This Certificate We Are Proud To Entitle



Having satisfactorily completed the course of study is herewith and henceforth recognized as

CERTIFIED BASIC HUMAN CAPITAL MANAGEMENT (CBHCM)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of Our Participants as Certified Basic Human Capital Management.

August 15th, 2021

Certificate Number : CBHCM-002082021



DR. HENDY TANNADY

DIRECTOR





Having satisfactorily completed the course of study is herewith and henceforth recognized as

CERTIFIED COMPENSATION & BENEFIT PROFESSIONAL (CCBP)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of Our Participants as Certified Compensation & Benefit Professional.

November 11th, 2021



DR. HENDY TANNADY

DIRECTOR

CCBP



IEEEL INSTITUTE Indonesia Excellent Education For Excellent Life

Certificate Number : CCBP-004112021





Having satisfactorily completed the course of study is herewith and henceforth recognized as

CERTIFIED CONFLICT

MANAGEMENT ANALYST (CCMA)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of Our Participants as Certified Conflict Management Analyst.

January 18th, 2022





DR. HENDY TANNADY

DIRECTOR



IEEEL INSTITUTE Indonesia Excellent Education For Excellent Life







Having satisfactorily completed the course of study is herewith and henceforth recognized as

CERTIFIED EMOTIONAL FREEDOM TECHNIQUE (CEFT)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of Our Participants as Certified Emotional Freedom Technique.

December 28th, 2021



CEFT

Certificate Number : CEFT-003122021

DR. HENDY TANNADY

DIRECTOR



IEEEL INSTITUTE

Indonesia Excellent Education For Excellent Life



Hereby With This Certificate We Are Proud To Entitle



Having satisfactorily completed the course of study is herewith and henceforth recognized as

CERTIFIED FUNDAMENTAL HANDWRITING ANALYST (CFHA)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of Our Participants as Certified Fundamental Handwriting Analyst.

August 05th, 2021

Mario Kojongian

MARIO XAVERIUS KOJONGIAN, SS., CHA.

TRAINER



DR. HENDY TANNADY DIRECTOR Certificate Number : CFHA-006082021



INSTITUTE

Hereby With This Certificate We Are Proud To Entitle



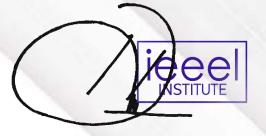
Having satisfactorily completed the course of study is herewith and henceforth recognized as

CERTIFIED HANDWRITING ANALYST (CHA)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of Our Participants as Certified Handwriting Analyst.



August 05th, 2021



DR. HENDY TANNADY

DIRECTOR



IEEEL INSTITUTE Indonesia Excellent Education For Excellent Life









Having satisfactorily completed the course of study is herewith and henceforth recognized as

CERTIFIED HUMAN CAPITAL BUSINESS PARTNER (CHCBP)



In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of Our Participants as Certified Human Capital Business Partner.

August 15th, 2021



DR. HENDY TANNADY

DIRECTOR

Certificate Number : CHCBP-002082021





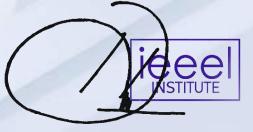
Having satisfactorily completed the course of study is herewith and henceforth recognized as

CERTIFIED HUMAN CAPITAL MANAGEMENT PROFESSIONAL (CHCMP)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of Our Participants as Certified Human Capital Management Professional.

September 12th, 2021





DR. HENDY TANNADY

DIRECTOR



IEEEL INSTITUTE Indonesia Excellent Education For Excellent Life

Certificate Number : CHCMP-012092021





Having satisfactorily completed the course of study is herewith and henceforth recognized as

CERTIFIED HYPNOTHERAPY FOR COUNSELING PRACTITIONER (CHCP)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of Our Participants as Certified Hypnotherapy For Counseling Practitioner.

