CURRICULUM VITAE

Name: Rene Anand

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Citizenship: USA

Education:

Undergraduate

1978-81	University of Madras (Loyola College), B.S. (Chemistry)
1981-83	Indian Institute of Technology, Madras, M.S. (Chemistry)

Graduate

1983-89	The Ohio State University, Ph.D. (Molecular Biology) **Mentor: Dr. Elio Vanin** (Postdoctoral Fellow of Dr. Oliver Smithies, Nobel Laureate in Medicine, 2007)

Postdoctoral

1989-90	The Salk Institute, San Diego, California (Neuroscience)
1990-94	University of Pennsylvania, Philadelphia (Neuroscience) **Mentor: Dr. Jon Lindstrom** (discoverer of autoimmune basis of Myasthenia Gravis, Trustee Professor, University of Pennsylvania)

Awards and Honors:

1979-80	College Gold Medal for Excellence in Chemistry
1991-92	Ossermann Fellowship, Myasthenia Gravis Foundation
1992-94	National Research Service Award
2000	Epilepsy Meeting Travel Award, NIH (NINDS)
2006	Essel Independent Investigator Award, NARSAD
2009	Roche-Nature Medicine Conference Travel Award
2009	Gordon Conference Presenter

2011	Autism Speaks sponsored "Autism Translational Medicine Research" Panelist
2010-2013	Program Committee Member, Society for Neuroscience
2011-	Scientific Advisory Board Member, Autism Speaks
2011-2012	OSU Medical Center Strategic Planning Committee Member

Academic, Professional, and Research Appointments:

2009-	Professor & Vice Chair, Department of Pharmacology The Ohio State University College of Medicine
2007-2009	Associate Professor & Vice Chair, Department of Pharmacology The Ohio State University College of Medicine
2003-2006	Associate Professor Neuroscience Center of Excellence and Department of Neurology Louisiana State University Health Sciences Center
1997-2003	Assistant Professor Neuroscience Center of Excellence and Department of Neurology Louisiana State University Health Sciences Center
1994-1997	Research Assistant Professor Department of Pharmacology, University of Pennsylvania

Grants and Contracts:

Submitted

2016-2018

NIH CEBRA; PI; R. Anand
Human Brain Organoid Model of Addiction
Total Costs: $385, 000

Goals: The central focus of this proposal is to test extend the newly developed brain organoid model for drug abuse studies and use it to screen for drug abuse cessation medications.

2016-2020

NIH R01; PI: R. Anand
Advancing Autism Genotypes From Correlation to Causation Using Human Brain Organoids
Total Costs: $2, 487, 483

Goals: Whole-exome sequencing (WES) and genome (WGS) of genomes has identified a large number of risk genes and strong candidate genes that are both noncoding and coding variants that increase the risk of autism. Our goal is to modulate the mTOR pathway during the development of the brain organoid in vitro and thus identify genes within the

feedback/feedforward networks acting at different scales - molecular, cellular, synaptic and circuits. The studies will use transcriptomics, proteomics, metabolomics and high resolution imaging techniques to accomplish the goals of the aims.

Funded

2009-2015 **Wexner Medical Research Fund**; **PI: R. Anand**
Autism & Developmental Disorders Research Program
Amount: $130,000
Autism is a devastating neurodevelopmental disorder requiring care of affected individuals for the rest of their lives. Our goal is to bridge findings from human genetic studies with preclinical models to develop a better understanding of ASD and to develop therapeutic strategies.

Completed

2006-2011 **NIH** (RO1); **PI: R. Anand**
Modulation of Nicotinic Receptors by Cytosolic Proteins
Total Costs: $1, 514, 625
Goals: The objectives are to test specific hypotheses about α4β2 nicotinic acetylcholine receptors (α4β2 AChRs) determinants and their complementary interactors that regulate the biogenesis of α4β2 AChRs. The results obtained from these studies will provide a better understanding of biological mechanisms that regulate plasticity in structure, transport, functional organization and surface expression of α4β2 AChRs. α4β2 AChRs dysfunctions are reported in both neurodegenerative diseases like Alzheimer's disease and mental illnesses like schizophrenia and autism spectrum disorders.

2009-2011 **NIH**
F32 NRSA Postdoctoral Fellowship
Mentee: Stephanie Amici; **Mentor**; **R. Anand**
Nicotine Dependence and Modulation of Synapse Maturation
Goals: This is a mentoring grant to help train a postdoctoral fellow in my laboratory to study the functions of neurexins and nicotinic receptors, both of which have been implicated in not only nicotine dependence, but also in autism spectrum disorders and schizophrenia.

2009-2013 **NIH** (**EUREKA** RO1); **PI: R. Anand;** Co-PI; G. Wells
Fish Electric Organ as a Factory for Membrane Proteins
Total Costs: $1, 505, 899
Goal: The goal of this grant is to test whether a new expression system can be developed by understanding how electric organs evolved to overexpress electrogenic proteins and then to implement these findings to express large amounts of membrane proteins such as α4β2 nicotinic receptors to first understand their structure by X-ray crytallography and

then use that information to guide the development of therapeutics for multiple disorders where membrane proteins are therapeutic targets such as Alzheimer's disease, Parkinson's Disease, Autism Spectrum Disorders and Cancer.

2011-2013 **Autism Speaks; PI: R. Anand**
Deficiency of Nicotinic Receptor-Neurexin Interactions in Autism
Amount: $119, 233
This preclinical study will ascertain whether neurexins can also modulate the functions of nicotinic receptors and whether the activation of nicotinic receptors by drugs that bind them will increase neurexin 1 expression in the brain.

2012-2014 **Ingram Autism Research Fund; PI: R. Anand**
Amount: $75, 000
This grant was awarded to develop human stem cell models of autism

Completed

2007-2010 **NIH (R21) PI: R. Anand**
Proteomics of Nicotinic Receptor Complexes
Total Costs: $351, 538
Goals: The objectives of this grant are to identify, using advanced proteomic techniques, the molecular composition of AChRs that are deficient in a number of neurodegenerative and neurodevelopmental disorders including autism spectrum disorders.

2007-2010 **National Alliance for Research on Schizophrenia and Depression (NARSAD) Independent Investigator Award; PI: R. Anand**
Dysfunctional Modulation of Nicotinic Receptors in Schizophrenia
Total Costs: $98, 000
Goals: The objectives are to study the functional modulation of $\alpha 4\beta 2$ nicotinic acetylcholine receptors by associated proteins in an animal model of mental illness.

1994-2000 **NIH (NS-33625); PI: R. Anand**
Topology & Stoichiometry of Glutamate Receptor Subunits
Total Costs: $569, 228

2001-2004 **NSF/EPSCoR (Program Project); Co-PI: R. Anand**
Synaptic Organization of Nicotinic Receptors
Direct Costs of Subproject: $426, 714

2002-2005 **Research Management Group; PI: R. Anand**
Proteomic Analysis of Nicotinic Receptor Complexes

Activated by Nicotine in Tobacco Smoke
Total Costs: $677, 227

2002-2007 **HEF/SCP (Program Project) PI: R. Anand**
Nicotine Addiction and Modification by Menthol: Molecular, Cellular, and Behavioral Correlates;
Direct Costs: $ 1, 250, 000

2002-2007 **NIH COBRE (PO1); PI: N. Bazan; Co-PI: R. Anand**
Mentoring Neuroscience in Louisiana
Molecular Core Unit Co-director
Direct Costs of Molecular Core Unit: $606, 135

Research Review Committees:

