BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2.
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NAME	POSITION TITLE
Jorge D. Miranda	**Professor**
eRA COMMONS USER NAME (credential, e.g., agency login) **JDMIRANDA**	

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
University of Puerto Rico, Rio Piedras Campus	B.S.	05/88	Biology
University of Puerto Rico, Rio Piedras Campus	M.S.	05/90	Biology
Baylor College of Medicine, Houston, TX	Ph.D.	10/96	Neuroscience
Univ. of Miami School of Medicine-Miami Project To Cure Parlysis	Postdoc	12/98	Regeneration

Please refer to the application instructions in order to complete sections A, B, C, and D of the Biographical Sketch.

A. Personal Statement → website: http://md.rcm.upr.edu/physiology/dt_team/dr-jorge-d-miranda/

My research experience began at the UPR-Rio Piedras Campus, studying the role of second messengers (Ca^{2+}, cAMP, cGMP and IP3) in the phagocytic process of *Tetrahymena thermophila*. This experience exposed me to concepts in Molecular Physiology and cellular strategies that increased my skills to answer specific questions. At Baylor College of Medicine (Houston, TX), I decided to pursue my doctoral research project in a laboratory working with the regulation of the alpha subunit of the GABAa receptor at the transcriptional, post-transcriptional, translational and post-translational level. This experience exposed me to Cellular & Molecular Neuroscience concepts and issues, as well as to extensive array of molecular, cellular and biochemical techniques. At the end of my PhD graduate training, I decided to continue my postdoctoral training in an environment related to neural development but with emphasis in clinical conditions. Many of the events that are initiated after spinal cord injury are recapitulation of the same molecular and cellular events that takes place during early stages of neural development. The challenge of establish a hypothesis about a biological problem and develop experiments to answer the questions is something that always attracted me. That is why, I decided to move to the Miami Project to Cure Paralysis and expose myself to the most recent issues related to this condition. I accepted a postdoctoral position with Dr. Scott Whittmore and he introduced me to the topics, research models and controversial issues in the field of spinal cord injury. This research center was an excellent place to perform my postdoctoral training because the environment was suitable to ask questions and share information at all the levels (ions, molecules, proteins, cells, systems, behavior). The publication of my research project was the first article about Eph receptors after spinal cord injury. Since then, we are the group with most publications of this topic in the field. After two years of postdoctoral training, I joined the Physiology Department at UPR-Medical Sciences Campus in 1999 with a lot of energy and enthusiasm to pass to others what I have learned. At the same time, I developed a collaboration with a group at the Kentucky Spinal Cord Injury Research Center in Louisville, KY. This experience gave me the opportunity to expand my knowledge and skills to answer specific questions related to spinal cord trauma. Although the main focus of my laboratory is on the role of repulsive molecules (Eph receptors) expressed after trauma, several new projects have been developed recently. For example, role of purinergic receptors in the formation of the glial scar, role of Flotilin-2 lipid raft protein in the repulsive environment for axonal regeneration, role of ephexin in generating the cellular events for growth cone collapse after spinal cord injury and more recently, the neuroprotective role of estradiol and tamoxifen after injury. So far, I trained three postdoctoral fellows, seven PhD graduate students, and over 15 undergraduate students confirming my motivation and leadership to stimulate others to get involved in science. The research experience and concepts obtained during my graduate and postdoctoral training support my qualification to accomplish the research project presented in this proposal. Moreover, the technical skills that will be used in the student's proposal are routinely used in my laboratory (and published in several peer review journals) and no difficulties are expected.

B. Positions and Honors

Positions

1986-1988 Undergraduate Research Assistant (Cel. & Mol. Biol. Lab.), University of Puerto Rico
1988-1989 Teaching Assistant (General Biology Course), University of Puerto Rico
1989-1990 Graduate Research Assistant (Cel. & Mol. Biol. Lab.), University of Puerto Rico
1990 Microbiology Teacher, Technological College of San Juan
1992-1996 Graduate Research Assistant (Biochemistry Depart.), Baylor College of Medicine
1996-1998 Senior Research Associate (Miami Project), University of Miami School of Medicine
1999-2004 Assistant Professor, Physiology Department, UPR - School of Medicine
2001-2004 Coordinator of the Graduate Program in the Physiology Department
2004-2011 Associate Professor, Physiology Department, UPR- School of Medicine (Tenure 2006)
2006-2010 Coordinator of the Graduate Program- Graduate Biomedical Sciences Program
2012- Professor, Physiology Department, UPR- School of Medicine
2010-2013 Associate Dean & Director of Biomedical Sci. Graduate Program, UPR-Sch. of Medicine

