

***CURRICULUM VITAE***  
***José A. Lasalde Dominicci, Ph.D.***

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<http://www.nachr.org/>  
<http://www.cifupr.org/>

**EDUCATION**

|           |  |  |
|-----------|--|--|
| 1983-1988 | Ph.D. Biochemistry<br>(mentors-Dr. Gladys Escalona<br>and Dr. José del Castillo) | Department of Chemistry<br>University of Puerto Rico<br>Río Piedras Campus |
| 1977-1982 | B.S. Chemistry & Biology   | Department of Chemistry<br>University of Puerto Rico<br>Río Piedras Campus |

**POSTDOCTORAL TRAINING**

|                    |  |   |
|--------------------|--|---|
| 11/91-7/1996       | Research Associate<br>Ion-Channel Structure<br>(Dr. Mark McNamee)  | Department of Biochemistry & Biophysics<br>UC Davis, Davis CA                     |
| 1988-1991          | Research Associate<br>Electrophysiology<br>Patch-Clamp Techniques<br>(Mentors: Dr. José del Castillo and Dr. Conchita Zuazaga) | Institute of Neurobiology<br>University of Puerto Rico<br>Medical Sciences Campus |
| 6/26/ al 9/25/1990 | Summer Training<br>Molecular Biology<br>(Dr. William Gilly)  | Stanford University<br>Hopkins Marine Station of<br>Stanford University           |

**OTHER TRAINING**

|               |   |  |
|---------------|---|--|
| 5/1996-9/1996 | Summer Sabbatical<br>(Dr. Stuart Forman's laboratory) | Harvard Medical School<br>Department of Anesthesiology<br>Boston, MA |
| 2002          | Summer Research<br>(Dr. Raymond Steven's Laboratory)  | Scripps Clinics, San Diego, California                               |

## ACADEMIC APPOINTMENTS

|                    |  |   |
|--------------------|--|---|
| 9/16/2013-present  | Vice President for<br>Research and Technology ( <i>in kind</i> ) | University of Puerto Rico   |
| 5/2013-9/15/2013   | Interim President- UPR   |   |
| 11/22/2010-5/2013  | Vice President for<br>Research and Technology ( <i>in kind</i> ) | University of Puerto Rico   |
| 12/2011-present    | Adjunct Professor  | Institute of Neurobiology<br>University of Puerto Rico<br>Medical School                    |
| 6/2006-present     | Adjunct Professor  | Department of Comparative Medicine<br>University of Puerto Rico<br>Medical School           |
| 6/2003-present     | Professor  | Department of Biology<br>University of Puerto Rico<br>San Juan, Puerto Rico                 |
| 7/1998-present     | Associate Professor  | Department of Biology<br>University of Puerto Rico<br>San Juan, Puerto Rico                 |
| 8/6/1996-6/31/1998 | Assistant Professor  | Department of Biology<br>University of Puerto Rico<br>San Juan, Puerto Rico                 |
| 8/1994-8/1997      | Associate Biochemist   | Molecular & Cellular Biology<br>Division of Biological Sciences<br>UC Davis, Davis CA 95616 |

## OTHER PROFESSIONAL APPOINTMENTS AND MAJOR VISITING APPOINTMENTS

|                  |                                  |  |
|------------------|----------------------------------|--|
| 10/2012-present  | Material Characterization Center | Board of Directors-President                           |
| 11/2011-present  | UPR-Molecular Science Building   | Board of Directors-Vice President                      |
| 10/2010- present | INDUNIV (PRIDCO)                 | Board of Directors-Vice President                      |
| Summer 1997      | Visiting Scientist               | Department of Anesthesiology<br>Harvard Medical School |
| 01-05/1987       | Professor of Biochemistry        | University of Puerto Rico<br>Río Piedras, P.R.         |

#### **AWARDS AND HONORS**

|                |  |
|----------------|--|
| 1981-1983      | National Institutes of Health -MBRS undergraduate Student fellowship     |
| 1998.          | National Institutes of Health -MBRS Graduate Student fellowship          |
| 1989-1992      | National Institutes of Health -MARC Post-Doctoral Fellowship award       |
| 1992-1996      | National Institutes of Health -NIGMS –Post-doctoral Research Award       |
| 5/1999         | National Science Foundation Productivity Award                           |
| 7/1999         | Glaxo-Wellcome Research Award  |
| 6/2000         | Academia de Artes y Ciencias de Puerto Rico.                             |
| 6/2008-present | Member Editorial Board of Cellular and Molecular Neurobiology (Springer) |
| 8/2008-present | Member of the IUPAC DIVISION-III BIOMOLECULAR SUBCOMMITTEE               |