2004-2008	Alzheimer's Association reviewer
2006-2007	NIH Cutting Edge Basic Research Awards ZDA1 MXS-M Panel Reviewer
2007	NIH MNPS study section *Ad hoc* reviewer
2008-2011	California Tobacco-Related Disease Research Program (TRDRP), University of California, Berkley
2009	NIDA RC2 ARRA study section *Ad hoc* reviewer
2008-2009	External Advisory Board Member, NERT program, Louisiana Tech
2007-2010	External Advisory Board Member for NINDS Human DNA Repository
2009-2011	Lytmos Group, Inc, *Ad hoc* reviewer
2010	Hong Kong Research Grants Council, *Ad hoc* reviewer
2010	Israel Science Foundation, *Ad hoc* reviewer
2010	American Association for Advancement of Science; RCS grant study section *Ad hoc* reviewer
2010-	Autism Speaks, Trailblazer Grants *Ad hoc* reviewer
2014-	Brain Canada study section, *Ad Hoc* reviewer
2016	California Tobacco-Related Disease Research Program (TRDRP), University of California, Berkley
2016	NIMH SEP ZMH1 ERB-L (03)
2016	NIDA SEP ZDA1 JXR-G (01)

Membership in Professional Organizations:

Society for Neuroscience, USA

Teaching Experience/Responsibilities:

1983-1989	Teaching Assistant in Chemistry, Biochemistry and Mol. Biology Department of Biochemistry, Ohio State University
1989-1994	Supervised graduate students, technicians and postdoctoral associates in Jon Lindstrom's laboratory
1996	Team taught Graduate Molecular Pharmacology Course

	Department of Pharmacology, University of Pennsylvania
1998	Team taught Graduate Molecular Biology Course, Department of Biochemistry and Molecular Biology, LSUHSC
1998	Team taught Dental Biochemistry Course Department of Biochemistry and Molecular Biology, LSUHSC
1998-2003	Team taught Graduate Investigative Neuroscience Course, Interdisciplinary Neuroscience Program, LSUHSC
1999-2003	Course Co-Director and lecturer in Graduate Molecular Neurobiology Course, Interdisciplinary Neuroscience Program, LSUHSC
2003-2006	Neurology Residency Training Program, Lecturer
2007-2010	Lecturer in Grant Writing IBGP-707 Fundamentals of Grant Writing Course
2007	Panelist in IBGP Ethics Course
2008-2010	Lecturer in Module 6 IBGP Molecular Pharmacology
2009	Lecturer in IBGP 851 Advanced Seminar Course
2009-2010	Lecturer in IBGP 707 Advanced Seminar Course
2009-2010	Lecturer in IBGP 705 Neurobiology of Disease
2010	Lecturer in NGSP 726 Seminars in Behavioral Neurosciences
2013	Lecturer in Pharm 5600
2014	Articulate lecturer for Neuroblock for Medical students
2015-16	BSGP Seminar Course
2016	Stem Cell Biology and Applications to Human Regenerative Medicine

Graduate Students:

2002-2006	Jayanta Mukherjee (Ph.D. Thesis Advisor)
2003-2006	Tania Das (Ph.D. Thesis Advisor)
2010-11	Jordan Robson (Ph.D. Thesis Advisor)

Mentor for Post-Doctoral Fellows:

1998-2001	Dr. Elisabeth Jeanclos (PD Fellow)
1998-2003	Dr. Lin Lin (PD Fellow)
2002-2006	Dr. Xiaoqin Ren (PD Fellow)
2002-2006	Dr. Shibin Cheng (PD Fellow)
2002-2003	Dr. Heming Xhou (Co-Postdoctoral Mentor)

OSU

2007-2013	Dr. Stephanie Amici (PD Fellow)
2009-2013	Dr. Gerald Ponath (PD Fellow)
2009-2010	Dr. Hans Hu (PD Fellow)

Mentor for Junior Tenure Track Faculty

2004-2006	Dr. Laura Harrison, COBRE Junior Faculty
2004-2006	Dr. Mark DeCoster, COBRE Junior Faculty
2005-2006	Dr. Hugh Xia, COBRE Junior Faculty
2007	Dr. Kirk Mykytyn; Department of Pharmacology (Faculty)
2008-2009	Steve Kolb, M.D., Ph.D., Department of Biochemistry and Neurology (Faculty)
2008-2009	David Pitt, M.D., Department of Neurology (Faculty)

Journal Publications:

Refereed

1. **Anand, R.,** Boehm, C.D., Kazazian Jr., H.H., and Vanin, E.F. (1988) Molecular characterization of a β^o-Thalassemia resulting from a 1.4 Kb deletion. *Blood* 72, 636-641.

2. **Anand, R.,** and Lindstrom, J. (1990). Nucleotide sequence of the human nicotinic acetylcholine receptor β2 subunit gene. *Nucl. Acids Res.* 18, 4272.

3. Saedi, M.S., **Anand,R.,** Conroy, W.G., and Lindstom, J. (1990) Determination of amino acids critical to the main immunogenic region of intact acetylcholine receptors by *in vitro* mutagenesis. *FEBS Lett.* 267, 55-59.

4. **Anand, R.,** Conroy, W.G., Schoepfer, R., Whiting, P., and Lindstrom, J. (1991) Neuronal nicotinic acetylcholine receptors expressed in *Xenopus* oocytes have a pentameric quaternary structure *J. Biol. Chem.* 266, 11192-11198.

5. **Anand, R.,** and Lindstrom, J. (1992). Chromosomal localization of seven neuronal nicotinic acetylcholine receptor subunit genes in humans. *Genomics* 13, 962-967.

6. **Anand, R.,** Peng, X., and Lindstrom, J. (1993) Homomeric and native α7 acetylcholine receptors exhibit remarkably similar but nonidentical pharmacological properties suggesting that the native receptor is a heteromeric protein complex. *FEBS Lett.* 327, 241-246

7. **Anand, R.,** Bason, L., Saedi, M. S., Gerzanich, V., Peng, X., and Lindstrom, J. (1993) Reporter Epitopes: A novel approach to examine transmembrane topology of integral membrane proteins applied to the α1 subunit of the nicotinic acetylcholine receptor. *Biochemistry* 32, 9975-9984.

8. **Anand, R.,** Peng, X., Ballesta, J. J., and Lindstrom, J. (1993) Pharmacological characterization of αBungarotoxin-sensitive AChRs immunoisolated from chick retina: Contrasting properties of α7 and α8 subunit-containing subtypes. *Mol. Pharmacol.* 44, 1046-1050.

9. Gerzanich, V., **Anand, R.,** and Lindstrom, J. (1994) Homomers of α8 and α7 subunits of nicotinic receptors exhibit similar channel but contrasting binding site properties. *Mol. Pharmacol*. 45, 212-220.

10. Peng, X., Katz, M., Gerzanich, V., **Anand, R.,** and Lindstrom, J. (1994) Human α7 acetylcholine receptor: Cloning of the α7 subunit from SH-SY5Y cell line and determination of pharmacological properties of native receptors and functional α7 homomers expressed in *Xenopus* oocytes. *Mol. Pharmacol*. 45, 546-554.

11. Steinlein, O., Smigrodzki, R., Lindstrom, J., **Anand, R.,** Kohler, M., Tocharoentanaphol, C., and Vogel, F. (1994). Refinement of the localization of the gene for neuronal nicotinic acetylcholine receptor α4 subunit (AChR α4) to human chromosome 20q13.2-q13.3. *Genomics* 22, 493-495.

12. Peng, X., Gerzanich, V., **Anand, R.,** Whiting, P.J., and Lindstrom, J. (1994) Nicotine-induced increase in neuronal nicotinic receptors results from a decrease in the rate of receptor turnover. *Mol. Pharmacol*.46, 523-530.

