# Jeffry B. Lansman, Ph.D.

# **Professor Emeritus** University of California, San Francisco

EDUCATION			
1971 - 1973	Purchase College	B.A.	Biology
1976 - 1978	Tufts University	M.S.	Biology

1978 - 1982 University of California, Los Angeles Ph.D. Physiology/Biophysics

## PRINCIPAL POSITIONS HELD

1982 - 1983	Department of Physiology University of California, Los Angeles	NIMH Postdoctoral Fellow
1983 - 1984	Department of Physiology Yale School of Medicine	NIH Postdoctoral Fellow
1985 - 1986	Physiological Laboratory University of Cambridge	National Science Foundation Postdoctoral Fellow
1987 - 1992	Department of Pharmacology University of California, San Francisco	Assistant Professor
1992 - 2012	Department of Cellular & Molecular Pharmacology University of California, San Francisco	Associate Professor
2012 - 2017	Department of Cellular & Molecular Pharmacology	Professor
2017 - present	Department of Cellular & Molecular Pharmacology	Professor Emeritus
2017 - present	Turex Marine BioPharma Drug discovery	Founder and CSO
2023 - 2024	Cardio AI Multimodal AI precision CVD screening	Senior Scientific Advisor and Executive Vice-President R&D

## **AFFILIATED ACADEMIC PROGRAMS**

**Neuroscience Graduate Program** 

Weill Institute of Neurosciences

Cardiovascular Research Institute

# **CERTIFICATE COURSES**

1975	Course in Neurobiology	Marine Biological Laboratory, Woods Hole
1976	Course in Invertebrate Physiology	Marine Biological Laboratory, Woods Hole
1977	Course in Synaptic Structure and Function	Cold Spring Harbor Laboratory
1979	Invertebrate Embryology	Hopkins Marine Station, Stanford University
1980	Course in Invertebrate Ecology	Bermuda Biological Station for Research
1988	Course in Biological Imaging	Marine Biological Laboratory, Woods Hole
2021	Entrepreneurship	Wharton School, University of Pennsylvania

# **HONORS AND AWARDS**

1980	Sigma Xi, Tufts University
1985	NATO Postdoctoral Fellow, Cambridge University National Science Foundation
1986	Syntex Scholars Achievement in Cardiovascular Research Syntex Corporation
1987	Basil O'Connor Scholar Award March of Dimes Foundation
1991	Dunaway-Burnam Visiting Professor of Physiology Dartmouth Medical School
2002	Long Prize "Teacher of the Year" UCSF School of Pharmacy
2004	Joseph M. Long Foundation Prize for Excellence in Teaching, UCSF School of Pharmacy (Awarded by the Class of 2004)
2004	Long Prize "Teacher of the Year" UCSF School of Pharmacy
2006	Joseph M. Long Foundation Prize for Excellence in Teaching, UCSF School of Pharmacy (awarded by the graduating Class of 2006)
2006	Dean's Recognition for Excellence in Teaching UCSF School of Pharmacy (Winter)
2006	Nominated Academic Senate Distinction in Teaching
2006	Long Prize "Teacher of the Year" UCSF School of Pharmacy

2007	Dean's Recognition for Excellence in Teaching UCSF School of Pharmacy (Fall)
2008	Dean's Recognition for Excellence in Teaching UCSF School of Pharmacy (Winter)
2008	Dean's Recognition for Excellence in Teaching UCSF School of Pharmacy (Spring)
2008	Long Prize "Teacher of the Year" UCSF School of Pharmacy
2008	Dean's Recognition for Excellence in Teaching UCSF School of Pharmacy (Fall)
2008	Nominated: Essential Core Teaching Award for Excellence in Small Group, UCSF School of Medicine
2008	Nominated for Kaiser Award for Excellence Teaching UCSF School of Medicine
2009	Joseph M. Long Foundation Prize for Excellence in Teaching UCSF School of Pharmacy (awarded by the Graduating Class of 2009)
2009	AACP Teacher of the Year American Association Colleges of Pharmacy
2009	Dean's Recognition for Excellence in Teaching UCSF School of Pharmacy (Winter)
2009	Dean's Recognition for Excellence in Teaching UCSF School of Pharmacy (Spring)
2010	Dean's Recognition for Excellence in Teaching UCSF School of Pharmacy (Winter)
2010	Joseph M. Long Foundation Prize for Excellence in Teaching UCSF School of Pharmacy (awarded by the Graduating Class of 2010)
2010	AACP Teacher of the Year American Association Colleges of Pharmacy
2010	Dean's Recognition for Excellence in Teaching UCSF School of Pharmacy (Spring)
2011	Long Prize "Teacher of the Year" UCSF School of Pharmacy
2012	Dean's Recognition for Excellence in Teaching UCSF School of Pharmacy (Winter)
2013	Dean's Recognition for Excellence in Teaching UCSF School of Pharmacy (Winter)

