# CURRICULUM VITAE
# JEROLD CHUN

**Short Bio:** Jerold Chun, MD, PhD, is Professor and Senior Vice President, Neuroscience Drug Discover at Sanford Burnham Prebys (SBP) Medical Discovery Institute in La Jolla, CA where he conducts basic and translational research, and oversees development of neuroscience programs having commercial and/or philanthropic potential. He is also Adjunct Professor in the Departments of Pharmacology and Neuroscience at the University of California at San Diego (UCSD) School of Medicine, and in the Department of Molecular and Cellular Neuroscience at The Scripps Research Institute (TSRI).

He received his MD and PhD (Neuroscience) degrees through the Medical Scientist Training Program at Stanford University School of Medicine with Kavli Prize recipient Carla Shatz, moving east as a Helen Hay Whitney Postdoctoral Fellow at the Whitehead Institute for Biomedical Research–Massachusetts Institute of Technology where he worked with National Medal of Science recipient Dr. Rudolf Jaenisch and Nobel Laureate David Baltimore. He then joined the faculty at the UCSD School of Medicine, where he became Professor of Pharmacology and Neurosciences and directed the Neurosciences Graduate Program. He subsequently became Senior Director and Department Head of Molecular Neuroscience at Merck Research Laboratories, later returning to academia as Professor at TSRI, to arrive at his current position at SBP.

He has made important contributions to our understanding of the brain and its diseases, including the discovery that our brains are composed of genomically distinct cells; that this genomic mosaicism offers a new mechanism for understanding the most common forms of Alzheimer's disease and possibly other brain disorders; and in separate work, identified the first lysophospholipid receptor, which is a growing class of lipid receptors that has led to new neuroscience drugs (*e.g.,* Gilenya for Multiple Sclerosis) and an understanding of other diseases including hydrocephalus, schizophrenia and fibrosis. Authoring more than 300 scientific papers, he has been recognized in Thomson Reuters' World's Most Influential Scientific Minds citation list, is a member of numerous editorial, advisory, and review boards; and has received many awards, including those from the NIH, Alfred P. Sloan Foundation, The Klingenstein Fund, and The March of Dimes.

Dr. Chun has 22 years of continuous experience with the Biotechnology and Pharmaceutical industry. He participated in all major stages of the development of fingolimod (Gilenya, Novartis), from basic science, preclinical studies through post-marketing and commercial activities: Gilenya is the top product at Novartis, with over $3.1 billion (USD) in 2017. He sat on the scientific advisory board for Amira Pharmaceutical (Versant Ventures), which was sold to Bristol-Meyers-Squibb for ~$475 million for a program based upon the receptor that he had discovered, $LPA_1$.

**Contribution to Science**

1. **Discovery of the first lysophospholipid receptor and initiation of the lysophospholipid receptor field.** Lysophospholipids (LPs) are small, membrane-derived lipids that were thought to produce extracellular effects by different mechanisms – *e.g.,* as detergents, calcium chelation, second messengers – with no receptors identified. Through studies of the embryonic brain, we discovered the first such receptor (Hecht, Weiner et al. 1996) for an LP known as lysophosphatidic acid (LPA), now known as $LPA_1$, allowing subsequent de-orphanization of other LP receptors for LPA, sphingosine 1-phosphate (S1P), and other LPs. This class of lipid receptors now

constitutes around 40% of the known lipid G protein-coupled receptors, with thousands of papers published since our first report in 1996, and the entry of the human medicine fingolimod (Gilenya) for treating multiple sclerosis. We have been involved in many advances in this area including the first LPA receptor knockout (Contos, Fukushima et al. 2000), receptor-mediated effects on the developing brain (Kingsbury, Rehen et al. 2003), and most recently, a crystal structure for $LPA_1$ (Chrencik, Roth et al. 2015) that provided a first structural link between LP and endocannabinoid signaling.

a. Chrencik JE, Roth CB, Terakado M, Kurata H, Oumi R, Kihara Y, Warshaviak D, Nakade S, Asmar-Rovira G, Mileni M, Mizuno H, Griffith MT, Rodgers C, Han GW, Velasquez J, Chun J*, Stevens RC*, Hanson MA*. Crystal structure of human lysophosphatidic acid receptor 1. **Cell** 2015;161:1633-1643. *co-senior authors. PMC4476059
b. Contos JJA, Fukushima N, Weiner JA, Kaushal D, Chun J. Requirement for the $lp_{A1}$ lysophosphatidic acid receptor gene in normal suckling behavior. **Proc Natl Acad Sci USA** 2000;97:13384-13389. PMC27233
c. Hecht JH, Weiner JA, Post SR, Chun J. Ventricular zone gene -1 (Vzg-1) encodes a lysophosphatidic acid receptor expressed in neurogenic regions of the developing cerebral cortex. **J Cell Biol** 1996;135:1071-1083. PMC2133395
d. Kingsbury MA, Rehen SK, Contos JJA, Higgins C, Chun J. Non-proliferative effects of lysophosphatidic acid enhance cortical growth and folding. **Nature Neurosci** 2003;6:1292-1299.

