

BIOGRAPHICAL SKETCH
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NAME: Larre Perez, Maria Isabel

eRA COMMONS USER NAME (credential, e.g., agency login): PEREZIM

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Metropolitan Autonomous University of Mexico	B.S	2002	Experimental Biology
Center for Research and Advanced Studies of National polytechnic Institute (CINVESTAV).	M. Sc.	2005	Cellular and Molecular Physiology
Center for Research and Advanced Studies of National polytechnic Institute (CINVESTAV).	Ph.D	2012	Cellular and Molecular Physiology
Center for Research and advanced Studies of National polytechnic Institute (CINVESTAV).	Postdoctoral	2013	Cellular and Molecular Physiology

A. Personal Statement

I have the expertise, training and motivation necessary to successfully carry out the proposed research project for this COBRE, focused on cellular transport physiology in obesity related conditions. I have specific training in epithelial physiology. One of the features of these cells is the presence of tight junctions. Key technologies to study tight junctions were pioneered by the group I trained under as a Ph.D. student. My research includes the regulation of the function and the molecular composition of tight junctions by the Na/K-ATPase ligand ouabain, which is the foundation of the proposed research as a junior investigator in this COBRE. In addition, I have had numerous fruitful collaborations with other researchers in the field of gap junctions. These accomplishments demonstrate my ability to participate in productive, collaborative teams requiring frequent communication among project members to define realistic research goals and to publish relevant manuscripts. I have been invited to write book chapters detailing the techniques for studying tight junction. As a junior investigator at Marshall Institute for Interdisciplinary Research (MIIR) and in the Marshall University School of Medicine, my interest is in studying how the signaling function sodium pump regulates epithelial phenotype. With the newly developed technology that allows the expression of mutants of alpha 1 Na/K-ATPase with defects in signaling function, it becomes possible for me to study how Na/K-ATPase signaling function regulates kidney function. This COBRE will allow me the financial support and time to complete this important work. Support and collaborative work with the Genomics Core at Marshall University for RNA-seq will allow determination of the differential regulation of tight junction genes (a unique feature of epithelial cells) and other genes that are important for the epithelial phenotype, which will lead to more knowledge and more efficacious treatment of kidney disease.

1. The emergence of the concept of tight junctions and physiological regulation by ouabain. [Larre I](#), Ponce A, Franco M, Cerejido M. Semin Cell Dev Biol. doi: 10.1016.
2. Ouabain modulates ciliogenesis in epithelial cells. [Larre I](#), Castillo A, Flores-Maldonado C, Contreras RG, Galvan I, Muñoz-Estrada J, Cerejido M. Proc Natl Acad Sci U S A. 2011;108(51):20591-62.
3. Ouabain modulates cell contacts as well as functions that depend on cell adhesion. [Larre I](#), Contreras RG, Cerejido M. Methods Mol Biol. 2011;763:155-68.
4. Ouabain modulates epithelial cell tight junction. [Larre I](#), Lazaro A, Contreras RG, Balda MS, Matter K, Flores-Maldonado C, Ponce A, Flores-Benitez D, Rincon-Heredia R, Padilla-Benavides T, Castillo A, Shoshani L, Cerejido M. Proc Natl Acad Sci U S A. 2010;107(25):11387-92.

5. Tight junction and polarity interaction in the transporting epithelial phenotype. Cereijido M, Contreras RG, Shoshani L, Flores-Benitez D, Larre I. *Biochim Biophys Acta*. 2008;1778(3):770-93.

Book chapters

1. Book: Tight junctions in Cancer Metastasis. Larre, I, Flores-Maldonado C and Marcelino C. Methods to study tight junctions, (Martin, T.A. and Jiang W.G Eds). Chapter 3 (19), pp. 65-80, 2013.
2. Book: Permeability Barrier: Methods and Protocols, Methods in Molecular Biology. Larre, I, Contreras, R.G., Cereijido, M. Hormone ouabain modulates cell contacts as well as functions that depend on cell adhesion, (Kursad, Turksen Ed), Chapter 10 (763), pp.155-168, 2011

B. Positions and Honors

Positions and Employment

- | | |
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| 2012-13 | Postdoctoral Fellow, Department of physiology Biophysics and Neurosciences, Center of research and Advanced Studies of National Polytechnic Institute, Mexico. |
| 2013-14 | Visiting Professor, Department of physiology Biophysics and Neurosciences, Center of research and Advanced Studies of National Polytechnic Institute, Mexico. |
| 2014 | Instructor of Neurophysiology, Metropolitan Autonomous University, Mexico. |
| 2014-2015 | Assistant Investigator or residence at MIIR, Marshall University, WV. |
| 2014- | Assistant Investigator at MIIR, Marshall, University, WV. |
| 2014- | Assistant Professor, Joan C. Edwards School of Medicine, Marshall University, WV. |

Other Experience and Professional Memberships

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| 2012- | Member of American Society of Cell Biology, USA. |
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Honors

