

Ximena M. Bustamante Marin, PhD

Research Assistant Professor

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EDUCATION

Pontificia Universidad Católica de Chile December, 2009
PhD in Biological Sciences with mention in Physiological Sciences
Thesis Title: Role of metabolic substrates in the regulation of physiological apoptosis during rat spermatogenesis.

Pontificia Universidad Católica de Valparaíso, Chile April 2006
Professional Degree: Biochemist
Thesis Title: Substrate cycles during glycolysis in rat spermatocytes: Activity of 6 phosphofructose-2 kinase, fructose-1,6-bisphosphatase and fructose-2,6-bisphosphatase.

Pontificia Universidad Católica de Valparaíso, Chile December, 2004
B. S. Biochemistry

RESEARCH EXPERIENCE

Research Associate, University of North Carolina, Chapel Hill 2017 – 2019
Cystic Fibrosis Center and Pulmonary Diseases

- Investigating the role of ciliary clearance in neonatal respiratory distress associated with Primary ciliary dyskinesia.
- Characterizing the gene expression pattern of different ciliated cells across the tissues using a mouse model expressing *Foxj1-GFP*.

This research is competing for funds at the American Thoracic Society.

Postdoctoral Associate, University of North Carolina, Chapel Hill

2014 – 2017

Cystic Fibrosis Center and Pulmonary Diseases

Advisor: Lawrence Ostrowski, PhD

- Using exome sequencing to discover pathogenic genetics variants in GAS2L2 that lead to development of Primary Ciliary Dyskinesia.
- Developed a novel methodology to expand and culture human nasal epithelial cells and mouse embryonic trachea cells to perform *in vitro* analysis of ciliary function.
- Discovered new ciliated cells specific proteins using proteomic and super resolution confocal imaging.
- Collaboration with Dr. Knowles and Dr. Zariwala to investigate other genetic variant in cilia specific genes that cause Primary ciliary dyskinesia.

This work resulted in 2 publication as a first author, one publication as collaborator, and two other manuscripts are under preparation.

Research Scholar, Duke University, Durham

2010 – 2014

Cell Biology Department

Advisor: Blanche Capel

- Demonstrated that metabolic differences arise from body axis asymmetry. Established a collaboration with Dr. Newgard at Duke University.
- Developed a methodology to demonstrate that differences in oxygen availability, associated to left/right body asymmetry, modulate signal pathways that regulate germ cell fate decision leading to teratoma formation or cell death in *Dnd1^{Ter/+}* mice. Established a collaboration with Dr. Piantadosi at Duke University.
- Developed a methodology to rescue ovary function after chemotherapy.

This work was funded through the Lalor Foundation Postdoctoral Fellowship and Chancellor's discovery grant.

Assistant Professor, Universidad de Antofagasta, Chile

2010 – 2010

Faculty of Health Sciences.

Role of Na⁺/ H⁺ Exchanger sperm- Specific during human sperm capacitation and acrosomal reaction.

Research Assistant Universidad Católica de Chile

2006 – 2008

Laboratory of Embryology, Pontificia Universidad Católica de Chile, Santiago, Chile.

Advisor: Ricardo Moreno Mauro

- Investigated the Glucose –dependent generation of reactive oxygen species sensibility of rat spermatocytes to Fas-mediated apoptosis.
- Evaluated the role of p38 Map kinase activation on physiological and stress-induced germ cell apoptosis during rat spermatogenesis.

This work resulted in one publication as a co-author and one book chapter.

Doctoral Training, Universidad Catolica de Chile

2005 - 2009

- Investigated the role of metabolic substrates in the regulation of physiological apoptosis during rat spermatogenesis.

This work resulted in one publication as a first author.

Undergraduate Research, Universidad Catolica de Valparaiso, Chile

2000 – 2004

- Characterized Substrate cycles during glycolysis in rat spermatocytes: Activity of 6 phosphofructose-2 kinase, fructose-1,6-bisphosphatase and fructose-2,6-bisphosphatase.

RESEARCH GRANTS

Contribution to Ongoing Funded Research

Project Title: Functional Studies of Novel Genes Mutated in Primary Ciliary Dyskinesia. R01-HL117836-02

Advisor: Lawrence Ostrowski

Contributions to prior Funded Research

Project Title: Regulation of germ cell pluripotency through RNA Binding protein. R01-GM087500-001A2, NIH

Advisor: Blanche Capel

Project Title: Rescue of Fertility and ovarian Function after chemotherapy.