2013	Joseph M. Long Foundation Prize for Excellence in Teaching UCSF School of Pharmacy (awarded by the Graduating Class of 2013)
2013	Dean's Recognition for Excellence in Teaching UCSF School of Pharmacy (Fall)
2013	Dean's Recognition for Excellence in Teaching UCSF School of Pharmacy (Winter)
2014	Dean's Recognition for Excellence in Teaching School of Pharmacy (Winter)
2014	Dean's Recognition for Excellence in Teaching UCSF School of Pharmacy (Spring)
2015	Dean's Recognition for Excellence in Teaching, UCSF School of Pharmacy (Winter)

## **AREAS OF INTEREST**

Degenerative disease of nerve and muscle Calcium channels and signaling

Mechanosensitive ion channels **Drug Discovery** 

## **SERVICE TO PROFESSIONAL PUBLICATIONS**

ACS Chemical Biology Journal of Physiology

**Biophysical Journal** Journal of Neurophysiology

**FASEB Journal** Neuroscience

Plos One Journal Cell Biology

Journal of General Physiology Plos One Computational Biology

## **SCIENTIFIC CONTRIBUTIONS**

- Discovery of If, a novel sodium channel subsequently shown to be the cardiac pacemaker (UCLA, 1982)
- Discovery of the calcium-activated sodium channel current which controls the duration of individual action potentials in many cells including nerve and sensory cells (UCLA, 1982)
- First identification of L- and T-type calcium channels in ventricular heart cells and elucidation of the mechanism of the action of dihydropyridine dugs and beta receptor agonists on the heart that stimulate the increase in heart rate and contractility by sympathetic nervous system activity (Yale, 1984)

- First direct measurement of the lifetime of a single calcium ion in the pore of a single calcium channel molecule which provided proof of a two binding site model to explain the high permeability of calcium channels to extracellular Ca<sup>2+</sup> ions over Na<sup>+</sup> ions (Yale, 1985)
- Discovery of mechanosensitive ion channels in vascular endothelial cells as the primary sensor for detecting blood pressor and blood flow in the vascular system (Cambridge, 1986)
- Discovery of mechanosensitive ion channels as a pathway for abnormal Ca<sup>2+</sup> entry in muscular dystrophy and the major pathway for pathophysiological Ca<sup>2+</sup> entry in degenerative disease. (UCSF, 1990)
- Discovery of functionally distinct L-type Ca<sup>2+</sup> channels in the brain that contribute to facilitation of Ca<sup>2+</sup> entry and signal processing. First description of a new pathway for intracellular Ca<sup>2+</sup> store refilling in which intracellular Ca<sup>2+</sup> store depletion activates L-type channels in the cell membrane (UCSF, 2001).
- Discovery of L-type and NMDA receptor upregulation in the pathogenesis of cerebellar neurodegenerative disease and ataxia (UCSF, 2012)

## **SERVICE TO PROFESSIONAL ORGANIZATIONS**

2016 - 2017	Annals of Pharmacology and Therapeutics	Editorial Board
2016 - 2017	Brain and Neuroscience	Editorial Board

## **INTERNATIONAL INVITED PRESENTATIONS**

1984	Physiological Society, Oxford University Invited Speaker		
1984	Department of Physiology, Oxford University	Invited Seminar	
1986	Physiological Laboratory, Cambridge University	Invited Speaker	
1990	International Symposium on the Regulation of Coronary Circulation, Kobe, Japan	i invited speaker	
1990	International Symposium on Basic Neurophysiology, Okazaki, Japan	Invited Speaker	
1991	International Symposium on Mechanoreceptors, Nagoya, Japan	Invited Speaker	
1991	Third International Congress of Comparative Physiology, Tokyo	Invited Speaker	
1995	Université Montpellier, France	Ph.D. Committee	
2004	Australian Physiological Society Symposium "Stretchactivated ion Channels"  Invited Speaker		

#### **MEMBERSHIPS**

1986 - 2022	Biophysical Society
1986 - 2022	Society of General Physiologists

#### UNIVERSITY OF CALIFORNIA SYSTEM-WIDE LEADERSHIP

## MEMBER, ACADEMIC SENATE BOARD ON ADMISSION & RELATIONS WITH SCHOOLS

(2003-2005) The Board on Admissions and Relations with Schools sets system-wide admissions policy for all nine undergraduate campuses of the University of California. I reviewed and amended admission requirements and policies regarding "Eligibility in a Local Context," admission metrics as correlated with future success at UC, principles and policies for undergraduate admissions testing, UC subject admission requirements, and inclusiveness indicators in admissions policy.