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| 2014-2016 | Fellowship for National Researcher from National Research System (SNI), (http://www.conacyt.mx/index.php/el-conacyt/sistema-nacional-de-investigadores), Mexico |
| 2012 | Postdoctoral Fellowship from Institute of Science and Technology of D.F. (ICyTDF) for women, Rosalind Franklin, 2012, Mexico. |
| 2006 | Research fellowship from National Council for Science and Technology, "Becas Mixtas en el Extrajero", to stay in the University College of London, U.K. Mentor: María Susana Balda. |
| 2003-2009 | Research fellowship from National Council for Science and Technology (CONACYT) Mexico. |
| 2002 | Fellowship from the Mexican Academy of Science, "Summer of Scientific Research" (http://www.amc.edu.mx/p5/index.php?option=com_content&id=139). |
| 2002 | Degree in Experimental Biology with Honors, Metropolitan Autonomous University (UAM-Iztapala). |

C. Contribution to Science

1. My early publications showed that ouabain regulates cell adhesion. The binding of ouabain to Na/K-ATPase modified different cell-cell adhesion and cell-substrate adhesion. Also, cells that are sensitive to ouabain became resistant to ouabain by establishing gap junctions. We used high concentrations of ouabain that inhibited and affected both pumping and signaling function, but this was the first evidence of the existence of a relationship between Na/KATPase and Tight Junction regulation.
 - a. Ouabain binding to Na⁺,K⁺-ATPase relaxes cell attachment and sends a specific signal (NACos) to the nucleus. Contreras RG, Flores-Maldonado C, Lázaro A, Shoshani L, Flores-Benitez D, Larré I, Cereijido M. *J Membr Biol*. 2004;198(3):147-58.
 - b. Contacts and cooperation between cells depend on the hormone ouabain. Larre I, Ponce A, Fiorentino R, Shoshani L, Contreras RG, Cereijido M. *Proc Natl Acad Sci U S A*. 2006; 103(29):10911-6.
2. In 1991, Hamlyn et al. and Mathews et al. demonstrated the presence of a substance in plasma that they could not distinguish from ouabain of vegetal origin, a finding confirmed with more advanced methods

such as 1H-NMR and mass ionization spectrometry. Now endogenous ouabain is well accepted and recognized as a hormone. Using physiological concentrations of ouabain, we showed that it was able to regulate the two features of a transporting epithelium: Tight Junctions and Polarity. Specifically, the binding of ouabain to Na/K-ATPase triggers the c-Src/ERK pathway, which in turn regulates paracellular permeability (Tight Junctions) and ciliogenesis (polarity). Those results suggested for first time that the signaling function of Na/K-ATPase could be involved in the regulation of Tight Junctions.

- a. Ouabain modulates ciliogenesis in epithelial cells. Larre I, Castillo A, Flores-Maldonado C, Contreras RG, Galvan I, Muñoz-Estrada J, Cereijido M. Proc Natl Acad Sci U S A. 2011;108(51):20591-62.
 - b. Ouabain modulates cell contacts as well as functions that depend on cell adhesion. Larre I, Contreras RG, Cereijido M. Methods Mol Biol. 2011;763:155-68.
 - c. Na, K-ATPase is the putative membrane receptor of hormone ouabain. Larre I and Cereijido M. Commun Integr Biol. 2010 (6):625-8.
 - d. Ouabain modulates epithelial cell tight junction. Larre I, Lazaro A, Contreras RG, Balda MS, Matter K, Flores-Maldonado C, Ponce A, Flores-Benitez D, Rincon-Heredia R, Padilla-Benavides T, Castillo A, Shoshani L, Cereijido M. Proc Natl Acad Sci U S A. 2010;107(25):11387-92.
3. In addition to the contribution described above, with a team of collaborators, I investigated the effect of ouabain on gap junctions. This type of cell communication is important in tissue morphogenesis, not only in epithelial but also in the heart, liver, etc. Finally, I was invited to collaborate in studying the effect of Epidermal Growth Factor on Tight Junctions.
- a. Ouabain increases gap junctional communication in epithelial cells. Ponce A, Larre I, Castillo A, García-Villegas R, Romero A, Flores-Maldonado C, Martinez-Rendón J, Contreras RG, Cereijido M. Cell Physiol Biochem. 2014;34(6):2081-90.
 - b. The polarized distribution of Na⁺,K⁺-ATPase: role of the interaction between {beta} subunits. Padilla-Benavides T, Roldán ML, Larre I, Flores-Benitez D, Villegas-Sepúlveda N, Contreras RG, Cereijido M, Shoshani L. Mol Biol Cell. 2010;21(13):2217-25.
 - c. Control of tight junctional sealing: roles of epidermal growth factor and prostaglandin E2. Flores-Benitez D, Rincon-Heredia R, Razgado LF, Larre I, Cereijido M, Contreras RG. Am J Physiol Cell Physiol. 2009;297(3):C611-20.
 - d. Tight junction and polarity interaction in the transporting epithelial phenotype. Cereijido M, Contreras RG, Shoshani L, Flores-Benitez D, Larre I. Biochim Biophys Acta. 2008;1778(3):770-93.

Complete List of Published Work in MyBibliography:

<https://www.ncbi.nlm.nih.gov/sites/myncbi/1bEO8ejAe9v5N/bibliography/49260018/public/?sort=date&direction=ascending>

D. Additional Information: Research Support and/or Scholastic Performance