September 26th, 2021







Having satisfactorily completed the course of study is herewith and henceforth recognized as

CERTIFIED INDUSTRIAL RELATION PROFESSIONAL (CIRP)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of Our Participants as Certified Industrial Relation Professional.

October 13th, 2021







Having satisfactorily completed the course of study is herewith and henceforth recognized as

CERTIFIED LEADERSHIP SUCCESSION PLANNER (CLSP)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of Our Participants as Certified Leadership Succession Planner.

December 16th, 2021





DR. HENDY TANNADY

DIRECTOR



IEEEL INSTITUTE Indonesia Excellent Education For Excellent Life

Certificate Number : CLSP-022122021





Having satisfactorily completed the course of study is herewith and henceforth recognized as

CERTIFIED NLP FOR COUNSELING PRACTITIONER (CNCP)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of Our Participants as Certified NLP For Counseling Practitioner.

September 26th, 2021



Certificate Number : CNCP-005092021

DIRECTOR







Having satisfactorily completed the course of study is herewith and henceforth recognized as

CERTIFIED NLP FOR EXCELLENT PARENTING (CNEP)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of Our Participants as Certified NLP for Excellent Parenting.

November 25th, 2021



Seiso NLP International

CNEP

DR. HENDY TANNADY DIRECTOR





Having satisfactorily completed the course of study is herewith and henceforth recognized as

CNET

CERTIFIED NLP FOR EXCELLENT TEACHER (CNET)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of Our Participants as Certified NLP for Excellent Teacher.

November 24th, 2021



Certificate Number : CNET-001112021





Having satisfactorily completed the course of study is herewith and henceforth recognized as

CERTIFIED NLP LIFE HARMONY PRACTITIONER (CNLHP)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of Our Participants as Certified NLP Life Harmony Practitioner.

January 26th, 2022





Certificate Number : SEISO-001012022





Having satisfactorily completed the course of study is herewith and henceforth recognized as

CERTIFIED NLP FOR SELF HEALING PRACTITIONER (CNSHP)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of Our Participants as Certified NLP For Self Healing Practitioner.

November 22nd, 2021



DR. HENDY TANNADY

DIRECTOR

CNSHP

Certificate Number : CNSHP-002112021







Having satisfactorily completed the course of study is herewith and henceforth recognized as

CERTIFIED NLP FOR THERAPEUTIC WRITING **PROFESSIONAL (CNTWP)**

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of Our Participants as Certified NLP For Therapeutic Writing Professional.

January 25th, 2022



DR. HENDY TANNADY

Certificate Number : CNTWP-003012022

DIRECTOR







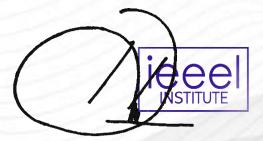
Having satisfactorily completed the course of study is herewith and henceforth recognized as

CERTIFIED ORGANIZATION

DEVELOPMENT PROFESSIONAL (CODP)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of Our Participants as Certified Organization Development Professional.

October 4th, 2021



Certificate Number : CODP-004102021

DR. HENDY TANNADY



Certificate



REVOLUTION MIND INDONESIA

Number: 0039/RMI/CPABC/XI/2021

Hereby Certifies That

Dito Anurogo

Has satisfactorily completed the required course of study in Certified Professional Activity Based Costing (CPABC)

Sukabumi, November 14th 2021



Mulyani Trainer

Muhammad Hadi Nur Yahya Tasman Director



Hereby With This Certificate We Are Proud To Entitle

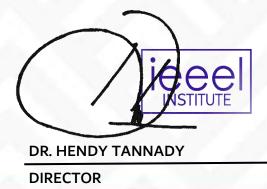


Having satisfactorily completed the course of study is herewith and henceforth recognized as

CERTIFIED PROFESSIONAL GENERAL AFFAIR (CPGA)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of Our Participants as Certified Professional General Affair.