MEMBER, UNIVERSITY COMMITTEE ON PRIVILEGE AND TENURE (2012-2013) Privilege and Tenure is an Academic Senate Committee charged as a quasi-judicial body to hear faculty grievances and to provide due process adjudication of faculty disciplinary cases. At the system-wide level, I reviewed and revised policies and procedures that govern the Privilege and Tenure hearings on the ten UC campuses.

CHAIR, UNIVERSITY COMMITTEE ON PRIVILEGE AND TENURE (2013-2016) I reviewed and revised policy related to concerns from incidents of racial discrimination and sexual harassment on several campuses. Under my direction, the committee evaluated how divisional Privilege and Tenure Committees interact with their respective administrations and Title VII and IX Offices, particularly in relation to investigative procedures and evidentiary standards. I drafted guidelines for procedures for handling sexual harassment cases on all campuses, which coordinated Title IX Office investigations with University investigations.

http://senate.universityofcalifornia.edu/\_files/committees/ucpt/UCPT2013-14AnnualReport.pdf http://senate.universityofcalifornia.edu/\_files/committees/ucpt/UCPT2013-14AnnualReport.pdf

MEMBER, PRESIDENT NAPOLITANO'S WORK GROUP ON DISCRIMINATION AND BIAS (2013-2014) University of California President Janet Napolitano formed an independent task force headed by former California State Supreme Court Justice Carlos Moreno to investigate university policies and procedures for addressing racial bias and discrimination. The report of the Moreno Task Force concluded campus procedures "...failed to adequately record, investigate, or provide for disciplinary sanctions for incidents which, if substantiated, would constitute violations of university nondiscrimination policy." Based on these conclusions the President formed a work group to propose new policies and procedures for both dealing effectively with acts of discrimination and ensuring a university climate of respect and recognition of all members of the campus community. The report can be found at:

http://www.ucop.edu/moreno-report/moreno-senate-admin-work-group-12-23-13.pdf

## **UCSF CAMPUS LEADERSHIP**

MEMBER, ACADEMIC SENATE GRADUATE COUNCIL (2004-2006) The Graduate Council is charged with making reports and recommendations to the Academic Senate, periodic external quality reviews of existing graduate programs, setting policies and standards concerning graduate students' progress towards their degrees and the conduct of examinations for degrees, overseeing standards for part-time degree status, making recommendations for the awards of fellowships, and advising the administration on foundation and research institution issues related to graduate education.

CHAIR, ACADEMIC SENATE GRADUATE COUNCIL (2007-2009) I directed external review of UCSF's doctoral programs in Neuroscience, Chemistry and Chemical Biology, Developmental Biology, Bioengineering, Medical Anthropology, and the Masters in Clinical Sciences. In addition, he evaluated program proposals, defined support and teaching staff needs, and determined cost and revenue structures for new Master's degree programs in Global Health, Science and Technology Studies in Medicine, and Dental Hygiene, and a Ph.D. program in Epidemiology and Translational Sciences.

http://senate.ucsf.edu/2006-2007/i-gradc-2006-07-annualreport.pdf http://senate.ucsf.edu/2007-2008/i-gradc-2007-08-annualreport.pdf

CHAIR, ACADEMIC TASK FORCE ON THE UCSF INSTITUTE OF QUANTITATIVE BIOSCIENCES (2008) The Institute of Quantitative Biology is a consortium of UC faculty whose goal is to advance quantitative biosciences using the methods of physics, chemistry, and computer science to solve fundamental problems in human biology. The Institute fosters transfer of basic science to commercial start-ups.

CHAIR, TASK FORCE TO REVIEW NEW DEPT. OF BIOENGINEERING AND THERAPEUTIC SCIENCE (2008)

MEMBER, CHANCELLOR'S EXECUTIVE BUDGET COMMITTEE (2009)

CHAIR, ACADEMIC SENATE COMMITTEE ON PRIVILEGE AND TENURE (2012-2014) I presided over evidentiary hearings involving faculty disciplinary and grievance cases and also negotiated settlements with administration counsel and grievant. I led in developing policies to extend Privilege and Tenure due process rights to faculty in the Adjunct Series.

MEMBER, ACADEMIC COMMITTEE ON COURSES OF INSTRUCTION (2014-2017) The Committee on Courses of Instruction reviews and approves all new courses at UCSF. Working with faculty throughout the university, I worked with program instructors to define specific skill sets, methods to evaluate student progress and skill and knowledge acquisition, and define course content within the context of existing courses and the specific program.