2. **Discovery of somatically derived genomic mosaicism in the brain and its role in sporadic Alzheimer's disease.** Cells of the brain – as with almost all cells of the body – were historically thought to have identical and constant genomes. We identified recombination-activating gene 1 (RAG1) in the brain (Chun, Schatz et al. 1991), supporting the possibility of individually altered genomes in the brain, and stimulating a search for genomic diversity. We discovered the first evidence for this through aneuploidies (Rehen, McConnell et al. 2001) – gains and/or losses of chromosomes representing the first described somatic copy number variants (CNVs) in neural cells – which produce mosaicism and are part of the normal brain, with aneuploid neurons integrated into functional neural circuitry (Kingsbury, Friedman et al. 2005). Multiple other forms of somatic genomic mosaicism have subsequently been identified and we recently reported its operation in sporadic Alzheimer's disease (Bushman, Kaeser et al. 2015) (accounting for ~99% of cases vs. familial disease), which may help to understand and treat AD, and serve as a model for other sporadic or idiopathic brain disorders. These studies have driven single-cell analyses to reveal an enormously diverse landscape of distinct genomic and transcriptomic signatures within and amongst individual brain cells.

a. Bushman DM, Kaeser GE, Siddoway B, Westra JW, Rivera RR, Rehen SK, Yung YC, Chun J. Genomic mosaicism with increased amyloid precursor protein (APP) copy number in single neurons from sporadic Alzheimer's disease brains. **eLife** 2015;4:e05116. doi:10.7554/eLife.05116. PMC4337608
b. Lake BB, Ai R, Kaeser GE, Salathia NS, Yung YC, Liu R, Wildberg A, Gao D, Fung H-L, Chen S, Vijayaraghavan R, Wong J, Chen C, Sheng X, Kaper F, Shen R, Ronaghi M, Fan J-B, *Wang W, *Chun J, *Zhang K. Neuronal subtypes and diversity revealed by single-nucleus RNA sequencing of the human brain. **Science** 2016;352(6293):1586-1590. *Co-senior authors
c. Chun JJM, Schatz DG, Oettinger MA, Jaenisch R, Baltimore D. The recombination activating gene-1 (RAG-1) transcript is present in the murine central nervous system. **Cell** 1991;64:189-200.
d. Kingsbury MA, Friedman B, McConnell MJ, Rehen SK, Yang AH, Kaushal D, Chun J. Aneuploid neurons are functionally active and integrated into brain circuitry. **Proc Natl Acad Sci USA** 2005;102:6143-6147. PMC1087909

e. Rehen SK, McConnell MJ, Kaushal D, Kingsbury MA, Yang AH, Chun J. Chromosomal variation in neurons of the developing and adult mammalian nervous system. **Proc Natl Acad Sci USA,** 2001;98:13361-13366. PMC60876

3. **Discovery of major disease links involving disruption of lysophospholipid signaling.** A major emphasis for our lab has been identifying lysophospholipid (LP) receptor roles in disease. A genuinely remarkable spectrum of pathogenic activities have emerged affecting multiple organ systems and we have driven studies identifying novel roles for LPA or S1P receptors in medically important areas that include: infertility (Ye, Hama et al. 2005), CNS mechanisms in multiple sclerosis (Choi, Gardell et al. 2011), hypoxic brain damage (Herr, Herr et al. 2011), and hydrocephalus (Yung, Mutoh et al. 2011).

   a. Choi JW, Gardell SE, Herr DR, Rivera R, Lee CW, Noguchi K, Teo ST, Yung YC, Lu M, Kennedy G, Chun J. FTY720 (fingolimod) efficacy in an animal model of multiple sclerosis requires astrocyte sphingosine 1-phosphate receptor ($S1P_1$) modulation. **Proc Natl Acad Sci USA** 2011;108(2):751-756. PMC3021041
   b. Herr KJ, Herr DR, Lee CW, Noguchi K, Chun J. Stereotyped fetal brain disorganization is induced by hypoxia and requires lysophosphatidic acid receptor 1 ($LPA_1$) signaling. **Proc Natl Acad Sci USA** 2011;108(37):15444-15449. PMC3174597
   c. Ye X, Hama K, Contos JJ, Anliker B, Inoue A, Skinner MK, Suzuki H, Amano T, Arai H, Aoki J, Chun J. $LPA_3$-mediated lysophosphatidic acid signalling in embryo implantation and spacing. **Nature** 2005;435:104-108. PMC1369590
   d. Yung YC, Mutoh T, Lin ME, Noguchi K, Rivera RR, Choi JW, Kingsbury MA, Chun J. Lysophosphatidic acid signaling may initiate fetal hydrocephalus. **Sci Transl Med** 2011;3:99ra87. PMC3653407