September 6th, 2021





Certificate Number : CPGA-005092021







Having satisfactorily completed the course of study is herewith and henceforth recognized as

СРНА

CERTIFIED PROFESSIONAL

HANDWRITING ANALYST (CPHA)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of Our Participants as Certified Professional Handwriting Analyst.

September 15th, 2021

DIRECTOR

Certificate Number : CPHA-002092021





Indonesia Excellent Education For Excellent Life

Hereby With This Certificate We Are Proud To Entitle

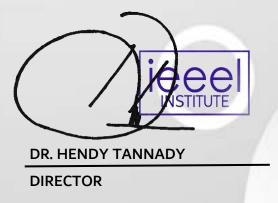
Dito Anurogo

Having satisfactorily completed the course of study is herewith and henceforth recognized as

CERTIFIED PROFESSIONAL HUMAN CAPITAL ENTERPRISE PARTNER (CPHCEP)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of Our Participants as Certified Professional Human Capital Enterprise Partner.

September 12th, 2021



Certificate Number : CPHCEP-012092021

CPHCEP





Having satisfactorily completed the course of study is herewith and henceforth recognized as

CERTIFIED PROFESSIONAL HUMAN RESOURCE MANAGEMENT (CPHRM)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of Our Participants as Certified Professional Human Resource Management.

December 11th, 2021



iceel

DR. HENDY TANNADY

DIRECTOR



IEEEL INSTITUTE Indonesia Excellent Education For Excellent Life

Certificate Number : CPHRM-037122021





Hereby With This Certificate We Are Proud To Entitle

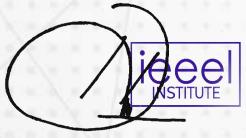


Having satisfactorily completed the course of study is herewith and henceforth recognized as

CERTIFIED PERFORMANCE MANAGEMENT PROFESSIONAL (CPMP)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of Our Participants as Certified Performance Management Professional.

September 9th, 2021



DR. HENDY TANNADY

DIRECTOR

Certificate Number : CPMP-006092021



ieee INSTITUTE



Hereby With This Certificate We Are Proud To Entitle



Having satisfactorily completed the course of study is herewith and henceforth recognized as

CERTIFIED PROFESSIONAL PROJECT MANAGER (CPPM)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of Our Participants as Certified Professional Project Manager.

December 18th, 2021



IEEEL INSTITUTE Indonesia Excellent Education For Excellent Life

Certificate Number : CPPM-007122021







Hereby With This Certificate We Are Proud To Entitle



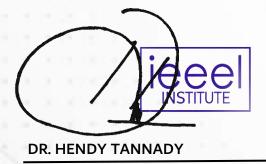
Having satisfactorily completed the course of study is herewith and henceforth recognized as

CERTIFIED PROFESSIONAL TRAINING NEEDS ANALYST (CPTNA)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of Our Participants as Certified Professional Training Needs Analyst.

August 16th, 2021





DIRECTOR

Certificate Number : CPTNA-003082021





Having satisfactorily completed the course of study is herewith and henceforth recognized as

CERTIFIED PROFESSIONAL WORKLOAD ANALYST (CPWA)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of Our Participants as Certified Professional Workload Analyst.

September 3rd, 2021



Certificate Number : CPWA-005092021





Sertifikat Statement Analysis Indonesia

kami serahkan kepada

Dito Anurogo

atas pencapaiannya dalam menyelesaikan workshop

Statement Analysis Practitioner

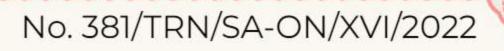
dan dengan demikian, berhak menyandang gelar non akademik

Certified Statement Analyst (C.SA)



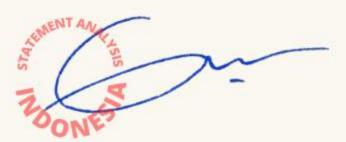
27 Februari 2022

Tanggal









Guruh Taufan H, SE, M.KOM





Hereby With This Certificate We Are Proud To Entitle

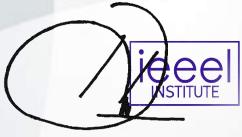
Dito Anurogo

Having satisfactorily completed the course of study is herewith and henceforth recognized as

CERTIFIED STRATEGIC ENTREPRENEURIAL MINDSET (CSEM)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of Our Participants as Certified Strategic Entrepreneurial Mindset.