#### **MAJOR COMITTEE ASSIGNMENT**

|            |                     |   |
|------------|---------------------|---|
| 1992-1996: | Laboratory Security | Molecular & Cellular Biology<br>Division of Biological Sciences<br>UC Davis, Davis CA 95616 |
| 1996-1998  | Library Committee   | Department of Biology   |

|                 |   |  |
|-----------------|---|--|
|                 |   | University of Puerto Rico<br>Río Piedras Campus                                |
| 1998-present    | MBRS Advisory committee   | Faculty of Natural Sciences<br>University of Puerto Rico<br>Río Piedras Campus |
| 1998-present    | MARC Advisory committee   | Faculty of Natural Sciences<br>University of Puerto Rico<br>Río Piedras Campus |
| 1998-2003       | RCMI Advisory committee   | Universidad Central del Caribe<br>School of Medicine (UCC)                     |
| 6/2000-present  | Director Confocal Imaging Facility<br>( <a href="http://www.cifupr.org">www.cifupr.org</a> )  | Department of Biology<br>University of Puerto Rico<br>Río Piedras Campus       |
| 8/2000-2002     | Graduate School committee   | Department of Biology<br>University of Puerto Rico<br>Río Piedras Campus.      |
| 8/2002-2004     | Personnel committee   | Department of Biology<br>University of Puerto Rico<br>Río Piedras Campus.      |
| 8/2001-8/2003   | National Science Foundation, Neuronal & Glial Mechanisms Panel member   |  |
| 5/2004-5/2005   | MD Anderson-UPR Steering Committee  |  |
| 7/2003-5/2004   | Chair UPRRP Biomolecular Building Committee   |  |
| 6/2003-6/2005   | National Institute of Health, National Research Service Award (NRSA) panel member,<br>Structural Biology.   |  |
| 6/2005-5/2007   | Reviewer for the Philip Morris External Research Program  |  |
| 6/-2000-11/2005 | Mentor for the “successful grant writing” NIGMS initiative at the University of<br>Kentucky.  |  |
| 04/2005-3/2011: | Appointed as Scientific Director for the SNRP program at UPR-RCM campus ( <a href="http://snrp.rcm.upr.edu/investig.html">http://<br/>snrp.rcm.upr.edu/investig.html</a> ). |  |

## MAJOR RESEARCH INTEREST

Acetylcholine receptor structure and function, lipid-protein interactions in biological membranes, neuronal acetylcholine receptor and nicotine addiction, electrophysiological analysis of slow-channel congenital myasthenic syndromes (SCCMS) associated with point mutations in the genes encoding acetylcholine receptor subunits. Molecular basis for neuronal nicotinic receptor upregulation: potential implications in HIV associated dementia.

## RESEARCH FUNDING INFORMATION

### *Past*

1988-1991: National Institute of Health MARC Postdoctoral fellowship, “Membrane cholesterol affects acetylcholine receptor-channel function.” (\$90,000)

1992-1996: National Institute of Health NIGMS Postdoctoral fellowship, “Mutagenesis of nicotinic acetylcholine receptor-channel function.” (\$200,000).

7/97-7/99 National Science Foundation-EPSCOR- 7/97 to 7/99, P.I., “Molecular basis of Neuronal Acetylcholine receptor desensitization” (\$146,000) (Principal Investigator).

1/99-12/2001, National Institute of Health “Postdoctoral Research Supplement” 5/1/997- 4/30/2002 (\$223,000) (Principal Investigator José A. Lasalde Dominicci, Co-PI Mark McNamee UC Davis).

6/2000-8/2004, “General anesthetic interaction with lipid-exposed domains of the acetylcholine receptor”. period: 6/2000-8/2004 National Institute of Health-NIGMS-SCORE. Principal Investigator: José A. Lasalde Dominicci, Type: Institutional Minority Training Grant SCORE program NIGMS NIH MBRS S06 GM08102, cost \$595,482. The goal of this project is to define the allosteric sites of the M4 transmembrane segment of the *Torpedo* AChR. This project focus on the interaction of general anesthetics with lipid exposed mutations on the M4 domain and also the analysis of 3 lipid exposed allosteric positions. Principal Investigator: José A. Lasalde Dominicci, Ph.D. Type: Institutional Minority Training Grant SCORE program NIGMS (NIH MBRS S06 GM08102).