2006 Vice-President of the Puerto Rico Neuroscience Chapter
2007 President of the Puerto Rico Neuroscience Chapter
2008-2010 Coordinator of the Human Physiology Course for Medical Students UPR-MSC
2010-2012 Coordinator of the Human Physiology Course for Dental Students UPR-MSC
2012-2015 Coordinator of the Vertebrate Physiology Course for Graduate Students UPR-MSC
2011 Vice-President of the Puerto Rico Physiological Society Chapter
2012 President of the Puerto Rico Physiological Society Chapter

Honors and Professional Memberships

1990-1995 MARC Predoctoral Fellowship (NIGMS)
1992-1996 Dean's Award for Excellence, Baylor College of Medicine
1995-1996 American Psychological Association Fellowship
1996- Member, Society for Neuroscience
1996-1997 Research Supplement for Minorities (NIH-NINDS: #NS26887)
1997-1998 F32 Postdoctoral Fellowship (NIH-NINDS: #NS10304)
1999-2009 Organizing Committee, Puerto Rico Annual Neuroscience Meeting
2000-2008 Member, International Society for Developmental Neuroscience
2000- Member, Society for Neurotrauma
2002 Distinguished Faculty, UPR - School of Medicine (Betances Award)
2003-2006 Outstanding Professor, Physiology Department, UPR - School of Medicine
2006 Alumni Achievement Award for Research, American Psychological Association (Atlanta,GA)
2011-2014 Member, American Physiological Society (APS)
2009- Member, Puerto Rico Physiological Society (PRPS)
2012 Distinguished Faculty, UPR-School of Medicine – Class of Medicine 2012 and 2013
2012 Distinguished Faculty, UPR-School of Medicine – Class of Graduate Students 2012
2008-2015 Outstanding Professor, Physiology Department, UPR - School of Medicine

Reviewer of the journal: Neural Regeneration Research
Adhoc Reviewer of the journals: 1) Neurological Research; 2) Neuroscience; 3) Brain Research; 4) Molecular and Cellular Endocrinology

C. Selected Peer-reviewed Publications

Colon JM and Miranda JD (2016) Tamoxifen: an FDA approved drug with neuroprotective effects for spinal cord injury recovery. (*In revision after resubmission to Neural Regeneration Research*).

Cruz N, Miranda JD and Crespo MJ (2016) Modulation of Vascular ACE by Oxidative Stress in Young Syrian Cardiomyopathic Hamsters: Therapeutic Implications. Journal of Clinical Medicine. 5(7). PMID: 27420103

Martinez NA, Ayala AM, Martinez M, Martinez-Rivera FJ, Miranda JD and Silva WI (2016) Caveolin-1 Regulates the P2Y2 Receptor Signaling in Human 1321N1 Astrocytoma Cells. J. Biol Chem. 291 (23): 12208-22. PMID: 27129210.

Colón JM, Torrado AI, Cajigas A, Santiago JM, Salgado IK, Arroyo Y and Miranda JD (2016) Tamoxifen administration immediately or 24 hours after spinal cord injury improves locomotor recovery and reduces secondary damage in female rats. J. Neurotrauma – Epub ahead of print; PMID: 26896212.

Figueroa JD, Serrano-Illan M, Licero J, Cordero K, Miranda JD and De Leon M. (2016) Expression and roles of the lipid chaperone, FABP5, in the restorative actions mediated by docosahexaenoic acid (DHA) following experimental spinal cord injury. J. Neurotrauma – Epub ahead of print; PMID: 26715431

Mosquera L, Arocho L, Torrado A, Torres Y, Miranda JD and Segarra AC (2015) Comparison of two methods of estradiol replacement: their physiological and behavioral outcomes. J. Vet. Sci. & Technology. 6(6): 276-284. PMID: 26962471; Manuscript ID: NIHMS749972

Salgado IK, Torrado AI, Santiago JM, Miranda JD (2015) Tamoxifen and Src kinase inhibitors as neuroprotective/neuroregenerative drugs after spinal cord injury. Neural Regeneration Research. 10(3): 385-390. PMID: 25878585; PMC4396099

Rosas OR, Torrado AI, Santiago JM, Rodriguez AE, Salgado IK, Miranda JD (2014) Long-term treatment with PP2 after spinal cord injury resulted in functional locomotor recovery and increased spared tissue. Neural Regeneration Research. 9 (24): 2164-2173. PMID: 25657738; PMC4316450