4. **Discovery of extensive programmed cell death in the embryonic brain.** In the early 1990s, programmed cell death – apoptosis – was assumed to be non-existent or trivial in the embryonic brain. We developed more sensitive detection techniques to show that death amongst neuroprogenitor cells was occurring (Blaschke, Staley et al. 1996, Blaschke, Weiner et al. 1998), which provided a mechanistic explanation for the phenotypes of caspase-null mice (that have grossly enlarged brains). The techniques stemming from these studies have been used in the field (Yung, Kennedy et al. 2009), and continue to reveal linkage to developmental mechanisms such as genomic mosaicism (Peterson, Yang et al. 2012).

   a. Blaschke AJ, Staley K, Chun J. Widespread programmed cell death in proliferative and postmitotic regions of the fetal cerebral cortex. **Development** 1996;122:1165-1174.
   b. Blaschke AJ, Weiner JA, Chun J. Programmed cell death is a universal feature of embryonic and postnatal neuroproliferative regions throughout the CNS. **J Comp Neurol** 1998;396:39-50.
   c. Peterson SE, Yang AH, Bushman DM, Westra JW, Yung YC, Barral S, Mutoh T, Rehen SK, Chun J. Aneuploid cells are differentially susceptible to caspase-mediated death during embryonic cerebral cortical development. **J Neurosci** 2012;32(46):16213-16222. PMC361449
   d. Yung YC, Kennedy G, Chun J. Identification of neural programmed cell death through the detection of DNA fragmentation *in situ* and by PCR. In **Current Protocols in Neuroscience**, Unit 3.8, Taylor G (Ed.), John Wiley & Sons, July 2009. PMC2774705

5. **Defining subplate neurons in the developing cerebral cortex.** The subplate is a developmentally transient structure that has importance in organizing the cerebral cortex. Anatomical studies in the 1980s suggested that some of the cells were neurons, however this was not proven. My PhD work defined them as peptidergic neurons (Chun, Nakamura

et al. 1987, Chun and Shatz 1989) representing both subplate and Cajal-Retzius cells that received synaptic connections (Chun and Shatz 1988), with a small sub-population surviving as what had been known as “interstitial neurons” (Chun and Shatz 1989).

a. Chun JJM, Nakamura MJ, Shatz CJ. Transient cells of the developing mammalian telencephalon are peptide-immunoreactive neurons. **Nature** 1987;325:617-620.
b. Chun JJM, Shatz CJ. Redistribution of synaptic vesicle antigens is correlated with the disappearance of a transient synaptic zone in the developing cerebral cortex. **Neuron** 1988;1:297-310.
c. Chun JJM, Shatz CJ. The earliest-generated neurons of the cat cerebral cortex: characterization by MAP2 and neurotransmitter immunohistochemistry during fetal life. **J Neurosci** 1989;9:1648-1667.
d. Chun JJM, Shatz CJ. Interstitial cells of the adult neocortical white matter are the remnant of the early generated subplate neuron population. **J Comp Neurol** 1989;282:555-569.

**Complete List of Published Work in my Bibliography**
http://www.ncbi.nlm.nih.gov/sites/myncbi/jerold.chun.1/bibliography/43724733/public/?sort=date&direction=ascending

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**Citizenship** USA

**Education**

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| 1988-1991 | Postdoctoral Fellow, Whitehead Institute for Biomedical Research/MIT |
| 1981-1988 | M.D.-Ph.D. (Neurosciences), Stanford University School of Medicine |
| 1977-1981 | B.A. (High Honors) in English and Biology, The University of Hawaii at Manoa |