13. Gerzanich, V., Peng, X., Wang, F., **Anand, R.,** Fletcher, S., and Lindstrom, J. (1995) Comparative pharmacology of epibatidine- A potent agonist for neuronal nicotinic acetylcholine receptors. *Mol. Pharmacol*. 48, 774-782.

14. Wang, F., Gerzanich, V., Wells, B., **Anand, R.,** Peng, X., Keyser, K., and Lindstrom, J. (1996). Assembly of human neuronal nicotinic receptor α5 subunit with α3, β2, and β4 subunits. *J. Biol. Chem.* 271, 17656-17665.

15. Gerzanich, V., Kuryatov, A., **Anand, R.,** and Lindstrom, J. (1997) "Orphan" α6 nicotinic AChR subunit can form a functional heteromeric receptor. *Mol. Pharmacol.* 51, 320-327.

16. Peng, X., Gerzanich, V., **Anand, R.,** Wang, F., and Lindstrom, J. (1997) Chronic nicotinic treatment up-regulates α3 AChRs and α7 AChRs expressed by the human neuroblastoma cell line SH-SY5Y. *Mol. Pharmacol.* 51, 776-784.

17. Wells, G. B., **Anand, R.,** Wang, F., and Lindstrom, J. (1998). Water-soluble nicotinic acetylcholine receptor formed by α7 subunit extracellular domains. *J. Biol. Chem.* 273, 964-973.

18. **Anand, R.,** Nelson, M.E., Gerzanich, V., Wells, G. B., and Lindstrom, J. (1998). Determinants of channel gating located in the N-terminal extracellular domain of nicotinic α7 receptor. *J. Pharmacol. Exp. Ther.* 287, 469-479.

19. Anegawa, N.J., Grant, E.R., Guttmann, R.P., **Anand, R.,** Lindstrom, J., and Lynch, D.R. (2000). NMDA receptor mediated toxicity in a neuronal cell line: Characterization using fluorescent measures of cell viability and reactive oxygen species production. *Brain Res. Mol. Brain Res.* 77, 163-175.

20. **Anand, R.** (2000). Probing the topology of the glutamate receptor GluR1 subunit using epitope tag insertions. *Biochem. Biophy. Res. Comm.*276, 157-161.

21. Wells, G. B., Lin, L., Jeanclos, E.M., and **Anand, R.**, (2001) Assembly and ligand binding properties of the water-soluble extracellular domains of the glutamate receptor 1 subunit.. *J.Biol. Chem.* 276, 3031-3036.

22. Jeanclos, E. M, Lin, L., Treuil, M., Jayaraman, A., DeCoster, M., and **Anand, R**. (2001). The chaperone protein 14-3-3η interacts with the nicotinic acetylcholine receptor □4□subunit: Evidence for a dynamic role in subunit stabilization *J. Biol. Chem.* 276, 28,281-28, 290

23. Braunewell, K-H., Brackmann, M., Schaupp, M., Spilker, C., **Anand**, **R**., and Gundelfinger, E.D. (2001). Intracellular neuronal calcium sensor (NCS) protein VILIP-1 modulates cGMP signalling pathways in transfected neural cells and cerebellar granule neurones. *J. Neurochem. 78, 1277-1286.*

24. Lin, L, Jeanclos, E.M., Braunewell, K.-H., Gundelfinger, E.D., and **Anand, R**. (2002). Functional Analysis of Calcium-binding EF-hand of Visinin-like protein-1 *Biochem. Biophy. Res. Comm.* 296, 827-832.

25. Lin, L, Jeanclos, E.M., Magdalen Treuil, Braunewell, K.-H., Gundelfinger, E.D., and **Anand, R.** (2002). The calcium sensor protein VILIP-1 modulates the surface expression and agonist-sensitivity of the nicotinic α4β2 acetylcholine receptor *J. Biol. Chem. 277, 41872-41878.* ***.** Highlighted by "Faculty of 1000 Biology"***

26. Brackmann, M, Schuchmann, S., **Anand , R.**, and Braunewell, K-H. Neuronal Ca++ sensor protein VILIP-1 affects cGMP signalling by regulating receptor recycling of guanylyl cyclase B in hippocampal neurons. *J. Cell Science, 118, 2495-2505, 2005*

27. Ren, X-Q, Cheng, S-B, Treuil M.W., Mukherjee, J., Rao, J., Lindstrom, J.M., and **Anand, R.** (2005). Structural determinants of α4β2 nicotinic acetylcholine receptor trafficking *J. Neurosci.25, 6676-6686.*

28. Ruskin, D.N., **Anand, R.** and LaHoste G.J. Menthol and nicotine oppositely modulate body temperature in the rat. (2007). *Eur. J. Pharmacol*. 559, 161-164.

29. Ruskin, D.N., **Anand, R.** and LaHoste, G.J. Chronic menthol attenuates the effect of nicotine on body temperature in adolescent rats (2008). *Nicotine & Tobacco Research* 10, 1753-1759

30. Gierke, P., Zhao, C., Bernstein, H-G., Noack, C., **Anand, R.,** Heinemann, U., and Braunewell, K-H. Implication of neuronal *Ca*2 + −*Sensor* Protein VILIP-1 in the glutamate hypothesis of Schizophrenia. (2008*). Neurobiology of Disease* 32, 162-175. ***Editor-Selected Cover article***

31. Zhao, C., Noack, C., Brackmann, M., Gloveli, T., Maelicke, A., Heinemann, U., **Anand, R.,** and Braunewell, K.H. Neuronal Ca^{2+} Sensor Protein VILIP -1 leads to the up-regulation of □α4β2 nicotinic acetylcholine receptor in hippocampal Neurons (2009). *Mol. Cell. Neurosci*. 40, 280-292.

32. Zhao C, **Anand R,** Braunewell KH. Nicotine-induced Ca(2+)-myristoyl Switch of Neuronal Ca(2+) Sensor VILIP-1 in Hippocampal Neurons: A Possible Crosstalk Mechanism for Nicotinic Receptors. (2009). *Cell Mol. Neurobiol.* 29, 273-286.

33. Cheng SB, Amici SA, Ren XQ, McKay SB, Treuil MW, Lindstrom JM, Rao J, **Anand R.** Presynaptic targeting of alpha4beta 2 nicotinic acetylcholine receptors is regulated by neurexin-1beta. ***J. Biol Chem.*** 2009; 284:23251-9. PMID: 19567877**.**** ***Highlighted by "Faculty of 1000 Biology"***

34. Mukherjee, J. Kuryatov, A., Moss, S.J., Lindstrom, J.M., and **Anand, R.** (2009). Mutations in the cytosolic loop residues impair assembly and maturation of α7 nicotinic acetylcholine receptors ***J. Neurochem.*** 110, 1885-1894. PMID: 19627445

35. Anand R, Amici SA, Ponath G, Robson JI, Nasir M, McKay SB. (2011). Nicotinic Acetylcholine Receptor Alterations in Autism Spectrum Disorders: Biomarkers and Therapeutic Targets. InTech Open Access Publisher, Accepted Book Chapter, "Autism / Book 2", edited by Dr. Valsamma Eapen, ISBN 978-953-307-493-1.

36. Amici SA, McKay SB, Wells GB, Robson JI, Nasir M, Ponath G, Anand R. (2012). A highly conserved cytoplasmic cysteine residue in the α4 nicotinic acetylcholine receptor is palmitoylated and regulates protein expression. J. Biol Chem. 287:23119-27**.** PMID:22593584.