Mosquera L, Colón JM, Santiago JM, Torrado AI, Melendez M, Segarra AC, Rodriguez-Orengo, JF, Miranda JD (2014) Tamoxifen and estradiol improved locomotor function and increased spared tissue in rats after spinal cord injury: their antioxidant effect and role of estrogen receptor alpha. Brain Research. 1561: 11-22. PMID: 24637260; PMC4046634

Santos-Vera B, Vázquez-Torres R, Marrero HG, Acevedo JM, Arencibia-Albite F, Vélez-Hernández ME, Miranda JD, Jiménez-Rivera CA. (2013) Cocaine sensitization increases I h current channel subunit 2 (HCN_2) protein expression in structures of the mesocorticolimbic system. J Mol Neurosci. 50(1):234-45. PMID: 23203153; PMC3742011

Santiago JM, Torrado AI, Arocho LC, Rosas OR, Rodríguez AE, Toro FK, Salgado IK, Torres YA, Silva WI, Miranda JD. (2013) Expression Profile of Flotillin-2 and Its Pathophysiological Role After Spinal Cord Injury. J. Mol. Neurosci. 49(2): 347-59. PMID: 22878913; PMC3545048

Figueroa JD, Cordero K, Baldeosingh K, Torrado AI, Walker RL, Miranda JD, and De Leon M (2011) Docosahexaenoic Acid Pretreatment Confers Protection and Functional Improvements after Acute Spinal Cord Injury in Adult Rats. J Neurotrauma . 29(3), 551-66. PMID: 21970623; PMC3278822

Rodriguez-Zayas AE, Torrado AI, Rosas OR, Santiago JM, Figueroa JD and Miranda JD (2011) Blockade of P2 Nucleotide Receptors After Spinal Cord Injury Reduced the Gliotic Response and Spared Tissue. J. Mol. Neurosci. 46(1), 167-176. PMID: 21647706; PMC3522077

Arocho LC, Figueroa JD, Torrado AI, Santiago JM, Vera AE and Miranda JD (2011) Expression Profile and Role of EphrinA1 Ligand After Spinal Cord Injury. Cell Mol. Neurobiology. 31(7), 1057-1069. PMID: 21603973; PMC3216482

Rosas O, Figueroa JD, Torrado A, Rivera M, Konig-Toro F and Miranda JD (2011) Expression and activation of Ephexin Expression is altered after spinal cord injury. Developmental Neurobiology. 71(7): 595-607. PMID: 20949525; PMC3514508

Rodríguez-Zayas A, Torrado A, Miranda JD (2010) $P2Y_2$ Receptor Expression is Altered in Rats after Spinal Cord Injury. International J. of Devel. Neurosci. Int. Journal of Developmental Neurosc. 28(6), 413-21. PMID: 20619335; PMC3225399

Santiago JM, Rosas O, Torrado AI, González MM, Kalyan-Masih PO, and Miranda JD (2009) Molecular, Anatomical, Physiological and Behavioral studies of rats treated with Buprenorphine. J. Neurotrauma. 26 (10), 1783-1793. PMID: 19653810; PMC2864459

Cruz-Orengo L, Figueroa JD, Torrado A, Puig A, Whittemore SR and Miranda JD (2007) Reduction of EphA4 receptor expression after spinal cord injury does not induce axonal regeneration or return of tcMMEP response. Neuroscience Letters. 418(1), 49-54. PMID: 17418490; PMC2570091

Willson CA, Foster RD, Onifer SM and Whittemore SR and Miranda JD (2006) EphB3 receptor and ligand expression in the adult rat CNS. J. Mol. Histol. 37(8-9), p.369-380. PMID 17103029

Cruz-Orengo L, Velázaquez I, Torrado A, Ortiz C, Hernández C, Puig A, Segarra A, Whittemore SR and Miranda JD (2006) Blocking EphA4 upregulation after spinal cord injury results in enhanced chronic pain. Experimental Neurology. 202, p.421-433. PMID: 16959251

Figueroa JD, Benton R, Willson CA, Velázquez I, Torrado A, Ortiz C, Whittemore SR and Miranda JD (2006) Inhibition of EphA7 Upregulation after spinal cord injury reduces Apoptosis and Promotes Locomotor Recovery. J. Neurosc. Res. 84(7), p. 1438-51. PMID: 16983667