## PEER-REVIEWED PUBLICATIONS

- 1. Lansman, J. and Haynes, D.H. (1975) Kinetics of a Ca<sup>2+</sup>-triggered membrane aggregation reaction of phospholipid membranes. Biochimica Biophysica Acta 394:335-347.
- 2. Lansman, J.B. and Haynes, D.H. (1979) Charge asymmetry does not affect the rate of Ca<sup>2+</sup>induced aggregation of phospholipid vesicles. Biophysical Journal 26:335-337.
- 3. Haynes, D.H., Lansman, J.B., Cahill, A.L. and Morris, S.J. (1979) Kinetics of cation-induced aggregation of Torpedo electric organ synaptic vesicles. Biochimica Biophysica Acta 557:340-
- 4. Lansman, J.B. and Cochrane, D.E. (1979) Wheat germ agglutinin stimulates exocytotic histamine secretion from rat mast cells in the absence of extracellular calcium. Biochemical Pharmacology 29:455-458.
- 5. Cochrane, D.E., Distel, D.L., Lansman, J.B. and Paterson, B.M. (1982) Stimulus-secretion coupling in rat mast cells: Inactivation of calcium-dependent secretion. Journal of Physiology 323:423-435.

- 6. Carraway, R., Cochrane, D.E., Lansman, J.B., Leeman, S.E., Paterson, B.M. and Welch, H.J. (1982) Neurotensin stimulates histamine secretion from rat mast cells and elevates plasma histamine levels. Journal of Physiology 323:403-414.
- 7. Moody, W.J. and Lansman, J.B. (1983) Developmental regulation of Ca<sup>2+</sup> and K<sup>+</sup> currents during hormone-induced meiotic maturation of starfish oocytes. Proceedings of the National Academy of Sciences USA 80:3096-3100.
- 8. Lansman, J.B. (1983) Voltage clamp study of the conductance activated at fertilization in the egg of a starfish. Journal of Physiology 345:353-372.
- 9. Hess, P., Lansman, J.B. and Tsien, R.W. (1984) Different modes of calcium channel gating behavior favored by dihydropyridine agonists and antagonists. *Nature* 311:538-544.
- 10. Nilius, B., Hess, P., Lansman, J.B. and Tsien, R.W. (1985) A novel type of cardiac calcium channel in ventricular cells. *Nature* 316:443-446.
- 11. Hess, P., Lansman, J.B. and Tsien, R.W. (1986) Calcium channel selectivity for divalent and monovalent cations. Voltage and concentration dependence of single channel current in ventricular heart cells. Journal of General Physiology 88:293-319.
- 12. Lansman, J.B., Hess, P. and Tsien, R.W. (1986) Blockade of current through single calcium channels by Cd, Mg, and Ca. Voltage-and concentration-dependence of Ca entry into the pore. Journal of General Physiology 88:321-347.
- 13. Tsien, R.W., Bean, B.P., Hess, P., Lansman, J.B., Nilius, B. and Nowycky, M.C. (1986) Mechanisms of calcium channel modulation by beta-adrenergic agents and dihydropyridine agonists. Journal of Molecular and Cellular Cardiology 18:691-710.
- 14. Hess, P., Lansman, J.B., Nilius, B. and Tsien, R.W. (1987) Calcium channel types in cardiac myocytes: Modulation by dihydropyridines and beta-adrenergic stimulation. Journal of Cardiovascular Pharmacology 8 (suppl. 9):511-521.
- 15. Lansman, J.B. (1987) Calcium current and calcium-activated inward current in the oocyte of the starfish *Leptasterias hexactis*. *Journal of Physiology* 390:397-413.
- 16. Lansman, J.B., Hallam, T.J. and Rink, T.J. (1987) Single stretch-activated ion channels in vascular endothelial cells as mechanotransducers? Nature 325:811-813.
- 17. Nilius, B., Hess, P., Lansman, J.B. and Tsien, R.W. (1987) Two kinds of calcium channels in isolated ventricular cells form guinea pig heart. Fortschritte der Zoologie 33:83-98.
- 18. Franco, A. and Lansman, J.B. (1990) Calcium entry through stretch-inactivated ion channels in mdx myotubes. Nature 344:670-673.
- 19. Franco, A. and Lansman, J.B. (1990) Stretch-sensitive channels in developing muscle cells from a mouse cell line. Journal of Physiology 427:361-380.
- 20. Lansman, J.B. (1990) Blockade of current through single calcium channels by trivalent lanthanide cations. Effect of ionic radius on the rates of ion entry and exit. Journal of General Physiology 95:679-696.
- 21. Winegar, B. and Lansman, J.B. (1990) Voltage-dependent block by zinc of single calcium channels in mouse myotubes. Journal of Physiology 425:563-578.