37. Arnold LE, Aman MG, Hollway J, Hurt E, Bates B, Li X, Farmer C, Anand R, Thompson S, Ramadan Y, Williams C. (2012). Placebo-controlled pilot trial of mecamylamine for treatment of autism spectrum disorders**.** J. Child Adolesc Psychopharmacol. 22:198-205. PMID:22537359.

38. Arnold LE, Anand R, Aman M. (2013). Varenicline in autistic disorder: hypothesis and case report of single-patient crossover. J. Child Adolesc Psychopharmacol. 23:61-4. PMID:23350866.

39. Gallant et al., (2014). Genomic basis for convergent evolution of electric organs. Science 344; 1522-1525.

40. Traeger LL, Volkening JD, Moffett H, Gallant JR, Chen PH, Novina CD, Phillips GN Jr, Anand R, Wells GB, Pinch M, Güth R, Unguez GA, Albert JS, Zakon H, Sussman MR, Samanta MP. Unique patterns of transcript and miRNA expression in the South American strong voltage electric eel (Electrophorus electricus). BMC Genomics. 2015 Mar 26;16:243. doi: 10.1186/s12864-015-1288-8.PMID: 25887781

Books and Chapters:

1. Lindstrom, J., Schoepfer, R., Conroy, W., Whiting, P., Das, M., Saedi, M., and **Anand, R.** (1991) The nicotinic acetylcholine receptor gene family: structure of nicotinic receptors from muscle and neurons and neuronal alpha-bungarotoxin-binding proteins. *Adv. Exp. Med. Biol.* 287, 255-278.

2. Lindstrom, J., Schoepfer, R., Whiting, P., **Anand, R.,** Conroy, R., Saedi, M. and Das, M.(1991) Monoclonal Antibody Probes for Nicotinic Receptors of Muscles and Nerves, *Biochemical Society Transactions* 19, 115-120.

3. Lindstrom, J., **Anand, R.,** Peng, X., Gerzanich, V., Wang, F., and Li, Y. (1995) Neuronal nicotinic receptor subtypes. *Annals of the New York Academy of Sciences* (Eds: Lajtha, A. and Abood, L.) vol. 757, 100-116.

4. Lindstrom, J., **Anand, R.,** Peng, X., and Gerzanich, V. (1995) Neuronal nicotinic receptor structure and function. *Advances in pharmacological sciences* , 45-52.

5. Lindstrom, J., **Anand, R.,** Gerzanich, V., Peng, X., Wang, F., and Wells, G. (1996) Structure and function of neuronal nicotinic acetylcholine receptors. *Prog. Brain Res*. (Eds. Klein, J. and Loffelholz, K.) vol. 109, 125-137.

6. Lindstrom, J., Peng, X., Kuryatov, A., Lee, E., **Anand, R.,** Gerzanich, V., Wang, F., Wells, G., and Nelson, M. (1998) Molecular and antigenic structure of nicotinic acetylcholine receptors. *Annals of the New York Academy of Sciences* vol. 841, 71-86.

Papers Presented and Abstracts:

1. **Anand, R.,** Gerzanich, V., and Lindstrom J. (1994) Mapping amino acids responsible for the pharmacological differences observed between α7 and α8 homomers. *Soc. Neurosci. Abstr.* 20, 1134 (A466.37).

2. Peng, X., **Anand, R.,** Whiting, P.J., and Lindstrom, J. (1994) Nicotine-induced upregulation of neuronal nicotinic receptors results from a decrease in the rate of receptor turnover. *Soc. Neurosci. Abstr.* 20, 1128 (A466.3).

3. Peng, X., **Anand, R.,** Wang, F., and Lindstrom, J. (1995) Chronic nicotine treatment up-regulates α3 AChRs and α7 AChRs expressed by the human neuroblastoma cell line SH-SY5Y. *Soc. Neurosci. Abstr*: 21, 1333 (A527.5).

4. Wang, F., Gerzanich, V., **Anand, R.,** Peng, X., and Lindstrom, J. (1995) Characterization of human neuronal nicotinic acetylcholine receptor subunits α3, β2, β4, and α5 expressed in Xenopus oocytes. *Soc. Neurosci. Abstr*. 21, 1583 (A621.19).

5. **Anand, R.,** Nelson, M., Gerzanich, V., Wells, G., and Lindstrom, J. (1998) Determinants of channel gating located in the N-terminal extracellular domain of nicotinic α7 receptors. *Xth International Symposium on Cholinergic Mechanisms*, Arcachon, France.

6. Lin, L., Jeanclos, E., and **Anand, R.** (1999) Nicotine induced changes in gene expression in the CNS. Society for Neurochemistry, Annual Meeting, New Orleans, LA, February 13th-17th, 1999.

7. Jeanclos, E.M., Lin, L., and **Anand, R.** Dynamic interaction of 14-3-3 with nicotinic α4β2 acetylcholine receptors.(2000). *Soc. Neurosci. Abstr*: 26, 625 (A235.5).

8. Lin, L., Jeanclos, E.M., Braunewell, K.-H., Gundelfinger, E. D., and **Anand, R.** VILIP-1: A calcium sensor visinin-like protein-1 is associated with nicotinic α4β2 acetylcholine receptors (2000). *Soc. Neurosci. Abstr*: 26, 625 (A235.4).

9. **Anand, R,** Jeanclos, E.M., Lin, L., Treuil, M.A., Rao, J., and DeCoster, M.A. 14-3-3 Regulates the stability and surface expression of nicotinic α4β2 acetylcholine receptors (2001). *Soc. Neurosci. Abstr*: A146.1.

10. Lin, L., Jeanclos, E.M., Braunewell, K.-H., Gundelfinger, E. D., and **Anand, R.** VILIP-1: Characterization of VILIP-1 and its interaction with nicotinic α4β2 acetylcholine receptors (2001)**.** *Soc. Neurosci. Abstr*: A146.2.

11. **Anand, R,** and Lin, L. Menthol modulates the functional properties of nicotinic receptors. (2002).*Soc. Neurosci. Abstr.* .

12. Lin, L., Treuil, M., K.H. Braunewell, E.D. Gundelfinger, and **Anand, R.** VILIP-1 modulates the surface expression and agonist-sensitivity of the nicotinic α4β2 AChR. (2002). *Soc. Neurosci. Abstr.* .

13. T. Das, X.Q. Ren, M. W. Treuil, S. B.Cheng, L. Lin, H. J. Leblanc, L. A. Carver, J. Rao and **R. Anand**. 14-3-3 Proteins, Deficient in Parkinson's disease, Brains: Neuroprotective Role in Rotenone-Induced Neurotoxicity (2004). *Soc. Neurosci. Abstr.*

14. X.Q. Ren, S. B. Cheng, M. W. Treuil, J. Mukherjee, J. Lindstrom, K.-H. Braunewell and **R. Anand**. Cytoplasmic determinants of α4β2 AChR Surface Expression (2004). *Soc. Neurosci. Abstr.*

15. S. B. Cheng, M. W. Treuil, J. Mukherjee, L. Lin, T. Das, X. Q. Ren, H. J. LeBlanc, Larry A. Carver, J. Rao and **R. Anand**. 14-3-3 Proteins Essential for Cellular Resistance to beta-amyloid Neurotoxicity are Deficient in Alzheimer's Disease Brains (2004). *Soc. Neurosci. Abstr.*

16. J. Mukherjee, X. Q. Ren, S. B. Cheng, and **R. Anand**. Tandem Affinity Purification Strategy for Proteomic Analysis of α7 Nicotinic Acetylcholine Receptor Complexes. (2004). *Soc. Neurosci. Abstr.*

17. G. J. LaHoste, L.E. LeBon, **R. Anand** and D. N. Ruskin. Biased and Unbiased Place Preference with nicotine in rats. (2004). *Soc. Neurosci. Abstr.*

18. J. Mukherjee, X-Q Ren, M.W. Treuil, J. M. Lindstrom and **R. Anand**. Regulation of the Pharmacological Maturation of the α7 Nicotinic Acetylcholine Receptor. (2005). *Soc. Neurosci. Abstr.*

19. T. Das, X.Q. Ren, S.B Cheng, L. Lin, M.W. Treuil, J. Mukherjee, H. J. Leblanc, L. Carver, **J. Rao, R. Anand.** 14-3-3 Protein Dysfunction in Culture Models of Parkinson's and Alzheimer's disease. (2005). Soc. Neurosci. Abstr.