Irizarry-Ramírez M, Willson CA, Cruz L, Figueroa JD, Velázquez I, Jones H, Foster R, Whittemore SR and Miranda JD (2005) Upregulation of EphA3 Receptors After Spinal Cord Injry. J. of Neurotrauma 22(8), p.929-935. PMID: 16083359

Silva WI, Maldonado HM, Velázquez G, Rubio-Dávila M, Miranda JD, Aquino E, Mayol N, Cruz-Torres A and Salgado-Villanueva IK (2005) Caveolin isoforms expression during differentiation of C6 glioma cells. Internat. J. of Develpmental Neuroscience 23, p. 599-612. PMID: 16135403

Willson CA, Miranda JD, Foster RD, Onifer SM and Whittemore SR (2003) Transection of the adult rat spinal cord up-regulates EphB3 receptor and ligand expression. Cell Transplantation 12(3), p. 279-290. PMID: 12797382

Willson CA, Irizarry-Ramírez M, Gaskins HE, Cruz-Orengo L, Figueroa JD, Whittemore SR and Miranda JD (2002) Upregulation of EphA Receptor Expression in the Injured Adult spinal Cord. Cell Transplantation 11(3): p.229-239. PMID: 12075988

Miranda JD, White LA, Willson CA, Marcillo A, Jaggid J and Whittemore SR. (1999) Induction of Eph B3 after spinal cord injury. *Exp.Neurol*. 156, p.218. PMID: 10192794

Miranda JD, Sin-Chieh L, Díaz ME and Barnes EM, Jr. (1997) Developmental Expression of Chick $GABA_A$ Receptor α1 subunit *in vivo* and *in vitro*. *Dev. Brain Res*. 99, p.176-186.

Miranda JD and Barnes EM, Jr. (1997) Repression of $GABA_A$ Receptor α1 Polypeptide Biosynthesis Requires Chronic Agonist Exposure. *J. Biol. Chem*. 272 (26), p.16288-16294.

Renaud FL, Chiesa R, De Jesús JM, Lopez A, Miranda JD and Tomassini N. (1991) Hormones and Signal transduction in Protozoa. *Comp. Biochem. Physiol*. **100**A (1), p. 41-45.

Non-Peer review Communications:

1) Miranda JD. Puerto Rico Physiological Society (PRPS) Annual Meeting Report (2013) The Physiologist. vol. 56, No. 4, p. 95-97.
2) Miranda JD. Puerto Rico Physiological Society Newsletters: July 2012 and May 2013
3) Sosa M, Miranda JD, Perez-Acevedo N, Santos Quiñones L, Prado Otero J (2014) Las Ciencias Biomédicas en la Escuela de Medicina de la UPR. Buhiti (Publicacion de la Escuela de Medicina de la UPR). Vol. 18, No. 3, pag. 2
4) Cadilla CL and Miranda JD (2014) History, Impact, Achievements and Future Directions of the UPR Medical Sciences Campus MBR RISE Program. Buhiti (Publicacion de la Escuela de Medicina de la UPR). Vol. 18, No. 3, pag. 48

Past & Present doctoral students in the laboratory:

1999-2005	Lillian Cruz Orengo: now Assistant Professor at UC Davis, CA
1999-2005	Johnny Figueroa: now Assistant Professor in Loma Linda School of Medicine
2003-2011	Jose Santiago: now an Assistant Professor at UPR-Carolina Campus
2003-2011	Ana Rodríguez: now an Instructor at UMET
2003-2011	Luz Arocho: now a Research Specialist in Pfizer laboratories, MA
2003-2011	Laurivette Mosquera: finished her PhD and then completed her training in Dental School
2004-2012	Odrick Rosas: finished his PhD & now a resident in Physical Medicine & Rehabilitation
2011	Jennifer Colon: 6th year graduate student (Expected graduation date: May 2017)

Co-Advisor of Graduate Students:

2015-	Nilmary Grafals (with Dr. Pablo Vivas as Thesis Advisor-Biochemistry)
2015-	Cristina Roman (with Dr. Guillermo Yudowski as Thesis Advisor-Anatomy)

Past & Present Postdoctoral Fellows in the laboratory:

1) Dr. Margarita Irizarry (1999-2001)
2) Dr. Jose Santiago (2012-2013)
3) Dr. Iris K. Salgado (2013-present)

D. Research Support

Miranda, Jorge D.