- 22. Forsayeth, J.R., Rossi, A.B., Franco, A., Lansman, J.B., and Hall, Z. (1990). Expression of functional mouse muscle acetylcholine receptors in Chinese Hamster Ovary cells. Journal of Neuroscience 10(8):2771-2779.
- 23. Gu, Y., Franco, A., Gardner, P.D., Lansman, J.B., Forsayeth, J.R., and Hall, Z.W. (1990). Properties of embyronic and adult muscle acetycholine receptors transiently expressed in COS cells. Neuron 5:147-157.
- 24. Winegar, B., Kelly, R., and Lansman, J.B. (1991) Block of current through single calcium channels by Fe, Co, Ni. Location of the transition metal binding site in the pore. Journal of General Physiology 97:351-367.
- 25. Slesinger, P.A. and Lansman, J.B. (1991a) Inactivation of calcium currents in granule cells cultured from mouse cerebellum. Journal of Physiology 435:101-121
- 26. Slesinger, P.A. and Lansman, J.B. (1991b) Inactivating and non-inactivating dihydropyridinesensitive calcium channels in mouse cerebellar granule cells. Journal of Physiology 439:301-3
- 27. Franco, A., Winegar, B.D., and Lansman, J.B. (1991) Open channel block by gadolinium ion of the stretch-inactivated ion channel in mdx myotubes. Biophysical Journal 59:1-7.
- 28. Haws, C.M. and Lansman, J.B. (1991a) Calcium permeable ion channels open at negative membrane potentials in cerebellar neurons from mdx mice. Proceedings of the Royal Society of London B 244:185-189.
- 29. Haws, C.M. and Lansman J.B. (1991b) Developmental regulation of mechanosensitive Ca2+ channels in skeletal muscle from normal and mdx mice. Proceedings of the Royal Society of London B 245:173-177.
- 30. Slesinger, P.A. and Lansman, J.B. (1991c) Reopening of Ca<sup>2+</sup> channels in mouse cerebellar neurons at resting membrane potentials during recovery from inactivation. Neuron 7:755-762.
- 31. Haws, C.M., Slesinger, P.A., and Lansman, J.B. (1993) Dihydropyridine- and ω-conotoxin-sensitive Ca<sup>2+</sup> currents in cerebellar neurons. Persistent block of L-type channels by a pertussis toxinsensitive G protein. Journal of Neuroscience 13:1148-1156
- 32. Elam, T.R. and Lansman, J.B. (1993) Mechanosensitive ion channels in vascular endothelial cells. In, NATO Advanced Studies Workshop: The Role of Ion Flux in Pulmonary Vascular Control. ed., E. Kenneth Weir, Plenum Press: New York
- 33. Franco-Obregón, A. and Lansman, J.B. (1994) Mechanosensitive ion channels in skeletal muscle from normal and dystrophic mice. Journal of Physiology 481(2):299-309
- 34. Elam, T.R. and Lansman, J.B. (1995) The role of Mg<sup>2+</sup> in the inactivation of inwardly rectifying K<sup>+</sup> channels in aortic endothelial cells. Journal of General Physiology 105:463-484.
- 35. Franco-Obrégon, A. and Lansman, J.B. (1995) Spontaneous and agonist-induced activity of acetylcholine receptor channels in developing muscle cells from normal and dystrophic mice. Journal of Neuroscience Research 42:452-458.
- 36. Chavis, P., Fagni, L., Bockaert, J., and Lansman, J.B. (1995) Modulation of calcium channels by metabotropic glutamate receptors in cerebellar granule cells. Neuropharmacology 34(8):929-937.
- 37. Slesinger, P.A. and Lansman, J.B. (1996) Reopening of single L-type Ca<sup>2+</sup> channels in mouse cerebellar granule cells: Voltage- and ion concentration-dependence. Journal of Physiology 491.2:335-345.