20. S. Cheng, X. Ren, M.W. Treuil, J.M. Lindstrom and **R. Anand**. Neurexin induces pre-synaptic clustering of α4β2 nicotinic acetylcholine receptors. (2005). *Soc. Neurosci. Abstr.*

21. Karl-Heinz Braunewell, **Anand, R.** et al. Regulation of receptor trafficking by neuronal calcium sensor VILIP-1 in hippocampal neurons. (2007). *Soc Neurosci. Abstr. 2006-A-9025-SFN*

22. S. A. Amici, S.-B. Cheng, X.-Q. Ren, S. B. McKay, M. W. Treuil, J. Lindstrom, J. Rao, **R. Anand**. Neurexin-1β regulates targeting of α4β2 nicotinic acetylcholine receptors to presynaptic junctions: implications for nicotine dependence and autism (2008). *Soc Neurosci. Abstr. 104572* ****This work has the distinction that it was selected by the Society for Neuroscience for inclusion in Neuroscience 2008 media materials for national press in Washington DC.***

23. S. A. Amici, G. Ponath, J. I. Robson, S. B. McKay, J. M. Lindstrom and **R. Anand** Neurexins Modulate Synaptic Targeting of the Alpha 7 Nicotinic Receptor, a Mediator of Neuroimmune Signaling (2010). *International Congress of Neuroimmunology Abstr.*

24. S. Mckay and R. Anand. Human Organoids for Cancer, Neurodevelopmental, and Neurodegenerative Disorder Research. Comprehensive Cancer Center Research Meeting. (2014). Columbus, Ohio.

25. S. Mckay and R. Anand. Human Organoids for Cancer, Neurodevelopmental, and Neurodegenerative Disorder Research. Center for Regenerative Medicine and Cell based Therapies Meeting. (2014). Columbus, Ohio

Seminars and Invited Presentations

1995	Department of Neuroscience Albert Einstein Medical School, Bronx, NY
1995	CNS Research Division Bristol-Myer Squibb, Wallingford, CT

1995	Department of Medicinal Chemistry Purdue University, W. Lafayette, IN
1995	Department of Physiology and Biophysics University of Arkansas, Little Rock, AK
1995	Department of Pharmacology Ohio State University, Columbus, OH
1995	Department of Pharmacology University of Kentucky, Lexington, KT
1996	Department of Neuroscience Children's Hospital of Philadelphia, Philadelphia, PA
2002	Department of Cell Biology and Anatomy LSUHSC
2004	Capitol Day, Baton Rouge Nicotinic Receptor Functions in Addiction & Age-related Neurodegeneration
2004	Gordon Research Conference, Ventura, CA 14-3-3 Proteins modulate the biogenesis of nicotinic receptors deficient in Alzheimer's disease: therapeutic implications
2004	Department of Biochemistry LSUHSC
2004	Gene Therapy Consortium LSUHSC
2006	Department of Psychiatry, University of Colorado Health Sciences Center, Denver, CO
2006	Department of Pharmacology, Virginia Common Wealth University, Richmond, VA
2008	Wellcome Trust Nicotinic Receptor Symposium; Hinxton, UK
2008	XIII International Symposium on Cholinergic Mechanisms, Iguassu Falls, Brazil
2009	Roche -Nature Medicine translational Neuroscience Symposium 2009 Autism and Other Developmental Brain Disorders, Buonas, Switzerland
2009	Gordon Research Conference, Les Diablerets, Switzerland Excitatory Synapses and Brain Development
2011	**Autism Speaks** sponsored: "Autism Translational Medicine Research" meeting, Santa Monica, California
2014	Wellcome Trust Symposium on "Nicotinic Acetylcholine Receptors"
2014	OSU Neuroscience Signature Program Invited Speaker
2015	Health Science Innovation Conference, Mumbai, India
2015	Tata's Institute of Fundamental Research, Mumbai, India
2016	World CNS Summit, Boston, USA

Published Multimedia

Multimedia, Databases, and Websites

Rene Anand, **Narrator of discovery of a link between autism and nicotine receptors**. AUTISM. 1. web and video. Cold Spring Harbor Laboratory, Dana Foundation, CSHL, The Hewlett Foundation, and The Sanger Center, UK, January 2009. Forthcoming. http://www.g2conline.org/

Rene Anand; and coauthors Stephanie Amici and Susan McKay of Ohio State's Department of Pharmacology; Shi-Bin Cheng, Xiao-Qin Ren, Magdalen Treuil and Jay Rao of the LSUHSC in New Orleans; and Jon Lindstrom at U. Pennsylvania, Principal Investigator. 2008. **RESEARCHERS FIND LINK BETWEEN NICOTINE ADDICTION AND AUTISM**. 1. Web. NIH, NARSAD, and other autism-related sites, OSU, 2008. Forthcoming. http://medicine.osu.edu/pharmacology/article.cfm?id=4422

Radio and TV Shows
National Public Radio of Central Ohio. Scientific Contact. WCBE Stories. AUTISM. **OSU researcher finds proteins linked to both autism and nicotine addiction** [radio broadcast.]. 2008. [dir.] Mike Foley. [perfs.] Dr. Rene Anand. National Public Radio. WCBE. Columbus, OH. December 12, 2008.
http://www.publicbroadcasting.net/wcbe/news.newsmain?action=article&ARTICLE_ID=1443916.

Neural Organoids as pre-clinical models of brain disease.
Selected press reports from >1, 000

https://www.autismspeaks.org/blog/2015/09/21/breakthrough-science-walk-volunteer-turned-autism-researcher
https://audioboom.com/boos/3744835-professor-rene-anand-ohio-state-university
http://www.cnn.com/2015/10/06/health/pioneers-brain-organoids/
http://www.abc.net.au/news/2015-08-19/scientists-grow-model-brain-from-skin-cells/6708606
http://www.telegraph.co.uk/news/health/news/11811044/Nearly-fully-formed-human-brain-grown-in-laboratory.html
http://www.pcrm.org/sites/default/files/Alzheimers-special-report.pdf
http://www.nature.com/nature/journal/v526/n7572/full/nj7572-283a.html

Editorial Activities:

Editorial Board Member:
Molecular Neurobiology - current
Ion Channels
Journal of Biomedicine & Biotechnology (2009-2010)

***Ad hoc* Reviewer for:**
1998: Molecular Pharmacology
1999: Journal of Biological Chemistry
2000: Journal of Biological Chemistry & Neuropharmacology
2002: Molecular Neurobiology & Neurochemical Research
2003: Brain Research, Neuropharmacology & Biotechniques
2005: Journal of Neuroscience
2006; Journal of Neuroscience
2007: Journal of Neuroscience; J. Neurochemistry; Pharmacology, Biochemistry and Behavior
2008: Libertas Academia; Behavioral Brain Research
2009: Journal of Pharmaceutical and Experimental Therapeutics; Life Sciences

2010: Journal of Pharmaceutical and Experimental Therapeutics; Journal of Biological Chemistry; Molecular Pharmacology; Neuroscience; Journal of Neuroscience
2014: Journal of Neuroimmunology; Journal of General Physiology; Molecular Neurobiology;

Advisory Board/Committee Activities:

External Advisory Committee Member (2007-2008): **National Institutes of Neurological Stroke and Disease (NINDS)** human DNA repository at the Coriell Institute in New Jersey
My role on this advisory committee is to provide advice on creating a human DNA repository that would have wide utility to the research community. My advice is also sought on specific request from investigators seeking either to add samples to the repository or to request discounting pricing from the repository.

