BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
Perez-Reyes, Edward	Professor
eRA COMMONS USER NAME eperezreyes	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
University of North Carolina, Chapel Hill, NC	B.A.	1975-1978	Chemistry
University of Colorado, Denver, CO	Ph.D.	1980-1986	Pharmacology
Stanford University, Hopkin's Marine Station,		1989	Electrophysiology
Baylor College of Medicine, Baylor, TX		1986-1992	Post-doctoral

A. Positions and Honors.

Positions and Employment

1978-1980 Research Assistant, Laboratory of Environmental Biophysics, National Institute of Environmental Health Sciences, Research Triangle Park, NC.
1986-1991 Postdoctoral Fellow, Dept. Mol. Physiol. & Biophys., Baylor College of Medicine, Houston, TX.
1991-1992 Research Assistant Professor, Dept. Mol. Physiol. & Biophys., Baylor, Houston TX.
1993-1998 Assistant Professor, Department of Physiology, Loyola University Medical Center, Maywood, IL.
1998-1999 Associate Professor, Department of Physiology, Loyola University Medical Center, Maywood, IL.
1999-present Associate Professor, Department of Pharmacology, University of Virginia, Charlottesville, VA.

Honors

National Institute of Environmental Health Sciences Merit Award, 1979.
National Science Foundation Fellowship, 1980-1983.
University of Colorado Fellowship, 1983-1984.
National Research Service Award, National Heart, Lung, and Blood Institute, 1988-1991.
Shannon Award, National Heart, Lung, and Blood Institute, 1991
Established Investigator of the American Heart Association, 1996-2001

B. Selected peer-reviewed publications.

(118 total publications; 4657 citations, h-index = 37.

1. Dunwiddie, T.V., Perez-Reyes, E., Rice, K.C., and Palmer, M.R., Stereoselectivity of opiate antagonists in rat hippocampus and neocortex: responses to (+) and (-) isomers of naloxone. Neuroscience 7:1691-1702, 1982.
2. Perez-Reyes, E., Kim, H.S., Lacerda, A., Horne, W., Wei, X., Rampe, D., Campbell, K.P., Brown, A.M., and Birnbaumer, L., Induction of calcium currents by the expression of the alpha-1 subunit of the dihydropyridine receptor from skeletal muscle. Nature 340:233-236, 1989.
3. Perez-Reyes, E., Wei, X., Castellano, A., and Birnbaumer, L., Molecular diversity of L-type calcium channels: Evidence for alternative splicing of the transcripts of three non-allelic genes. J. Biol. Chem. 265:20430-20436, 1990.
4. Lacerda, A.E., Kim, H., Ruth, P., Perez-Reyes, E., Flockerzi, V., Hofmann, F., Birnbaumer, L., and Brown, A.M., Normalization of current kinetics by interaction between the α_1 and β components of the skeletal muscle dihydropyridine-sensitive Ca^{2+} channel. Nature 352:527-530, 1991.

