

BIOGRAPHICAL SKETCH

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NAME Ciria Carolina Quintero Hernandez, MD, PhD eRA COMMONS USER NAME(credential, e.g., agency login) hernanc1	POSITION TITLE Research Assistant Professor		
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
Lisandro Alvarado Center-West University , Barquisimeto, Venezuela.	MD	1997	Medicine
Federal University of Rio de Janeiro, Brazil.	PhD	2002	Biophysics
Federal University of Rio de Janeiro, Brazil.	Research Fellow/ Instructor	2002-03	Physiology/Biophysics
Federal University of Rio de Janeiro, Brazil.	Postdoctoral Fellow	2003 – 05	Physiology/Biophysics
University of Texas Health Science Center at San Antonio (UTHSCSA). TX.	Postdoctoral Fellow	2005 – 08	Neurophysiology/ Biophysics
Vanderbilt University Medical Center. Nashville. TN.	Research Fellow	2009 – 11	Neurophysiology/ Neuroscience

A. Personal Statement

My research is focused on understanding the basic mechanisms of epilepsy and how mutations, rare variants and polymorphisms alter the structure and function of recombinant and native gamma aminobutyric acid (GABA) type A (GABA_AR) receptor channels to cause epilepsy, and ultimately, to provide a mechanistic foundation for development of novel therapeutic strategies to treat or cure epilepsy. GABA_ARs are heteropentameric ligand-gated ion chloride channels responsible for the majority of fast inhibitory synaptic transmission and tonic extrasynaptic inhibition in the mammalian CNS. Seven subunit families have been identified, each composed of one or more subunit subtypes (α 1- α 6, β 1- β 3, γ 1- γ 3, δ , ϵ , π , and θ). At least four forms of monogenic human epilepsy have been linked to mutations in the α 1, β 3 and γ 2 GABA_A receptor subunits. Polymorphisms and novel rare variants associated with polygenic idiopathic generalized epilepsies (IGEs) have recently been found in GABA_AR α 4, α 5, α 6, β 1, β 2, γ 1, γ 3, δ , ϵ and π subunits. My overarching hypothesis is that GABA_AR subunit mutations, rare variants and polymorphisms promote neuronal hyperexcitability by disrupting GABA_AR functional properties, subunit assembly to form GABA_ARs, and/or GABA_AR surface trafficking, thus leading to impairment of the GABAergic synapse. My long-term goal is to provide insights into GABA_AR mutations linked to IGEs and developing more effective and new therapies for modeling epilepsy.

B. Positions and Honors

Positions and Employment

2012- Research Assistant Professor of Neurology, School of Medicine, Vanderbilt University.

Other Experience And Professional Memberships

1990-97 Peer Mentoring Program in Biochemistry. School of Medicina. Lisandro Alvarado University. Venezuela.

2002-05 Mentorship Support Program in Cardiovascular Physiology concepts. (IBCCF). Federal University of Rio de Janeiro, Brazil.

2007 - present Member, Biophysical Society.

2008 - present Member, The Physiological Society.

2008 - present Member, The American Association for the Advancement of Science (AAAS).

2008 Postdoctoral Program Coordinator. Department of Physiology. University of Texas Health Science Center. San Antonio, Texas.

2009 Member of the Scholarly Learning Postdoctoral Association Committee. BRET. Vanderbilt University. Nashville, Tennessee.

2010 - present Member, Society for Neuroscience.