External Advisory Board Member (2008) for **NERT** Proposal to NSF from Louisiana Tech, Ruston, LA
My role is to help provide advice to the participating investigators on how best to bridge biology and engineering through nanotechnological applications for biomedical endpoints.

Scientific Advisory Board Member, ICBI International, Inc., La Jolla, CA: My current role is to provide scientific and technical advice for the development of nano-technologies to overcome the challenges of blood brain barrier (BBB) to develop concomitant diagnostics and therapeutics for neurodegenerative diseases such as Alzheimer's disease (AD) and Parkinson's (PD).

Society for Neuroscience Program Committee Member: I served in this capacity for a 1-year term. Members are responsible for monitoring, advising and managing the activities of the meeting to help continually improve and enhance the SfN annual meeting experience by planning engaging scientific sessions containing cutting edge neuroscience research topics and speakers, and encouraging the exchange of information.

Chair, Steering Committee Member of Autism Center: I played a significant role in writing and developing the governance and scientific plan for the newly endowed **"Marci and Bill Ingram Center for Autism Spectrum Disorders"** at OSU**.** My role will be to provide scientific counsel to guide the development of the center and the investment of research funds in scientific projects.

Scientific Advisory Board Member, Autism Speaks (2012-2014): The advisory board members are responsible for reviewing proposals submitted to Autism Speaks to conduct basic and clinical research, pilot studies, and to support fellowships.

OSU Medical Center Strategic Planning Committee Member: I served in this capacity till 2012 to help Research Dean of the College Medicine, Dr. Clay Marsh, with the Strategic planning of the research agenda for the College of Medicine

OSU Center for Faculty Advancement, Mentoring and Engagement (FAME) member. I am the department of Pharmacology representative to this committee

University/Institutional Services

1995-1997	Member, Graduate Group in Pharmacological Sciences, University of Pennsylvania
1998-current	Neuroscience Faculty Recruitment Committee, LSUHSC
1998	School of Graduate Studies Task Force, LSUHSC
1998	Neuroscience Center HHMI Grant Application Task Force, LSUHSC
1997-1999	Host Committee, American Society For Neurochemistry Meeting
1999-current	Neuroscience Center Seminar Committee
1999	Planning Committee, Parkinson's Disease Centers of Excellence (NIH)
1999	Planning Committee, NIH COBRE Program Project
1999	Planning Committee, HEF Program Project
1999-current	Principal Investigator Advisory Committee, Neuroscience Center
1999-current	Planning and Coordination Committee, Molecular Neurobiology Core
2000-2001	Planning Committee, NSF/EPSCOR Program Project (Funded, June 1, 2001)
2000-2001	Planning Committee, Novartis Opthalmics Program Project
2000	Planning Committee, NIH COBRE Program Project (Funded, April 1, 2002)
2001	Planning Committee, HEF Program Project
2002	Project PI and Planning Committee, HEF/SCP Program Project (Funded, June 1, 2002)
2007	Member, Search Committee for Department of Pharmacology Chair The Ohio State University College of Medicine
2014-16	BSGP Graduate Student Selection Committee
2014-2016	Medical School Admission Selection Committee
2014-2016	MD-PhD Student Selection Committee

Thesis Committees

1995-1997	Neuropharmacology Graduate Student Thesis Committee (John Anegawa), University of Pennsylvania
1998-2001	Biochemistry Graduate Student Thesis Committee (Yolanda Fortenberry)
2000-2001	Neuroscience Graduate Student Thesis Committee (Scott Davis)
2000-2001	Neuroscience Graduate Student Thesis Committee (Neva West)
2000-2002	Neuroscience Graduate Student Thesis Committee (Akash Datwani)
2001-2002	Neuroscience Graduate Student Thesis Committee (Hande Pembe)
2001-2002	Neuroscience Graduate Student Thesis Committee (Xing Cheng)
2002-2003	Genetics Graduate Student Thesis Committee (Gauri Gaikwad)
2002-2003	Neuroscience M.S. Student Thesis Committee (Lisa Jaubert-Miazza)
2003	Cell Biology & Anatomy M.S. Student Thesis Committee (Paul Azar)
2004	Neuroscience Graduate Student Thesis Committee (Carmen Dermott)
2004	Neuroscience Graduate Student Thesis Committee (Sukjeevan Grewal)
2005	Neuroscience Graduate Student Thesis Committee (Gabriel Quintero)
2006	Neuroscience Graduate Student Thesis Committee (Jessica Waguespack)
2007	OSU External Examiner, Graduate Student Thesis Committee (Titipong Lertwiriyaprapa; Department of Electrical Engineering)
2009-2010	IBGP Graduate Student Thesis Committee (Eric Hill)
2009-2010	NGSP Graduate Student Thesis Committee (Allen Carpenter)

2010	OSU External Examiner, Graduate Student Thesis Committee (Brian Henslee; Department of Chemical Engineering)
2010-2011	IBGP Graduate Student Thesis Committee (Robert Moyer)
2010-2012	IBGP Graduate Student Thesis Committee (Bart Naughton)
2010-2013	NGSP Graduate Student Thesis Committee (Keerthi Thirtamara-Rajamani)
2014-2015	Psychology Graduate Student Thesis Committee (David Bortz)

Community Service/Mentoring Activities

1999	SUN Program Student Mentor (Pooja Dhume)
1999	High School Summer Student Mentor (Duncan Friedman)
1999	Parkinson's Disease Support Group Meeting, New Orleans, LA
2000	High School Summer Student Mentor (Jeffrey White)
2000	SUN Program Student Mentor (Duncan Friedman)
2001	University of New Orleans Summer Student Mentor (Danielle Levy)
2001	Tulane University Summer Student Mentor (Vanessa D'souza)
2002	SUN Program Student Mentor (Jeffrey White)
2002	SUN Program Student Mentor (Uzondu Agochukwu)
2004	SUN Program Student Mentor (William Steinhardt)
2007	OSUMC Research Day Poster Judge
2007 & 2008	Mentor for Society for Neuroscience (SFN) and National Institutes of Health Neuroscience Scholars Program; Mentees - 1. Dr. Shannon Hardie, Postdoctoral Fellow, Vanderbilt University Medical Center; 2. Dr. Odmara Chang, M.D. Ph.D., Stanford University College of Medicine
2008	Mentor for National Institutes on Drug Abuse Summer Research Program for Underrepresented Minority Students
2008	OSU Undergraduate Honors Research Student Mentor (Kevin Torma)
2008	OSU Summer Biomedical Sciences Student Mentor (Michael Marksz)
2008	Judge for the OSU Honors & Scholars Center Maximus Competition
2008	Judge for Chauncey Leake Award for Excellence in Pharmacology
2009	Judge for Medical Center Research Day
2010	Judge for Medical Center Research Day
2008 -2010	Executive Committee Member for **Autism Speaks** Fundraiser Walk
2014-	OSU Undergraduate Research Student Mentor (Kira Aldrich)
2014-	OSU Undergraduate Research Student Mentor (Alex Fishbach)
2014-	OSU Undergraduate Research Student Mentor (Abigail Zalenski)
2014-	OSU Undergraduate Research Student Mentor (Michael Valle)
2014-	OSU Undergraduate Research Student Mentor (Arun Rao)
2014-	OSU Undergraduate Research Student Mentor (Raeven Winn)
2014-	OSU SROP Diversity Student Mentorship (Crystal Carr)
2014	Judge for Medical Center Research Day
2014	Judge for Denman Forum Undergraduate Research Day