- 38. Haws, C.M., Winegar, B., and Lansman, J.B. (1996) Block of L-type Ca<sup>2+</sup> channels in skeletal muscle fibers by aminoglycoside antibiotics. *Journal of General Physiology* 107:421-432
- 39. Winegar, B., Haws, C.M. and Lansman, J.B. (1996) Subconductance block of mechanosensitive ion channels in skeletal muscle fibers by aminoglycoside antibiotics. *Journal of General Physiology* 107:433-443
- 40. Parri, H.R. and Lansman, J.B (1996) Multiple components of Ca<sup>2+</sup> channel facilitation in cerebellar granule cells. Expression of facilitation during development in culture. *Journal of Neuroscience* 16:4890-4902.
- 41. Chavis, P., Fagni, L, Lansman, J.B, and Bockaert, J. (1996) Functional coupling between ryanodine receptors and L-type calcium channels in neurons. *Nature* 382:719-722
- 42. Franco-Obrégon, A. and Lansman, J.B. (2002) Changes in mechanosensitive channel gating following mechanical stimulation in skeletal muscle myotubes from the mdx mouse. *Journal of Physiology* 539.2:391-407
- 43. Lansman, J.B. and Franco-Obregon, A. (2006) Mechanosensitive ion channels in skeletal muscle: a link in the membrane pathology of muscular dystrophy. *Clinical and Experimental Physiology and Pharmacology* 33:649-656
- 44. Vasquez, I., Tan, N., Boonyasampant, M, , Koppitch, K., and Lansman, J.B. (2012) Partial opening and subconductance gating of mechanosensitive ion channels in dystrophic skeletal muscle. *Journal of Physiology* 590(Pt 23):6167-6185.
- 45. Ho, T.C., Horn, N.A., Huyhn, T., Kelava, L. and Lansman, J.B. (2012) Evidence TRPV4 contributes to mechanosensitive ion channels in mouse skeletal muscle fibers. *Channels* 6(4):246-254.
- 46. Tan, N. and Lansman, J.B. (2014) Utrophin regulates modal gating of mechanosensitive ion channels in dystrophic skeletal muscle. *Journal of Physiology* 592(Pt 15):3303-3323
- 47. Lansman, J.B. (2015) Utrophin suppresses low frequency oscillations and coupled gating of mechanosensitive ion channels in dystrophic skeletal muscle. *Channels* 9(3):145-160.
- 48. Lansman, J.B. (2024) Compensatory changes in L-type and NMDA channels in cerebellar granule cells from leaner mice. (in revision)
- 49. Lansman, J.B. (2024) Hidden Markov Model analysis of individual subunit gating during single activations of mechanosensitive ion channels in dystrophic skeletal muscle. (in preparation)
- 50. Lansman, J.B. (2024) Analysis of the subconductance blocking mechanism of ruthenium red on single mechanosensitive channels in skeletal muscle fibers. (in preparation)
- 51. Lansman, J. (2024) The sodium and potassium currents in skeletal muscle from *mdx* and *mdx/utrophin* double knock out mice (in preparation)

#### **REVIEW ARTICLES**

- 1. Lansman, J.B. (1983) Components of the starfish fertilization potential: Role of calcium and calcium-dependent inward current. In, <u>Neurology and Neurobiology Vol. 5, The Physiology of Excitable Cells</u>. Grinnell, A. and Moody, W.J., eds., New York: Alan Liss, Inc.
- 2. Hess, P., Lansman, J.B. and Tsien, R.W. (1984) Mechanism of calcium channel modulation by dihydropyridine agonists and antagonists. In, <u>Control and Manipulation of Calcium Movement</u>. Parrat, ed., New York: Raven Press.
- 3. Tsien, R.W., Hess, P. and Lansman, J.B. (1985) Current views of cardiac calcium channels and their response to calcium antagonists and agonists. In, <u>Cardiac Electrophysiology and Arrhythmias</u>. Zipes, D.F. and Jalife, J., eds., Orlando, Grune and Stratton.
- 4. Hess, P., Fox, A.P., Lansman, J.B., Nilius, B., Nowycky, M.C. and Tsien, R.W. (1986) Calcium channel types in cardiac, neuronal and smooth muscle derived cells. Differences in gating, permeation and pharmacology. In, <a href="Ionic Channels in Neural Membranes">Ionic Channels in Neural Membranes</a>. Ritchie, J.M., and Keynes, R., eds., Alan R. Liss, Inc., New York
- 5. Fox, A.P., Hess, P., Lansman, J.B., Nilius, B., Nowycky, M.C., and Tsien, RW. (1986) Shifts between modes of calcium channel gating as a basis for pharmacological modulation of calcium in cardiac, neuronal and smooth muscle-derived cells. in: <a href="New Insights into Cell & Membrane">New Insights into Cell & Membrane</a> Transport Process A. Poste & S.J. Cooke, eds., Plenum Press: New York
- 6. Lansman, J.B. (1988) Endothelial mechanosensors. Nature 325:811-813.
- 7. Lansman, J.B. and Franco, A. (1991) What does dystrophin do in normal muscle? *Journal of Muscle Research and Cell Motility* 12:409-411.
- 8. Chavis, P., Fagni, L., Conquet, F., Lansman, J. and Bockaert, J. (1998) Metabotropic glutamate mGluR1 receptors couple L-type Ca<sup>2+</sup> channels and ryanodine receptors in neurons. In "Metabotropic Glutamate Receptors and Brain Function" Edited by Moroni, F., Nicoletti, F., and Pelligrini-Giampietro, D.E. London: Portland Press
- 9. Lansman, J.B. and Franco-Obregon, A. (2005) Stretch-inactivated channels in skeletal muscle. In, "Mechanosensitivity of Cells and Tissues." Ed, Kamkin, A. Moscow: Academia Press
- 10. Lansman, J.B. (2007) Mechanosensitive ion channels in dystrophic muscle. pp 467-484. <u>Current Topics in Membranes Volume 59</u>. Ed., Hamill, O. San Diego: Elsevier Press

Citations (total): 8800

h-index: 33 i10-index: 50

#### **FORMAL TEACHING**

Immuno- and Endocrine Pharmacology	Course Director, Lecturer	
Basic Concepts of Cellular & Molecular Neuroscience	Course Director, Lecturer	
Prologue, School of Medicine	Small Group Leader	
Autonomic & Cardiovascular Pharmacology	Course Director, Lecturer	
Neuropharmacology	Course Director, Lecture	

## PROFESSIONAL SCHOOL TEACHING

I directed and taught the second-year course in pharmacology for doctoral pharmacy students and cardiovascular pharmacology to medical students. The course covered Immunopharmacology and Endocrine Drugs, Autonomic and Cardiovascular Pharmacology, and Neuropharmacology. I also directed small group sessions in the School of Medicine, and lectured in the Biomedical Sciences basic science curriculum.