5. Perez-Reyes, E., Castellano, A., Kim, H.S., Bertrand, P., Baggstrom, E., Lacerda, A.E., Wei, X., and Birnbaumer, L., Cloning and expression of a cardiac/brain β subunit of the L-type calcium channel. J. Biol. Chem. 267:1792-1797, 1992.
6. Castellano, A., Wei, X., Birnbaumer, L., and Perez-Reyes, E., Cloning and expression of a third β subunit of calcium channels. J. Biol. Chem. 268:3450-3455, 1993.
7. Castellano, A., Wei, X., Birnbaumer, L., and Perez-Reyes, E., Cloning and expression of a neuronal β subunit of calcium channels. J. Biol. Chem. 268:12359-12366, 1993.
8. Schneider, T., Wei, X., Olcese, R., Costantin, J.L., Neely, A., Palade, P., Perez-Reyes, E., Qin, N., Zhou, J., Crawford, G.D., Smith, R.G., Appel, S.H., Stefani, E., and Birnbaumer, L., Molecular analysis and functional expression of the human type E α_1 subunit. Receptors & Channels 2:255-270, 1994.
9. de Leon, M., Wang, Y., Jones, L., Perez-Reyes, E., Wei, X., Soong, T.W., Snutch, T.P., and Yue, D.T., Essential Ca^{2+}-binding motif for Ca^{2+} -sensitive inactivation of L-type Ca channels. Science 270:1502-1506, 1995.
10. Perez-Reyes, E., Cribbs, L.L., Daud, A., Lacerda, A.E., Barclay, J., Williamson, M., Fox, M., Rees, M., and Lee, J.-H., Molecular characterization of a neuronal low voltage-activated T-type calcium channel. Nature, 391:896-900, 1998.
11. Cribbs, L.L., Lee, J.-H., Yang, J., Satin, J., Zhang, Y., Daud, A., Barclay, J., Williamson, M., Fox, M., Rees, M., and Perez-Reyes, E., Cloning and characterization of α1H from human heart, a member of the T-type calcium channel gene family. Circulation Research, 83:103-109, 1998.
12. Chien, A.J., Gao, T., Perez-Reyes, E., and Hosey, M.M., Determinants of palmitoylation and their effects on the subcellular localization of the β_{2a} subunit of L-type calcium channels. J. Biol. Chem. 273:23590-23597, 1998.
13. Chuang, R.S.-I., Jaffe, H., Cribbs, L.L., Perez-Reyes, E., and Swartz, K.J., Inhibition of T-type voltage-gated calcium channels by a new scorpion toxin. Nature Neuroscience, 1:668-674, 1998.
14. Talley, E.M., Cribbs, L.L., Lee, J.-H., Daud, A., Perez-Reyes, E., and Bayliss, D., Differential distribution of three members of a gene family encoding low voltage-activated (T-type) calcium channels. J. Neurosci., 19: 1895-1911, 1999.
15. Lee, J.-H., Daud, A., Cribbs, L.L., Lacerda, A.E., Pereverzev, A., Klöckner, U., Schneider, T., and Perez-Reyes, E., Cloning and expression of a novel member of the low voltage-activated T-type calcium channel family. J. Neurosci., 19:1912-1921, 1999.
16. Lee, J.-H., Cribbs, L.L., and Perez-Reyes, E., Cloning of a novel four repeat ion channel from rat brain. FEBS Letters, 445:231-236, 1999.
17. Dolphin, A.C., Wyatt, C.N., Richards, J., Beattie, R.E., Craig, P., Lee, J.-H., Cribbs, L.L., Volsen, S.G., and Perez-Reyes, E., The effect of α2-δ and other accessory subunits on expression and properties of the calcium channel α1G. J. Physiol. (Lond), 519.1:35-45, 1999.
18. Lee, J.-H., Gomora, J.C., Cribbs, L.L., and Perez-Reyes, E., Nickel block of three cloned T-type Ca channels: low concentrations selectively block α1H. Biophysical J., 77:3034-3042, 1999.
19. Talley, E.M., Solórzano, G., Depaulis, A., Perez-Reyes, E., and Bayliss, D., Low-voltage-activated calcium channel subunit expression in a genetic model of absence epilepsy in the rat. Mol. Brain Res., 75:159-165, 2000.
20. Gao, B., Sekido, Y., Maximov, A., Saad, M., Forgacs, E., Latif, F., Lerman, M., Lee, J.-H., Perez-Reyes, E., Bezprozvanny, I., and Minna, J.D., Functional properties of a new voltage-dependent calcium channel $\alpha_2\delta$ auxiliary subunit gene (*CACNA2D2*). J. Biol. Chem, 275:12237-12242, 2000.
21. Chemin, J., Monteil, A., Briquaire, C., Richard, S., Perez-Reyes, E., Nargeot, J., and Lory, P., Overexpression of T-type calcium channels in HEK-293 cells increases intracellular calcium without affecting cellular proliferation. FEBS Lett. 478: 166-172, 2000.
22. Schrier, A.D., Wang, H., Talley, E.M., Perez-Reyes, E., and Barrett, P.Q., The α1H T-type Ca^{2+} channel is the predominant subtype expressed in bovine and rat zona glomerulosa. Am. J. Physiol., 280:C265-C272, 2001.
23. Vajna, R., Klöckner, U., Pereverzev, A., Weiergräber, M., Chen, X., Miljanich, G., Klugbauer, N., Hescheler, J., Perez-Reyes, E., and Schneider, T., Functional coupling between R-type Ca^{2+} channels and insulin secretion in the insulinoma cell line INS-1. Eur. J. Biochem., 268:1066-1075, 2001.