Administrative Responsibilities:

2002-2006	Co-Director of the COBRE Molecular Neurobiology Core Facility
2007-	Department Representative, OSUMC Research Committee
2007-2008	OSU Department of Pharmacology Chair Search Committee
2009-	Vice Chair, Department of Pharmacology
2010	Department Representative on OSUCOM Council on Faculty Development
2011-2013	Scientific Advisory Board Member, Marci and Bill Ingram Center for Autism Spectrum Disorders
2011-2012	OSU Medical Center Strategic Planning Committee Member

RESEARCH SUMMARY

I. Stem cell models of human neurological diseases

Whole-exome sequencing (WES) of genomes has identified a large number of risk genes and strong candidate genes that are both noncoding and coding variants that increase the risk of autism (O'Roak et. al. 2012, Sanders et al, 2014). Furthermore, whole genome sequencing (WGS) is expected to identify additional noncoding and coding gene variants that increase the risk of autism, not previously identified by WES. An experimental human brain model system that allows one to discern which of these coding or noncoding gene variants cause autism would complement and accelerate other strategies used for this purpose. Towards this goal, our laboratory has independently investigated strategies to generate human specific brain organoids from iPSCs. We have engineered human brain organoids that exhibit a remarkable level of development typical of a human embryonic brain that is ~5 weeks old in utero, but after ~12 weeks of culture in vitro. These organoids express a complex milieu of markers characteristic of nearly all types of neurons in the human embryonic brain, as well as cells that are astrocytic, oligodendritic, microglial, and vascular in lineage. This conclusion is based on comparing the whole genome transcriptomic expression profile of the brain organoids to that of 1) a universal human brain reference standard, 2) the atlas of the developing human brain (BrainSpan) from the Allen Institute and 3) tissue other than the brain. Our analysis supports the formation of all the major regions of the brain including the cortex, midbrain, brain stem and the spinal cord in a single brain organoid and shows a >98% match for the ~15, 000 genes expressed in the CNS out of the ~20,800 protein coding genes in the human genome. More importantly, it largely fails to show matches to >800 genes examined that are unique to other tissues. **To the best of our knowledge, this is the first time this advanced milestone in human brain organogenesis from stem cells has been achieved compared to those recently reported** (cerebral - Lancaster et al., 2013; and cerebellar organoids - Muguruma et al., 2015 or in an organoid model of autism – Mariani et al 2015). Additionally, we demonstrate the ability to follow through transcriptomics the earliest impact of a gene mutation during brain development and the downstream consequences in brain organoids at different developmental stages in vitro.

A synopsis and impact of our most recent work on engineering human brain organoids can be found at these websites.

http://www.pcrm.org/sites/default/files/Alzheimers-special-report.pdf
http://www.nature.com/naturejobs/science/articles/10.1038/nj7572-283a
https://news.osu.edu/news/2015/08/18/human-brain-model/
http://www.cnn.com/2015/10/06/health/pioneers-brain-organoids/
http://www.bbc.co.uk/programmes/p0302wt6

II. Autism

We have recently adopted using iPSC-derived stem cell technology to advance our understanding of neurodevelopmental and neuropsychiatric disorders. Towards this goal, we have developed the skills to produce iPSC and iPSC-derived neurons and brain organoids.

Stem cell brain model of human embryonic brains.

We have made the first tuberous sclerosis model of brain organoids in a dish from TSC mutant iPSC line. Analysis of transcriptome is ongoing and preliminary data shows insight into the etiology of the disease

a. Cheng SB, Amici SA, Ren XQ, McKay SB, Treuil MW, Lindstrom JM, Rao J, Anand R. (2009). Presynaptic targeting of alpha4beta 2 nicotinic acetylcholine receptors is regulated by neurexin-1beta. J. Biol Chem. 284:23251-9. PMID: 19567877.** ***Highlighted by "Faculty of 1000 Biology"***

b. Arnold LE, Aman MG, Hollway J, Hurt E, Bates B, Li X, Farmer C, Anand R, Thompson S, Ramadan Y, Williams C. (2012). Placebo-controlled pilot trial of mecamylamine for treatment of autism spectrum disorders. J. Child Adolesc Psychopharmacol. 22:198-205. PMID:22537359.

c. Arnold LE, Anand R, Aman M. (2013). Varenicline in autistic disorder: hypothesis and case eport of single-patient crossover. J. Child Adolesc Psychopharmacol. 23:61-4. PMID:23350866.

We have engineered neural organoids (containing the retina, cortex, midbrain, hindbrain, brain stem and spinal cord) from normal and tuberous sclerosis (TSC2Arg1743Gln) patient skin cells. Transcriptomic results remarkably show comprehensive and accurate correlation of the dysregulated expression of hundreds of genes previously correlated with the clinical symptoms of autism and cancer. For tuberous sclerosis these include genes for tumor formation (A2M. AHSG, ADAM19, ATXN3L, ERG, HAS2), autism (NRXN1, PCDH19, DMD, ABAT, CDR1) blood pressure regulation (AGT, AGTR1), Zn++ ion homeostasis (ALB), Pb++ ion toxicity and round worm infections (HBE1), and cholesterol metabolism (DHCR7) among others. Our working hypothesis is that this massive dysregulation of genes in our neural organoid model system that correlates well with previously well-established genes for disease susceptibility occurs because the gene regulatory mechanisms governing the spatial-temporal fabric of coordinated gene expression in the nucleus is disrupted. This is best understood in the context of topology (TAD), laminin (LAD) and nucleolus (NAD) associated domains and their role in interactions with the inner laminin of the cell's nucleus.

III. Alzheimer's Disease

We have engineered neural organoids (containing the retina, cortex, midbrain, hindbrain, brain stem and spinal cord) from normal and Alzheimer's disease (APP gene duplication) patient skin cells. Transcriptomic results remarkably show comprehensive and accurate correlation of the dysregulated expression of hundreds of genes previously correlated with the clinical symptoms and/or pathologies of AD. These include the immune system (C1QB, C1QC, C1QL3, CD36, CD3G, CD4, CDS2), tau fibrils (EFHD2), lipid homeostasis (A2M, ABCA2, ABCA5) water homeostasis (AQP1) and others like late onset of AD (LRRTM3, COL13A1), AD (BRCA1, BET1, PCDHB18), DOWN (DSCAM, AURKA) and even longevity (ANK2) for AD. These results are consistent with recent and changing ideas of the cause of AD and the importance of inflammation and tau pathology being more prognostic of AD than formation of amyloidogenic plaques.