01/01/1999-7/31/2004, “Acetylcholine receptor genes in slow-channel syndrome” (\$1,400,000) Consortium Agreement Period: January 1, 1999 to July 31, 2004, Type: National Institute of Health-(2RO1-N33202) C0-PI (Principal Investigator- Christopher Gómez, J.A. Lasalde-Dominicci Co-Principal Investigator). The goal of this project is to understand the pathophysiology and molecular mechanisms involved in the impairment of neuromuscular transmission in the slow channel congenital myasthenic syndrome (SCCMS). Consortium agreement with University of Minnesota.

6/2000-7/2002. “**Development of pathogenic Neuronal Nicotinic Acetylcholine receptor models**” Postdoctoral Research training Supplement NIH, American Psychiatry Association (\$80,000) (Principal Investigator Maria Reyes, M.D., Co-Investigator: José A. Lasalde Dominicci. The long-term goal of this project is to develop transgenic mice models for pathogenic cholinergic pathways in the CNS. The proposed research will focus on the construction and electrophysiological characterization of two pathogenic mutations recently found in the muscle type AChR ( $\beta 1V229F$  and  $\alpha 1V249F$ ) at homologous positions in the  $\alpha 4$  neuronal subunit. These two mutations have been found in two myasthenic patients with the slow-channel (SCCMS).

7/2000-8/2003, “**Molecular Basis of neuronal nicotinic receptor up-regulation and nicotine addiction**” (\$30,000). The goal of this research proposal is to combine electrophysiological, biochemical, molecular biological techniques and confocal imaging in order to define the structural and functional basis for the relationship between up-regulation and desensitization of the  $\alpha 4\beta 2$  nAChR induced by nicotine. The mechanism by which the  $\alpha 4\beta 2$  nAChR number is increased in the cell surface following nicotine exposure is thought to involve reduced turnover of receptors, it has been suggested that a conformational change of the receptor prevent it from being removed from the cell surface. The long-range goal of the proposed experiments is to gain insight into a mechanism of upregulation of the  $\alpha 4\beta 2$  nAChR up-regulation that has been associated to nicotine tolerance and dependence. Principal Investigator: José A. Lasalde Dominicci, Ph.D. Type: Institutional Funds (FIPI) (Years 2000-2003) Period: July 1, 2000 to December 31, 2003.

10/1998-12/2000, “**Instrumentation for Confocal microscope**” Principal Investigator: José A. Lasalde Dominicci, Ph.D. Type: Competitive Instrumentation NIH-NCRR (1S10RR 13705-01). This project provided Confocal Laser Scanning microscope. This system includes Krypton/Argon mixed gas laser with lines 488, 568 and 647nm; scanning imaging head; fiberoptics laser delivery; three detector channels; multichannel data acquisition; Pentium based scan control and image acquisition system. Funds awarded \$236, 433.

10/1999-8/2000, “**Confocal Imaging Facility Upgrade**” Principal Investigator: José A. Lasalde Dominicci, Ph.D. Type: Instrumentation, National Science Foundation EPSCoR. This proposal up-grades the confocal imaging facility with an additional inverted microscope (coupled to the Zeiss 510 NLO confocal microscope) and computers programs and printers to support image analysis. Funds awarded \$226,000.

10/1998-10/1999, “**Automated DNA sequencing instrumentation Facility**” NSF-EPSCoR Shared Instrumentation grant, Awarded (3/15/1999) Principal Investigator: Owen McMillan, Ph.D. Co- Investigator: José A. Lasalde Dominicci, Ph.D. Funds awarded \$165,000.

5/1999-8/2000, “**A twophoton laser application for confocal imaging**” NSF EPSCoR co-funding Principal Investigator: Fernando Santana, Ph.D., Co-Principal Investigator: José A. Lasalde Dominicci, Ph.D. Funds awarded \$232,000

09/1997-04/31/2009 Type: 2R01GM56371-12, Funds awarded \$2,497,000. “**Cholesterol and lipid protein interactions affect acetylcholine channel function**” (*Investigates the effects of cholesterol and lipid exposed mutation on the Torpedo and muscle-type AChR channel function*). Principal Investigator: José A. Lasalde

Dominicci, Agency National Institute of General Medical Sciences (NIGMS). The conformational transitions of the Nicotinic Acetylcholine receptor (AChR). We decoded a network of hydrophobic allosteric sites located at lipid exposed of the M3 transmembrane segment. The main hypothesis is that an exclusive group of lipid-exposed positions might play a critical role in the channel function through physical interactions with membrane lipids that remain to be defined. This research explore specific, novel aspects of the interaction of these allosteric sites with the membrane bilayer using two approaches: lipid replacements in the intact oocyte, site specific mutagenesis of the M3 transmembrane domain of the *Torpedo* and muscle-type AChR and the use of nonsense suppressor methods to deliver unnatural amino acids to novel allosteric positions in transmembrane segments.