Honors

- 1989 Award for the 2nd place to the Best research work in Basic Sciences at the IV South American Scientific Congress of Medical Students and I Latin American Scientific Congress of Medical Students. National University of San Marcos (UNMSM). August 16-20. Lima. Peru.
- 1989 Recognition for Significant Advances in Science by the Dean of the Lisandro Alvarado University. October. Barquisimeto. Lara. Venezuela.
- 1990 Outstanding Basic Science Student Honor. Family and Youth Ministry, Barquisimeto, Venezuela.
- 1990, 92, 94-96 Recognition for Academic Achievements in Medicine by the Vice Chancellor for Academic Affairs of the Lisandro Alvarado University. Barquisimeto. Lara. Venezuela.
- 1991-1995 Undergraduate Research scholarship from the Council of Scientific and Technological Development, Lisandro Alvarado Center-West University, Barquisimeto, Venezuela.
- 1993 Award for the 1st, 2nd, and 3rd place to the Best research work in Basic Sciences at the II Venezuelan Congress of Medical Students. Lisandro Alvarado University. May 12-15. Barquisimeto. Lara. Venezuela.
- 1993 Travel Award from the VIII International Congress of the American Federation of Scientific Societies of Medical Students (FELSOCEM). August 20-24. Quito. Ecuador.
- 1993 Award for the 2nd place in Basic Sciences at the VIII International Congress of the American Federation of Scientific Societies of Medical Students (FELSOCEM). August 20-24. Quito. Ecuador.
- 1995 Recognition for Significant Advances in Science by the Vice Chancellor for Academic Affairs of the Lisandro Alvarado University. January. Barquisimeto. Lara. Venezuela.
- 1995 The Jose Felix Ribas Medal in its Second Class for outstanding achievements. Family and Youth Ministry, Caracas, Venezuela.
- 1995 The Jose Felix Ribas Medal in its Second Class for outstanding achievements. Family and Youth Ministry. February. Caracas. Distrito Federal. Venezuela
- 1995 Outstanding Basic Science Student Honor by the University Council of the Lisandro Alvarado University. March. Barquisimeto. Lara. Venezuela.
- 1995 Lisandro Alvarado Annual Research Award in Health Sciences. Lisandro Alvarado University. December. Barquisimeto. Lara. Venezuela.
- 1996 First and Second Prize in Undergraduate Basic Sciences Research at the V Venezuelan Congress of Medical Students. May. Valencia. Carabobo. Venezuela.
- 1997 J. M. Cortes Bastidas Annual Award. Barquisimeto. Lara. Venezuela.
- 1997 Button "Honor to whom Honor is due" by the Mayor of the County of Monseñor Jose Vicente de Unda for Invaluable Collaboration in Improving School Health System. April. Chabasquen. Portuguesa. Venezuela.
- 1997 Recognition for having obtained the Fifth place among 121 members of the XXXIV Class of Physicians by the Dean of the School of Medicine. Lisandro Alvarado University. July. Barquisimeto. Lara. Venezuela.
- 1997 – 1998 PhD scholarship from the National Research Council (CNPq). Rio de Janeiro. Brazil.
- 1998 – 2002 PhD scholarship from the Federal Agency for Post-Graduate Education (CAPES). Rio de Janeiro. Brazil.
- 2000 Award for the Best Poster at the IV Biophysics Congress of the Southern Cone on August 19-22. Campinas, SP. Brazil.
- 2002 Travel Fellowship Award For Young Scientists from the International Union for Pure and Applied Biophysics (IUPAB) and the XIV International Biophysics Congress. Buenos Aires. Argentina. April 27- May 1. 2002
- 2002-2003 Research Instructor scholarship from the Tissue Bioengineering Millennium Institute. Rio de Janeiro, Brazil.
- 2003-2005 Post-Doctoral scholarship from the National Research Council (CNPq), Rio de Janeiro, Brazil.

2007
2008

Post-Doctoral Award for the 2nd place to the Best Poster at the TX. USA.
Vernon Bishop Travel Award from the Department of Physiology, UTHSCSA.TX