## **GRADUATE TEACHING AND CURRICULUM DEVELOPMENT**

I directed and taught in Basic Concepts in Cellular and Molecular Neuroscience, the core course for first year neuroscience graduate students. Lectures covered the biophysics of nerve excitation, including the thermodynamics of electro-diffusion, the Nernst-Planck flux equation, origin of the membrane potential, voltage clamp methods, the Hodgkin and Huxley model for the nerve action potential, selective ion transport, and ion channel functional diversity relevant to the integrative properties of neurons for understanding information processing in the brain.

#### **MENTORING AND TRAINING**

# PRE-DOCTORAL STUDENTS SUPERVISED/MENTORED

Date	Name	Program or School	Role	Current Position
				Professor
1987 - 1991	Paul Slesinger	Neuroscience	PhD Advisor	Dept. Neuroscience,
				Mt. Sinai School of Medicine
1987 - 1993	Alfredo Franco-	Neuroscience	PhD Advisor	Professor Dept. of Surgery
1987 - 1993	Obregon	Neuroscience	PIID AUVISUI	National University of Singapore
1988 - 1993	Teryl Elam	Physiology	PhD Advisor	Private Practice, OB-GYN
1995 - 1996	Pascal Chavis	Visiting PHD	PhD Advisor	Institut de Neurobiologie de la
1990 - 1990		Student		Méditerranée, Marseille

### POSTDOCTORAL FELLOWS/RESIDENTS SUPERVISED/MENTORED

Date	Name	Fellow	Role	<b>Current Position</b>
1989 - 1993   Bruce Winegar, Ph.D.	Post-Doc	Research	Senior Scientist, Pherin	
1909 - 1993	Bruce Willegal, Fil.D.	POSI-DOC	Supervision	Pharmaceuticals
1987 - 1991	Christine Haws Ph.D.	Post-Doc	Research	Not known
1387 - 1331	Cilistille Haws Fil.D.	r ost-boc	Supervision	NOT KITOWIT
1997 - 1998	Panan Kally D Bhil	Post-Doc	Research	University Laboratory of
1997 - 1996	Ronan Kelly D.Phil.	POSI-DOC	Supervision	Physiology, Oxford
		Burroughs-	Research	
1993 - 1993	Munir Hussain Ph.D.	Wellcome	Wellcome Supervision	University of Leeds, Leeds UK
		Visiting Post-Doc	Super vision	
1993 - 1994	Rajeswari	Post-Doc	Research	Stanford University
1993 - 1994	Medicherla, Ph.D.	FUSI-DUC	Supervision	Staniord Oniversity
1992 - 1995	Rheinnalt Parri, Ph.D.	Post-Doc	Research	Senior Lecturer, Aston
1992 - 1995	Kneinnait Parri, Ph.D.		Supervision	University, Birmingham, UK
1996 - 1996 Leonard I	Loopard Koh M D	Visiting Clinical	Research	Dept. of Endocrinology,
	Leonard Koh M.D.	Fellow	Supervision	Singapore General Hospital
2000 - 2001	Gang Lu, M.D.	Post-Doc	Research	Senior Associate Scientist,
			Supervision	Hoffmann-La Roche

I have also mentored and supervised the research of 16 undergraduate or post -baccalaureate students who have gone on to enroll in highly rated Medical School and Ph.D. Programs.

## **RESEARCH AND CREATIVE ACTIVITIES**

## Biophysical basis of mechanical sensitivity and role in muscle disease

My research seeks to understand how cells and tissues sense and respond to mechanical forces. Mechanical forces control many fundamental physiological functions including touch, hearing, proprioception, cardiovascular and pulmonary function. There is strong evidence mechanical forces play a role in cellular growth, development, and cancer. How mechanosensitive (MS) channels detect mechanical forces in cells remains a major unsolved problem in biology. It is virtually impossible to study single MS channels in sensory cells because they are localized to structures too small or too imbedded in other tissue to be accessible to electrophysiological recording methods. Examples are tiny mechanosensory nerve endings in skin or structures like Pacinian corpuscles in muscle. Understanding how mechanical forces activate ion fluxes through channels requires understanding the physical properties the membrane bilayer, as well as the organization of submembrane cytoskeletal, which provides mechanical support to the membrane. MS channels differ fundamentally from conventional voltage-gated ion channels in which the events that link stimulation to channel opening occur primarily within the channel protein itself.