6/2004-8/2008, “**Mutagenesis of nicotinic acetylcholine receptors**”. period: 6/2004-8/2008 (\$740,000) National Institute of Health-NIGMS-SCORE. Principal Investigator: José A. Lasalde Dominicci, Type: Institutional Minority Training Grant SCORE program NIGMS NIH MBRS S06 GM08102, cost \$595,482. The goal of this project is to define the allosteric sites of the M4 trasmembrane segment of the *Torpedo* AChR. This project focus on the interaction of general anesthetics with lipid exposed mutations on the M4 domain an also the analysis of 3 lipid exposed allosteric positions. Principal Investigator: José A. Lasalde Dominicci, Ph.D. Type: Institutional Minority Training Grant SCORE program NIGMS (NIH MBRS S06 GM08102).

9/2009-11/2012 Principal Investigator: José A. Lasalde Dominicci, Ph.D. (NSF), Type: MRI Instrumentation Grant, “**Emission-Fingerprinting upgrade-Confocal and Two photon Facility–Multi Campus Initiative-UPR**” Submitted January 28, 2009. The main goal of this proposal is to upgrade the applications of an existing Confocal and Two-Photon Microscopy Facility of the University of Puerto Rico (UPR), Río Piedras Campus ([www.cifupr.org](http://www.cifupr.org)), to perform fluorecence emission fingerprinting - Budget allocation: \$322,000.

1/2010-7/2015 Type 2RO1-N33202 “**Acetylcholine receptor genes in slow-channel syndrome**” (\$1,400,000.013) Consortium Agreement: National Institute of Health (Principal Investigator-Christopher Gómez, J.A. Lasalde-Dominicci Co-Principal Investigator). The goal of this project is to understand the pathophysiology and molecular mechanisms involved in the impairment of neuromuscular transmission in the slow channel congenital myasthenic syndrome (SCCMS). Consortium agreement with University of Chicago.

10/2006-8/31/2013 - No Cost Extension - SNRP: “**Specialized Neurosciences Research Program in NeuroAIDS**”, (\$1,500,000 per year) Principal Investigator: Edmundo Kraiselburd, Scientific Director, José A. Lasalde Dominicci (time effort 25%, Scientific Director). National Institute of Neurological Disorder and Stroke (U54NS0430311), National Institutes of Health. The present NeuroAIDS Program of the UPR-MSU SNRP funded by NINDS provides the ideal instrument to upgrade the level of research in HIV and neuroscience's building on these existing clinical and basic research infrastructures and the collaboration with NIH funded scientists with skills and expertise otherwise not available in Puerto Rico. (for further information see <http://snrp.rcm.upr.edu/investig.html>).

10/2006-8/31/2013- No Cost Extension, - SNRP, NIH- U54NS0430311-NCE; Title: “**Molecular basis for neuronal nicotinic receptor upregulation: potential implications in HAD**” NCE P.I. José A. Lasalde-

Dominicci, Direct Cost \$350,000 per year (5 years) 11/2006-10/2013. In the project, we will use voltage-clamp whole-cell current electrophysiological recording to assess nAChR function, radioligand binding assays to ascertain numbers of  $\alpha 4\beta 2$ -nAChR in total cell membranes and on the cell surface, site-directed mutagenesis approaches, and confocal microscopy to study the upregulation of the  $\alpha 4\beta 2$  and  $\alpha 7$  nAChRs. The aims are to: (1) define the structural and functional basis for the up-regulation of the  $\alpha 4\beta 2$  nAChR induced by chronic nicotine exposure, (2) develop methods to incorporate fluorescent amino acids into the nAChR subunits using nonsense suppressor techniques that will allow the study nAChRs trafficking in vivo, (3) gain insight into the molecular basis for the upregulation of the  $\alpha 7$  nAChR induce by a combined treatment with HIV-1 gp120, nicotine and galantamine in vitro, (4) examine the functional state of the  $\alpha 7$  nAChR after chronic exposure to gp120 in macrophages from HIV infected patients and (5) express and purify the  $\alpha 7$  nAChR extracellular domain for crystallization trials.