**Academic Research and Professional Experience**

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| 2016- | Professor and Senior Vice President of Neuroscience Drug Discovery, Sanford Burnham Prebys Medical Discovery Institute |
| 2016- | Adjunct Professor, Neuroscience Department, Investigator, Dorris Neuroscience Center, TSRI |
| 2013-2016 | Professor, Molecular and Cellular Neuroscience Department, Investigator, Dorris Neuroscience Center, TSRI |
| 2003-2012 | Professor, Department of Molecular Biology, The Scripps Research Institute, Investigator, Dorris Neuroscience Center |
| 2003- | Adjunct Professor of Neuroscience, UC San Diego (UCSD) |
| 2002- | Adjunct Professor of Pharmacology, UCSD |
| 2001-2002 | Professor of Pharmacology, UCSD |
| 2000-2001 | Acting Director, Neurosciences Graduate Program, UCSD |
| 1999-2001 | Associate Director, Neurosciences Graduate Program, UCSD |
| 1998-2001 | Associate Professor (with tenure), Department of Pharmacology, and Member, Neurosciences and Biomedical Sciences Programs |
| 1995- | Executive Committee Member, Neurosciences Graduate Program, UCSD |
| 1991-1998 | Assistant Professor, Department of Pharmacology and Member, Neurosciences |

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| | and Biomedical Sciences Programs, UCSD School of Medicine |
| 1988-1991 | Postdoctoral Fellow, Whitehead Institute |
| 1981-1988 | M.D.-Ph.D. (MSTP) candidate, Department of Neurobiology, Stanford University School of Medicine |
| 1979-1981 | Undergraduate honors thesis student, Pacific Biomedical Research Center, University of Hawaii |

**Academic Review and Advisory Positions**

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| 2017 | Reviewer and Chair, NIA Alzheimer's Disease in the Post Genomics Era RFA |
| 2017 | Reviewer, NIH Vascular Cell and Molecular Biology |
| 2015- | Editorial Board Member, Scientific Reports (Nature) |
| 2013- | Member, Next Generation and Science Educator Awards Selection Committee, Society for Neuroscience |
| 2012- | Reviewer, Scientific and Medical Review Committee, Hydrocephalus Association |
| 2012- | Reviewer, Scripps Translational Science Institute Pilot Awards Program |
| 2012 | Reviewer, Swiss MS Society |
| 2012 | Reviewer, MS Research Australia (MSRA) |
| 2012 | Reviewer, French Multiple Sclerosis Society (ARSEP) |
| 2012 | Reviewer, BSF (United States-Israel Binational Science Foundation) |
| 2012- | Reviewer, The Wellcome Trust |
| 2011 | Chair, Hydrocephalus Association Review Panel |
| 2011 | Reviewer, Italian Multiple Sclerosis Society (FISM) |
| 2010 | Member, Board of Prostaglandins and Other Lipid Mediators |
| 2010 | Reviewer, NCI Discovery and Development Special Emphasis Panel P01 |
| 2010-2012 | Member, College of CSR Reviewers, NIH |
| 2010 | Reviewer, NIMH Sensitive Period RFA |
| 2010 | Reviewer, NCI, Discovery, Development, and Diagnosis P01 |
| 2009- | Editorial Board, Eye and Brain |
| 2009 | Reviewer, NIH ARRA Challenge Grants in Health and Science Research |
| 2009 | Reviewer, NIMH ARRA Autism RFA |
| 2008- | Co-Chair, Novartis FTY Mechanism of Action Advisory Board |
| 2008 | Reviewer, Special Emphasis Panel, Support of Competitive Research (SCORE) Awards, NIGMS |
| 2008- | Reviewer, Cancer Research, UK |
| 2007- | Editorial Advisory Board, Current Pharmaceutical Design |
| 2007- | Editorial Board Member, Open Neuroscience (ON) Journal |
| 2007- | Associate Editor, "Prostaglandin and Lipid Mediators," Bentham Science Pub |
| 2006- | Reviewer, Deutsche Forschungsgemeinschaft (DFG), Germany |
| 2006- | Reviewer, The Wellcome Trust, UK |
| 2006 | Byrd Alzheimer's Reviewer |
| 2006- | Chairman, External Advisory Committee, RCMI/NINDS University of Hawaii |
| 2005-2008 | Regular Member, NIH MBPP study section |
| 2004- | March of Dimes, Basil O'Connor Scholars Committee |
| 2004- | External Reviewer, Biotechnology and Biological Sciences Research Council (BBRC), UK |
| 2004 | External reviewer, The Netherlands Organisation for Health Research and Development |
| 2004 | External reviewer, Genome British Columbia |
| 2004- | Scientific Advisory Committee, Special Neuroscience Research Program (NINDS, University of Hawaii) |
| 2004 | External Reviewer, Sass Foundation |
| 2000-2005 | Editorial Board Member, Journal of Biological Chemistry |
| 2000-2003 | Permanent Member, MDCN-6, NIH |
| 2001- | Editorial Board, Journal of Molecular Medicine |

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