Active

R25 GM061838 09/01/12 – 08/31/17 1.20 calendar
NIH/NIMH- MBRS/RISE $120,000 for subproject #2 ($24,000/year)
Subproject: Interdepartamental Seminar Series (Activity #2)
Role: Coordinator Activity #2
The major goal of this activity is to coordinate a monthly seminar series. This involves the invitation of well-known investigators from the US mainland (different fields of research), and the coordination of seminars (and round table discussions) with the invited speaker and students/faculty.

PAR-11-286 07/01/13 – 06/30/18 6.0 calendar
NIH COBRE (1P20GM103642) $878,823 for subproject #1
Subproject 1: Estradiol and Tamoxifen as neuroprotective/neuroregenerative agents after spinal cord injury
Role: Principal Investigator of Subproject #1
The major goal of this activity is to determine the neuroprotective and neuroregenerative role of estrogen and the selective estrogen receptor modulator, tamoxifen, after spinal cord (SCI). Behavioral, anatomical, cellular and molecular analysis will be performed to analyze the effect of these agents in the injured spinal cord.
OVERLAP
There is no scientific overlap between the COBRE proposal and the MBRS/RISE grant.

Submitted

NINDS-R01 Miranda (PI) 06/01/16-05/31/21
Neuroprotective Effect of Tamoxifen and Exercise after Spinal Cord Injury
The major goal of this project is to determine the therapeutic window of tamoxifen treatment after spinal cord injury (SCI) and if there is any sex difference with this treatment in locomotor recovery. In addition, if tamoxifen produces changes at the anatomical and electrophysiological level. Moreover, the study includes the analysis of apoptotic, regenerative and repulsive proteins after SCI and if tamoxifen affect the expression of those factors. Finally, if the combinatorial treatment of tamoxifen with forced treadmill exercise improved the locomotor recovery in the injured animals.
Role: PI 50% effort-6 months calendar Direct cost: $1,250,000

NINDS-R21 Miranda (PI) 02/01/17 – 01/31/19
Effect of Tamoxifen and exercise in skeletal muscle after spinal cord injury.
The major goal of this project is to determine if tamoxifen, a selective estrogen receptor modulator, prevent the changes in the expression profile of myosin proteins after spinal cord injury and maintains the contractile properties of single muscle fibers. In addition, this activity will investigate the effect of early treatment with tamoxifen on Satellite cell proliferation and muscle regeneration, and if both events are potentiated by exercise.
Role: PI 25% effort – 3 months calendar Direct cost: $275,000

MBRS/RISE Dr. Carmen Cadilla (PI) 09/01/17 – 08/31/22
NIH/NIMH Role: Coordinator Activity #2 10% Effort (Total Direct Cost: $108K)
Interdepartmental Seminar Series (Activity #2)
The major goal of this activity is to coordinate a monthly seminar series and an annual departamental mini-symposium. This involves the invitation of well-known investigators from the US mainland (different fields of research), and the coordination of seminars (and round table discussions) with the invited speaker and students/faculty.

Completed Support

R25-GM061838 09/01/08 – 08/31/12 ($81,750)
NIH/NIMH Role: Coordinator of Activity #2
MBRS/RISE
Subproject: Interdepartamental Seminar Series (Activity #2)

R24-MH048190 07/01/05 – 06/30/09 ($178,081)
NIH/NIMH Role: PI of subproject #2
M-RISP (Expression Profile of Purinergic Receptors After spinal cord injury)

S06-GM08224 08/01/04-07/31/08 ($647,361)
NIH/NIGMS Role: PI of subproject #9
MBRS/SCORE (Role of Eph Receptors during Regeneration of the Nervous system)

S06-GM08224 08/01/01-07/31/04 ($102,832)
NIH/NIGMS Role: PI of subproject #12
MBRS/SCORE
The major goal of this pilot project was to analyze the spatial and temporal expression of the ephrin B ligands at the mRNA and protein level after spinal cord injury.

U54NS39405-03 09/01/99-08/31/04 ($1,519,370)
NIH/NINDS Role: PI of subproject #2
Specialized Program in Cellular and Molecular Neurobiology
The major goal of this subproject was to analyze the spatio-temporal expression of Eph A receptors at the mRNA and protein level after spinal cord injury (SCI) in adult rats. In addition, in this proposal we identified the cells that upregulate the EphAs molecules after SCI.

EPS-9874782 09/01/00-05/31/02 ($146,594)
NSF Role: PI of this project
The major goals of this project was to analyze the spatial and temporal expression of EphB receptors at the mRNA and protein level after spinal cord injury.