C. Selected Peer-reviewed Publications (in chronological order)

1. **Hernandez, C.C.**, Barcellos, L.C., Giménez, L.E., Bonfante-Cabarcas, R.A., Garcia ,S., Pedrosa, R.C., Nascimento, J.H., Kurtenbach, E., Masuda, M.O., Campos de Carvalho, A.C. (2003) Human chagasic IgGs bind to cardiac muscarinic receptors and impair L-type Ca²⁺ currents. *Cardiovasc Res*.58 (1):55-65. PMID: 12667946.
2. Gamper, N., Zaika, O., Li Y., Martin, P., **Hernandez, C.C.**, Perez, M.R., Wang, A., Jaffe, D.B. and Shapiro, M.S. (2006) Oxidative modification of M-type K⁺ Channels as a mechanism of cytoprotective neuronal silencing. *EMBO J*. 25:4996-5004. PMID: 17024175.
3. Soldovieri, M.V., Cilio, M.R., Miceli, F., Bellini, G., Miraglia del Giudice, E., Castaldo, P., **Hernandez, C.C.**, Shapiro, M.S., Pascotto, A., Annunziato, L., Tagliatela, M. (2007) Atypical gating of M-type potassium channels conferred by mutations in uncharged residues in the S4 region of KCNQ2 causing benign familial neonatal convulsions. *J Neurosci* 27:4919-28. PMID: 17475800.
4. **Hernandez, C.C.**, Zaika, O., Tolstikh, G., Shapiro, M.S. (2008) Regulation of neural KCNQ channels: signaling pathways, structural motifs and functional implications. *J Physiol* 586:1811-1821. Cover of the April 1 issue. PMID: 18238808.
5. **Hernández, C.C.**, Nascimento, J.H., Aguiar, E., Costa, P.C., Masuda, M.O., Kurtenbach, E, Campos de Carvalho A.C., Giménez L.E. (2008) Autoantibodies enhance agonist action and binding to cardiac muscarinic receptors in chronic Chagas' disease. *J Recept Signal Transduct Res*. 28:375-401. PMID: 18702010.
6. Miceli, F., Soldovieri, M.V., **Hernández, C.C.**, Shapiro, M.S., Annunziato, L., Tagliatela, M. (2008) Gating consequences of charge neutralization of arginine residues in the S4 domain of Kv7.2, an epilepsy-linked K⁺ channel subunit. *Biophys J*. 95:2254-64. PMID: 18515377.
7. **Hernandez, C.C.**, Zaika, O., Shapiro, M.S. (2008) A Carboxi-terminal inter-helix linker as the site of phosphatidylinositol 4,5 bisphosphate action on Kv7 (M-type) K⁺ channels . *J Gen Physiol*. 123:361-81. Cover of the September issue. PMID: 18725531.
8. Bal M., Zhang J., Zaika, O., **Hernandez, C.C.**, Shapiro, M.S. (2008) Homomeric and heteromeric assembly of KCNQ (Kv7) K⁺ channels assayed by TIRF/FRET and patch-clamp analysis. *J Biol Chem*. 283:30668-76. PMID: 18786918.
9. Zaika, O., **Hernandez, C.C.**, Bal M, Tolstikh, G., Shapiro, M.S. (2008) Determinants within the turret and pore-loop domains of KCNQ3 K⁺ channels governing functional activity. *Biophys J*. 95:1-17. PMID: 18790849.
10. **Hernandez, C.C.**, Falkenburger, B., Shapiro, M.S. (2009) Affinity for phosphatidylinositol 4,5-bisphosphate determines muscarinic agonist sensitivity of KV7 K⁺ channels. *J Gen Physiol*. 134(5):437-48. PMID: 19858360.
11. Tang, X., **Hernandez, C.C.**, Macdonald, R. L. (2010) Modulation of Spontaneous and GABA-Evoked Tonic $\alpha 4\beta 3\delta$ and $\alpha 4\beta 3\gamma 2L$ GABAA Receptor Currents by Protein Kinase A. *J Neurophysiol*. 103(2):1007-19. PMID: 19939957.
12. Bal, M., Zhang, J., **Hernandez, C.C.**, Zaika, O., Shapiro, M.S. (2010). Ca²⁺/calmodulin disrupts AKAP79/150 interactions with KCNQ (M-type) K⁺ channels. *J Neurosci*. 30(6):2311-23. PMID: 20147557.
13. Lo, Wen-yi., Lagrange, A.H., **Hernandez, C.C.**, Macdonald, R. L. (2010) Glycosylation of $\beta 2$ subunits regulates GABAA receptor biogenesis and channel gating. *J Biol Chem*. 285(41):31348-61. PMID: 20639197
14. **Hernandez C.C.**, Gurba K.N., Hu N., Macdonald, R. L. (2011). The GABRA6 mutation, R46W, associated with childhood absence epilepsy, alters $\alpha 6\beta 2\gamma 2$ and $\alpha 6\beta 2\delta$ GABAA receptor channel gating and expression. *J Physiol*. 589(23): 5857-78. PMID: 21930603.
15. Gurba K.N., **Hernandez C.C.**, Hu N., Macdonald, R. L. (2012). The GABRB3 mutation, G32R, associated with childhood absence epilepsy, alters $\alpha 1\beta 3\gamma 2$ GABAA receptor expression and channel gating. *J Biol Chem*. 287(15):12083-97. PMID: 22303015.
16. Huang X, Tian M, **Hernandez CC**, Hu N, Macdonald RL. (2012). The GABRG2 nonsense mutation, Q40X, associated with Dravet syndrome activated NMD and generated a truncated subunit that was partially rescued by aminoglycoside-induced stop codon read-through. *Neurobiol Dis*. 48(1):115-23. PMID: 22750526.

17. Choveau FS, **Hernandez CC**, Bierbower SM, Shapiro MS. (2012). Pore Determinants of KCNQ3 K(+) Current Expression. *Biophys J.* 102(11):2489-98. PMID: 22713564.
18. Mei D, Tian M, Freri E, **Hernandez CC**, Granata T, Shen W, Macdonald RL, Guerrini R. (2012). Impaired Surface $\alpha\beta\gamma$ GABAA Receptor Expression in Familial Epilepsy Due To a GABRG2 Frameshift Mutation. *Neurobiol Dis.* (submitted).
19. Lo, Wen-yi., Lagrange, A.H., **Hernandez, C.C.**, Gurba K.N., Macdonald, R. L. (2012) Coexpression of $\gamma 2$ subunits hinders processing of n-linked glycans attached to the N104 glycosylation sites of GABAA receptor $\beta 2$ subunits. *J Biol Chem* (submitted)

D. Research Support

None.