We first showed that MS channels in muscle from mice with Duchenne dystrophy remained open for tens of seconds rather than milliseconds and this was responsible for the high levels of intracellular Ca2+ that cause muscle death (Franco & Lansman, *Nature* 340: 377, 1990b; Franco-Obregon and Lansman, *Journal of Physiology* 481:299, 1994; Franco-Obregon and Lansman, *Journal of Physiology* 539.2:391, 2002. Work from the lab using a combined pharmacological and genetic approach recently showed that MS channels in skeletal muscle contain TRPV4 proteins (Ho, Horn, Huynh, Koppitch & Lansman, Channels 6.4:1, 2012). Mutations in the TRPV4 gene produce a wide variety of neurologic and skeletal disorders, including the autosomal dominant skeletal dysplasias, congenital distal spinal

muscular atrophy, and hereditary and motor neuropathies. This work shows that cytoskeletal abnormalities produce gain of function changes in TRPV4 channels causing enhanced Ca<sup>2+</sup> entry. Current work is focused on discovery of novel compounds that block TRPV4 containing MS channels as a cure for degenerative disease of cardiac and skeletal muscle.

# Neuronal L-type, voltage-gated calcium channels

While a postdoc at Yale with R.W. Tsien and Peter Hess, we were first to identify L- and T-type voltage - gated calcium channels in ventricular heart cells (Hess, Lansman, and Tsien, *Nature* 311:538; Nilius Hess, Lansman and Tsien, *Nature* 316: 1985). L-type Ca<sup>2+</sup> channels are sensitive to dihydropyridine agonists and antagonists and are responsible for contraction of cardiac and smooth muscle. Although receptors for dihydropyridine drugs had been found in brain tissue, the properties and physiological functions of L-type Ca<sup>2+</sup> channels in the brain were unknown.

At UCSF, I began studies aimed at understanding the diversity and function of L- type Ca<sup>2+</sup> channels in the brain. Studies focused on granule cells isolated from the cerebellum of mice because of the availability of a number of known spontaneous mutations that cause the selective loss of granule cells and produce a variety of neurologic disorders. Our initial work at UCSF characterized the whole-cell and single-channel Ca<sup>2+</sup> currents in granule cells, in which a large component is carried by L-type channels (Slesinger and Lansman, *J. Physiol.* 435:101, 1991; Slesinger and Lansman, *J. Physiol.* 439:301, 1991; Haws, Slesinger and Lansman, *J. Neurosci.* 13(3):1148). Subsequent studies revealed functionally distinct L-type channels: type 1 channels that re-opened at negative membrane potentials following a strong depolarization (Slesinger and Lansman, *Neuron* 7:755, 1991; Slesinger and Lansman, *J. Physiol.* 491.2:335; and type 2, facilitating channels, in which channel openings during a voltage step were prolonged by a strong pre-pulse to a positive voltage (Parri and Lansman, *J. Neurosci.*16(6):4890, 1996). The discovery of reopening and facilitating L-type channels expanded the physiological range over which L-type channels could control intracellular Ca<sup>2+</sup> levels.

L-type channels are often localized to postsynaptic sites. We asked whether synaptically released glutamate acting at metabotropic receptors regulates L- type channels in cerebellum (Chavis, Fagni, Bockaert, and Lansman, *Neuropharm* 34(8):929, 1996; Chavis, Fagni, Lansman and Bockaert, *Nature* 382:719, 1996). These studies revealed a novel form of oscillatory calcium signaling in which the depletion of intracellular Ca<sup>2+</sup> stores increased L-type channel current. This work suggested a direct physical interaction of membrane L-type Ca<sup>2+</sup> channel with intracellular Ca<sup>2+</sup> stores and suggested intracellular stores refill when depleted by Ca<sup>2+</sup> entry through L-type channels. More recently, we have shown that L-type channels are up-regulated in cerebellar granule cells from the *leaner* mutant mouse, which lacks presynaptic P-type Ca<sup>2+</sup> channels that normally control glutamate release. There is also a reduction of NMDA glutamate receptors. The changes in L- type and NMDA receptor channels represent physiological compensation for loss of presynaptic P-type Ca<sup>2+</sup> channels in the *leaner* mutant mouse. This compensatory process is important because Ca<sup>2+</sup> entry though NMDA receptor channels likely contributes to the selective degeneration of granule cells during early postnatal development of the cerebellum of *leaner* mice, which causes a profound ataxia and provides a useful model for elucidating the role of ion channels in neurodegenerative diseases.