IV. Nicotine Addiction

My laboratory has studied mechanism of neuropsychiatric disorders including addiction to nicotine. My laboratory has a long history of working in the field of tobacco addiction. We are also identifying the adverse effect of prenatal nicotine exposure on the developing human brain in utero using the organoids.

d. Jeanclos, E. M, Lin, L., Treuil, M., Jayaraman, A., DeCoster, M., and Anand, R. (2001). The *chaperone protein 14-3-3□ interacts with the nicotinic acetylcholine receptor □4-subunit: Evidence for a dynamic role in subunit stabilization. J. Biol. Chem. 276, 28281-90. PMID: 11352901*

e. Lin, L, Jeanclos, E.M., Magdalen Treuil, Braunewell, K.-H., Gundelfinger, E.D., and Anand, R. (2002). The calcium sensor protein VILIP-1 modulates the surface expression and agonist-sensitivity of the nicotinic □4□2 acetylcholine receptor. J. Biol. Chem**.** 277, 41872-41878. PMID: 12202488 **.** *Highlighted by "Faculty of 1000 Biology"***

f. Ren, X-Q, Cheng, S-B, Treuil M.W., Mukherjee, J., Rao, J., Lindstrom, J.M., and Anand, R. (2005). Structural determinants of □4□2 nicotinic acetylcholine receptor trafficking. J. Neurosci. 25, 6676-6686. PMID: 16014729

g. Gierke, P., Zhao, C., Bernstein, H-G., Noack, C., Anand, R., Heinemann, U., and Braunewell, K-H. (2008). Implication of neuronal Ca2+ -Sensor Protein VILIP-1 in the glutamate hypothesis of Schizophrenia. Neurobiology of Disease 32, 162-175**.** PMID: 18691652 *** *Cover article***

h. Amici SA, McKay SB, Wells GB, Robson JI, Nasir M, Ponath G, Anand R. (2012). A highly conserved cytoplasmic cysteine residue in the α4 nicotinic acetylcholine receptor is palmitoylated and regulates protein expression. J. Biol Chem. 287:23119-27**.** PMID:22593584.

i. Anand, R. COPI polices nicotine-mediated up-regulation of nicotinic receptors. J Gen Physiol. 2014 Jan;143 :49-50. doi: 10.1085/jgp.201311136.

V. Evolution of Fish Electric Organs

Funded by a **EUREKA RO1,** we reached a major milestone by a consortium: the completion of the genome and transcriptome of the electric organ (EO) of Electrophorus Electricus, an electric fish with special adaptations in its EO. We show by comparative transcriptomics of EO versus skeletal muscle expression genes that electric fish used a common molecular toolbox of (i) nuclear transcription factors, (ii) genes that regulate cell excitation, (iii) genes that regulate cell size, (iv) genes involved in contraction and excitation contraction coupling, and (v) genes encoding proteins that insulate individual electrocytes to form electric organs. Our work on the E. electricus genome and eight tissue-specific gene expression profiles will greatly facilitate future research on determining the coding and regulatory sequences that specify the function, development, and evolution of electric organs.

To explore new strategies to prevent or treat human neurodegeneration, we are developing a novel paradigm to investigate the highly stress resistant characteristics of electrocytes, electric organ cells of the strongly electric fish, *Electrophorus electricus*. *E. electricus* produces high voltage electric organ discharges (EODs) for predation and defense. Its electrocytes experience extraordinary levels of stress intrinsic to their highly electrogenic nature, for which they appear to be exquisitely well adapted. Adaptations in such cellular "extremophiles" support synthesis of high levels of proteins for electrogenic functions and augmented **energetics and metabolics**. Comparative transcript analysis from the EO of *E.*

electricus versus weakly electric fish (**Science 344, 1522-1525; 2014**), strongly supports our hypothesis—that evolution uniquely endowed *E. electricus* electrocytes with stress adaptations to generate high voltage EODs. Using this novel stress archetype, we propose to identify innovative strategies to prevent or mitigate analogous stress that leads to neurodegeneration in humans. A distinguishing feature of our ongoing work is that it aims to develop new human biological models highly resistant to neurodegeneration using evolutionary logic.

Normal brain activity has a high resting metabolic rate, consuming ~ 20% of the total metabolics compared to the rest of the body in humans. Moreover, the brain has a high energetic demand to fuel channels, pumps and transporters to constantly maintain membrane potentials, create large chemical gradients of Na^+ /K^+/Ca^{++} ions and generate action potentials for synaptic transmission underlying its wondrous capacity for motor, memory and cognitive functions. Unfortunately, modern human longevity has resulted in unanticipated consequences: age-related neurodegenerative disorders including Alzheimer's and Parkinson's disease. Neurodegeneration is presumably preceded by a dramatic escalation of energetic and metabolic demands to sustain cellular stress management systems such as the unfolded protein response (UPR), heat shock response, and ubiquitin-proteosomal clearance systems, as they are activated to mitigate protein aggregation and accumulation in neurons. Because these stressors are chronic, eventually energetic fatigue significantly contributes to neurodegeneration. We hypothesize that an apparent analogous stress response appears to have been experienced during the evolution of the electrocytes of strongly electric fish. This conclusion is based on adaptations deduced from our transcriptomic data. In order for the electric fish to sustain high-voltage EODs for predation and defense, their electrocytes synthesize very large quantities of membrane proteins—including voltage- and ligand-gated ion channels, as well as symporters, antiporters and pumps, supported by an augmented cellular stress management system. The endoplasmic reticulum (ER) of these electrocytes exhibits adaptations to manage physiological stresses associated with high rates of synthesis, folding and assembly of membrane proteins. Additionally, these electrocytes have evolved other adaptations that meet the extraordinary metabolic and energetic demands of high voltage EODs. Thus electrocytes are excitable cells much like neurons, but with highly evolved cellular "extremophile" characteristics to handle stress inherent to chronic, high-voltage, high-amperage EODs.

We postulate that a comprehensive analysis of the extreme adaptation of electrocytes through changes in transcripts, proteins and their posttranslational regulators as well as metabolites, will provide specific knowledge about how a highly advanced "stress management system" that evolved over ~100 million years, is regulated. Our current understanding of human neurophysiology was founded on historical work done in electric fish. By the same token, we reason that knowledge of stress adaptations in the electrocytes of the EO of *E. electricus* is likely to help mitigate stress in degenerating human neurons.

j. Gallant et al., (2014). Genomic basis for convergent evolution of electric organs. Science 344; 1522-1525. PMID 2490089

k. Traeger LL, Volkening JD, Moffett H, Gallant JR, Chen PH, Novina CD, Phillips GN Jr, Anand R, Wells GB, Pinch M, Güth R, Unguez GA, Albert JS, Zakon H, Sussman MR, Samanta MP. Unique patterns of transcript and miRNA expression in the South American strong voltage electric eel (Electrophorus electricus). BMC Genomics. 2015 Mar 26;16:243. doi: 10.1186/s12864-015-1288-8.PMID: 25887781

VI. Modulating human brain biology using time varying weak magnetic fields

We are developing a novel paradigm using time-varying weak magnetic fields (TVMF) to modulate the innate capacity for regeneration in human brains in collaboration with Dr. Vish Subramaniam, Chair, Dept of Aerospace and Mechanical, OSU. Such magnetic fields alter animal and human behaviors, yet, the mechanism(s) by which electromagnetic fields modulate biological systems is not well understood. We have recently engineered human brain organoids with all the major parts of the brain: cortex, midbrain, hindbrain and spinal cord for the first time. Our preliminary studies indicate that weak (microTesla) TVMF change the expression of genes regulating brain biology. We are now systematically investigating how TVMFs interact with biological systems to progressively change gene, protein and metabolite expression in neural stem cells and progenitors forming neurons of different lineages and during their proliferation and migration to form brain structures of the embryonic human brain. The impact of this study will provide a rational strategy to explore the ability to use TVMF to treat neurodegenerative disorders and brain cancers.

VII. Neurxstem (dba NeuRenaisson)

I am the founder and CEO of a new startup company, NeurXstem. Its goal is to commercialize the proprietary process for making complete human neural organoids from iPSCs. Our company is a recipient of a "Best University Startups 2016" award by NCET2 and a Third Frontier Award from the State of Ohio.