24. Todorovic, S., Jevtovic-Todorovic, V., Meyenburg, A., Mennerick, S., Perez-Reyes, E., Romano, C., Olney, J.W., and Zorumski, C.F., Redox modulation of T-type calcium channels in rat thermal nociceptors. Neuron, 31:75-85, 2001.
25. Barclay J., Balaguero, N., Mione, M., Ackerman, S.L., Letts, V.A., Brodbeck, J., Canti, C., Meir, A., Page, K.M., Kusumi, K., Perez-Reyes, E., Lander, E.S., Frankel, W.N., Gardiner, R.M., Dolphin, A.C., and Rees, M.,* *Ducky* mouse phenotype of epilepsy and ataxia is associated with mutations in the *Cacna2d2* gene and decreased calcium channel current in cerebellar Purkinje cells. J. Neurosci. 21: 6095-104., 2001.
26. Todorovic, S., Jevtovic-Todorovic, V., Mennerick, S., Perez-Reyes, E., and Zorumski, C. F., $Ca_v3.2$ is a molecular substrate for inhibition of T-type calcium currents in rat sensory neurons by nitrous oxide. Mol. Pharmacol., 60:603-610, 2001.
27. Gomora, J.C., Daud, A.N., Weiergräber, M., and Perez-Reyes, E., Block of cloned human T-type calcium channels by succinimide antiepileptic drugs. Mol. Pharmacol., 60: 1121-1132, 2001.
28. Wolfe, J.T., Wang, H., Perez-Reyes, E., and Barrett, P.Q. Stimulation of human $Ca_v3.2$, T-type, Ca^{2+} channel currents by CaMKIIγ_C heterologously expressed in HEK 293 cells. J. Physiol., 538: 343-355, 2002.
29. Chemin, J., Monteil, A., Perez-Reyes, E., Bourinet, E., Nargeot, J., and Lory, P., Specific contribution of human T-type calcium channel isotypes (α1G, α1H, and α1I) to neuronal excitability. J. Physiol. 540: 3-14, 2002.
30. Michels, G., Matthes, J., Handrock, R., Kuchinke, U., Groner, F., Cribbs, L.L., Pereverzev, A., Schneider, T., Perez-Reyes, E., and Herzig, S., Single channel pharmacology of mibefradil in human native T-type and recombinant $Ca_v3.2$ calcium channels. Mol. Pharmacol., 61:682-694, 2002.
31. Gomora, J.C., Murbartián, J., Arias, J.M.,Lee, J.-H., and Perez-Reyes, E., Cloning and expression of the human T-type channel $Ca_v3.3$: insights into prepulse facilitation. Biophysical J., 83:229-241, 2002.
32. Murbartián, J., Arias, J.M., Lee, J.H., Gomora, J.C., and Perez-Reyes, E., Alternative splicing of the rat $Ca_v3.3$ T-type calcium channel gene produces variants with distinct functional properties. FEBS Letters, 528:272-278, 2002.
33. Cataldi, M., Perez-Reyes, E., and Tsien, R.W., Differences in apparent pore sizes of low- and high-voltage-activated Ca^{2+} channels. J. Biol. Chem. 277:45969-45976, 2002.
34. Arias, J.M., Murbartián J., and Perez-Reyes E., Cloning of a novel one-repeat calcium channel-like gene. Biochem. Biophys. Res. Comm., 303:31-36, 2003.
35. Park, J.Y., Jeong, S.-W., Perez-Reyes, E., and Lee, J.-H., Modulation of $Ca_v3.2$ T-type Ca^{2+} channels by protein kinase C. FEBS Letters, 547:37-42, 2003.
36. Murbartián J., Arias, J.M., and Perez-Reyes E., Functional impact of alternative splicing of human T-type $Ca_v3.3$ calcium channels. J. Neurophysiol. 92:3399-3407, 2004.
37. Joksovic, P.M., Brimelow, B.C., Murbartián, J., Perez-Reyes, E., and Todorovic, S.M. Contrasting anesthetic sensitivities of T-type Ca2+ channels of reticular thalamic neurons and recombinant $Ca_v3.3$ channels. Br. J. Pharmacol., 144:59-70, 2005.
38. Shcheglovitov, A., Zhelay, T., Vitko, Y., Osipenko, V., Perez-Reyes, E., Kostyuk, P. and Shuba, Y. Contrasting the effects of nifedipine on subtypes of endogenous and recombinant T-type Ca^{2+} channels. Biochem. Pharmacol. 69: 841-854, 2005.
39. Vitko, I., Chen, Y., Arias, J.M., Shen, Y., Wu, X.-R., and Perez-Reyes, E. Functional characterization and neuronal modeling of the effects of Childhood Absence Epilepsy variants of CACNA1H, a T-type calcium channel, J.Neurosci. 25:4844-4855, 2005.
40. Arias, J.M., Murbartián J., Vitko, I., Lee, J.H., and Perez-Reyes E. Transfer of β subunit regulation from high to low voltage-gated Ca^{2+} channels, FEBS Letters, 579(18) 3907-3912, 2005.
41. Nelson, M.T., Joksovic, P.M., Perez-Reyes, E., and Todorovic, S.M., The endogenous redox agent L-cysteine induces T-type Ca^{2+} channel-dependent sensitization of a novel subpopulation of rat peripheral nociceptors. J. Neurosci. 25, 8766-8775, 2005.
42. Kang, H.-W., Park, J.-Y., Jeong, S.-W., Kim, J.-A., Moon, H.-J., Perez-Reyes, E., and Lee, J.-H., A molecular determinant of nickel inhibition in $Ca_v3.2$ T-type calcium channels. J. Biol. Chem. 281:4823-4830, 2006.