Grant Number P20 RR-016470 from the National Center for Research Resources (NCRR), Period: 05/01-2009-04/31-2014. P.I. Vibha Bansal, Ph.D. **“Screening of different sources of plasminogen activators, their inhibitors and development of new techniques for isolation of plasminogen activators”**, José A. Lasalde Dominicci, Ph.D. (in kind as Collaborator/Mentor).

Grant Number P20 RR-016470 from the National Center for Research Resources (NCRR), Period: 05/01-2009-04/31-2014. Margarita Ortiz, Ph.D., PI Project, José A. Lasalde Dominicci, Ph.D. (in kind Collaborator/Mentor) - **“Novel synthesis of nicotinic agonists for Alzheimer’s therapy”**

NIH Clinical Grant Award \$50K, PI Dr. Carlos Báez. Mentor, Dr. José Lasalde Dominicci **“Bupropion as adjunctive therapy to improve immune profile in HIV seropositive smokers”**, Awarded 02/11/2011 (in kind Mentor)

**Clinical Bioreagent Center in PR. HIV Vaccine pilot project** CRD OISE-14-60-828-01, 06/15/2015-01/15/2016 (José A. Lasalde Dominicci, Ph.D. PI 5% in kind)

### **Present Funding**

2/01/2013-1/31/2017, Principal Investigator: José A. Lasalde Dominicci, Ph.D. (NIH), Type: R01, 1R01GM098343-0, Structure of Membrane Proteins - submitted on February 28, 2012. **“A lipid-based approach towards the nAChR high resolution structure”**. This application responds to Program Announcement “Structural Biology of Membrane Proteins” (PA) Number: PA-10-228. We propose to develop a comprehensive lipid-based approach to assess the function and stability of detergent-solubilized nAChR. The main goal of this application is to define the manner in which detergents affects the lipid composition, ion channel function, agonist binding, state of aggregation of the solubilized-nAChR and ultimately the ability to form membrane protein crystals. The objective of this application is to develop a comprehensive lipid-based approach for the selection of detergents for membrane protein crystallization.

NIH/NINDS- **“The COBRE Center for Neuroplasticity at the University of Puerto Rico”**. Principal Investigator: Josh Rosenthal, Co-Investigator, Director of Confocal imaging facility, José A. Lasalde Dominicci, Ph.D. (NCRR), Type: U54 COBRE- Budget allocation: \$11,213,710. The goal of the COBRE Center



proposed in this application is to significantly enhance the quality and biomedical relevance of research by scientists at the Institute of Neurobiology, the University of Puerto Rico Medical Sciences Campus (UPR-MSC) and the UPR Río Piedras Campus (UPR-RP). Period: 01/2013-12/31/2017. Awarded on November 2012.

NIH-NIAID- ***“Optimization of HIV glycoproteins as vaccines candidates”***– Principal Investigator (R01AI122935) José A. Lasalde Dominicci, Ph.D. (*in kind*). More than thirty years after its discovery, the human immunodeficiency virus (HIV) continues to be a major global concern. Despite a reduction in the number of new infections worldwide (2.1 million new infections in 2013 vs. 5 million in 2005), the HIV pandemic is far from over. In the United States alone, there are nearly 45,000 new HIV diagnoses each year, with some ethnic groups being disproportionately affected. Thus, the search for a prophylactic vaccine against HIV is of paramount importance. In this project, a consortium that combines a research university, a startup biotech company and the advisory input from the local biopharmaceutical manufacturing sector, aim to optimize the pipeline for the production of HIV vaccines for clinical trials by addressing some of the hurdles that have hindered progress in this field over the years. Period: 07/01/2016 – 06/30/20

#### **COLLABORATIVE RESEARCH PROJECTS**

- 1997-present: Christopher Gómez, M.D., Ph.D., University of Chicago, Department of Neurology:  
*"Electrophysiological characterization of acetylcholine receptor genes in slow-channel congenital myasthenic syndrome"*
- 2001-present: Raymond Sevens Ph.D. and Vadim Cherezov, Scripps Institute, San Diego, CA:  
*"Crystallization of nicotinic acetylcholine receptor"*
- 2003-present: Enrique Ochoa, M.D., Ph.D., Department of Neurology, UC Davis Medical School, University of California at Davis. *"Molecular basis of neuronal nicotinic acetylcholine receptor desensitization"*.