September 17th, 2021



DR. HENDY TANNADY

DIRECTOR

Certificate Number : CSEM-003092021







> Certificate Number : CSEP-001092021

Hereby With This Certificate We Are Proud To Entitle



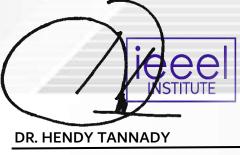
Having satisfactorily completed the course of study is herewith and henceforth recognized as

CERTIFIED SERVICE EXCELLENCE PROFESSIONAL (CSEP)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of Our Participants as Certified Service Excellence Professional.



September 1st, 2021









Having satisfactorily completed the course of study is herewith and henceforth recognized as

CERTIFIED SALARY STRUCTURE ANALYST (CSSA)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of Our Participants as Certified Salary Structure Analyst.

August 8th, 2021



DR. HENDY TANNADY

DIRECTOR

Certificate Number : CSSA-008082021







Having satisfactorily completed the course of study is herewith and henceforth recognized as

CERTIFIED STRUCTURED SELECTION INTERVIEW TECHNIQUE (CSSIT)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of Our Participants as Certified Structured Selection Interview Technique.

October 17th, 2021



IEEEL INSTITUTE

Indonesia Excellent Education For Excellent Life

Certificate Number : CSSIT-001102021



DR. HENDY TANNADY





Having satisfactorily completed the course of study is herewith and henceforth recognized as

CERTIFIED THERAPY FOR COUNSELING PRACTITIONER (CTCP)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of our Participants as Certified Therapy For Counseling Practitioner.

September 26th, 2021

Certificate Number : CTCP-005092021



DR. HENDY TANNADY



International Business Management Institute Berlin · Germany



This certifies that

Dito Anurogo

was awarded a program diploma in

Project Management

by completing the following courses:

Basics of Project Management

Leadership & Team Development

Change Management
 Risk Management



President

Program Director

Certificate ID: 487501-163-985-2074

www.ibm-institute.com/verify





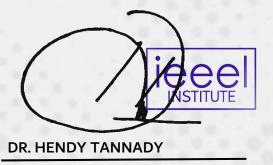


Having satisfactorily completed the course of study is herewith and henceforth recognized as

HUMAN CAPITAL MANAGEMENT PROFESSIONAL (HCMP)

In testimony thereof, after formal evaluations we acknowledge demonstrated knowledge and outstanding competence of Our Participants as Human Capital Management Professional.

September 12th, 2021



DIRECTOR



IEEEL INSTITUTE Indonesia Excellent Education For Excellent Life

Certificate Number: HCMP-012092021



REVOLUTION MIND INDONESIATM

Number: 0095/RMI/CSCAP/II/2022

Certificate Of Recognition Presented To

Dito Anurugo

Has successfully completed studies satisfactorily demonstrated competence and henceforth recognized as a

Certified Supply Chain Analyst Professional (CSCAP™)

Sukabumi, February 18th 2022

Mudjiyono Ridjan, S.T., M.M. Trainer



EEVOLIN

Muhammad Hadi Nur Yahya Tasman Director



THE ACADEMY OF MODERN APPLIED PSYCHOLOGY

CERTIFICATE OF COMPLETION

AWARDED TO

Dito Anurogo

DIPLOMA IN MODERN APPLIED PSYCHOLOGY

The holder of this certificate has successfully completed a Diploma certificate course in Modern Applied Psychology on Udemy.



Kain Ramsay Director of Training

February 20, 2021

Date