43. Uebachs, M., Schaub, C., Perez-Reyes, E., and Beck, H., T-type Ca^{2+} channels differentially encode subthreshold membrane potential changes and action potential firing as modulated recovery rates, J. Physiol., 571:519-536, 2006.
44. Joksovic, P.M., Nelson, M.T., Jevtovic-Todorovic, V., Patel, M.K., Perez-Reyes, E., Campbell K.P., and Todorovic, S.M., $Ca_v3.2$ (α1H) channel is the major molecular substrate for redox regulation of T-type calcium channels in the thalamus, J. Physiol., 574:415-430, 2006.
45. Lee, T.S., Kaku, T., Takebayashi, S., Uchino, T., Miyamoto, S., Hadama, T., Perez-Reyes, E., Ono, K., Actions of mibefradil, efonidipine, and nifedipine block of recombinant T- and L-type Ca^{2+} channels with distinct inhibitory mechanisms. Pharmacology, 78:11-20, 2006.
46. Vitko, I., Bidaud, I., Arias, J.M., Mezghrani, A., Lory, P., Perez-Reyes, E. (2007) The I-II loop controls plasma membrane expression and gating of $Ca_v3.2$ T-type Ca^{2+} channels: a paradigm for Childhood Absence Epilepsy. J. Neurosci. 27:322-330.
47. Xie X., Van Deusen, A.L., Vitko, I., Babu, D.A., Davies, L.A., Huynh, N., Cheng, H., Yang, N., Barrett, P.Q., and Perez-Reyes, E. Validation of high throughput screening assays against three subtypes of Ca_v3 T-type channels using molecular and pharmacologic approaches. Assay Drug Dev Technol 5:191-204, 2007.
48. Nelson, M.T., Woo, J., Kang, H.-W., Vitko, I., Barrett, P.Q., Perez-Reyes, E., Lee, J.H., Shin, H.S., and Todorovic, S.M., Reducing agents sensitize C-type nociceptors by relieving high-affinity zinc inhibition of T-type calcium channels. J. Neurosci., 27:8250-8260, 2007.
49. Nelson, M.T., Joksovic, P., Kang, H.-W., Van Deusen, A., Baumgart, J., Barrett, P.Q., Lee, J.H., Zorumski, C.F., Perez-Reyes, E., and Todorovic, S.M. Metal-catalyzed oxidation underlies subunit-specific inhibition of neuronal T-type calcium channels by ascorbate. J. Neurosci. *in press*.

C. Research Support

R01 NS038691, Perez-Reyes (PI) 7/5/99-5/31/09
NIH/NINDS
Molecular Analysis of Neuronal T-type Ca Channels
The specific aims of this project are to: 1) determine how mutations in Childhood Absence Epilepsy patients alter $Ca_v3.2$ channel activity; 2) since many of these mutations are in the cytoplasmic loop connecting repeat I to II, we plan on studying the structure-function relationships of this loop; 3) to determine if current antiepileptic drugs block recombinant T-currents, 4) to use a fluorescent dye based assay to map the chemical space of T channels using known channel blockers, and 5) to synthesize and test novel antiepileptic compounds.
Role on project: PI

R01 GM075229, Todorovic (PI) 6/1/06-5/31/08
NIH/NIGMS
Redox Pharmacology of T channels in DRG Neurons
The goals of this project are to characterize the mechanisms by which T channels are modulated by oxidation and reduction. The Perez-Reyes lab will use site-directed mutagenesis techniques to map the specific amino acid residues on the T-channel $Ca_v3.2$ responsible for this effect. An understanding of this regulation may lead to novel therapeutic strategies for the management of neuropathic pain. This subproject is only funded for 2 of the 4 years of the grant.
Role on project: Co-Investigator