Chancellor's Discovery Grant

FELLOWSHIPS

- Lalor Foundation, Post-Doctoral Fellowship, 2011 – 2012
- CONICYT, Postdoctoral Fellowship from, Chile 2011 – 2012 (declined)
- World Health Organization to attend the course "Frontiers in Reproductions", Marine Biological Laboratory, Woods Hole, USA., May 2008
- Fellowship from United Nations University/Biotechnology for Latin America and the Caribbean to attend the course "Influence of Genes Microenvironment in Regulation of Proliferation versus Apoptosis in Tumoral Cells". IVIC, Caracas, Venezuela, 2005
- MESESUP to attend the course "Generation and Analysis of mice genetically Modified" CECS, Valdivia, Chile 2005
- PhD Fellowship from Pontificia Universidad Católica de Chile. Santiago, Chile, 2005 – 2009
- Biochemistry Fellowship from Pontificia Universidad Católica de Valparaíso, Valparaíso, Chile, 1997 – 2004

HONORS & AWARDS

Travel Award, Gordon Research Conference Cilia, Mucus & Mucociliary Interactions 2017
Best Poster Award, Gordon Research Conference Cilia, Mucus & Mucociliary Interactions 2015

PUBLICATIONS

Bustamante-Marin X. M., Yin W. N., Sears P. R., Werner M. E., Brotslaw E. J., Mitchell B. J., Jania C. M., Zeman K. L., Rogers T. D., Herring L. E., Refabért L., Thomas L., Amselem S., Escudier E., Legendre M., Grubb B. R., Knowles M. R., Zariwala M. A., Ostrowski L. E. "Lack of GAS2L2 Causes PCD by Impairing Cilia Orientation and Mucociliary Clearance". *Am J Hum Genet.* 2019 Feb 7;104(2):229-245. doi: 10.1016/j.ajhg.2018.12.009. Epub 2019 Jan 18.

Bustamante-Marin X.*, **Blackburn K.***, Yin W., Goshe M. B., Ostrowski L. E. "Quantitative Proteomic Analysis of Human Airway Cilia Identifies Previously Uncharacterized Proteins of High Abundance" *J Proteome Res.* 2017 Apr 7;16 (4):1579-1592. (* **contributed equally to this research**)

Bustamante-Marin X. M. and Ostrowski L. E. "Cilia and Mucociliary Clearance" *Cold Spring Harb Perspect Biol.* 2017 Apr 3;9 (4). Review

Chen G., Volmer A. S., Wilkinson K. J., Deng Y., Jones L.C., Yu D., **Bustamante-Marin X. M.**, Burns K. A., Grubb B. R., O'Neal W. K., Livraghi-Butrico A., Boucher R. C. "Role of Spdef in the Regulation of Muc5b Expression in the Airways of Naïve and Muco-obstructed Mice" *Am J Respir Cell Mol Biol.* 2018 Mar 26. doi: 10.1165/rcmb.2017-0127OC

Batchvarov IS, Taylor RW, **Bustamante-Marín X.**, Czerwinski M, Johnson ES, Kornbluth S, Capel B. "A grafted Ovarian Fragment Rescues host Fertility after Chemotherapy" *Mol Hum Reprod.* 2016 Dec;22(12):842-851.

Bustamante-Marin X., Cook M. S., Gooding J., Newgard C. and Capel B. "Left-Biased Spermatogenic Failure in 129/SvJ Dnd1Ter/+ Mice Correlates with Differences in Vascular Architecture, Oxygen Availability, and Metabolites" *Biol Reprod.* 2015 Sep;93 (3):78.

Bustamante-Marín X., Garness J. A., and Capel B. "Testicular Teratomas: An intersection of Pluripotency, Differentiation, and Cancer Biology" *Int J Dev Biol.* 2013; 57(2-4):201-10. Review.

Bernhardt ML, **Bustamante-Marín X** "Triangle Consortium for Reproductive Biology 22nd Annual Meeting" *Mol Reprod Dev.* 2013 Jul;80 (7):504-7.

Bustamante-Marín X., Quiroga C, Lavandero S, Reyes JG, Moreno RD. "Apoptosis, Necrosis and Autophagy are Influenced by Metabolic Energy Sources in cultured Rat spermatocytes" *Apoptosis.* 2012 Jun;17 (6):539-50.

Moreno R. D., Lagos-Cabré R., Buñuay J., Urzúa N., and **Bustamante-Marin X.** “Molecular Basis of Heat Stress Damage in Mammalian Testis”_In: Heat Stress: Causes, Treatment and Prevention” Editor(s) Stanislas Josipovic and Elias Ludwig Publisher Nova Science Publishers. 2012; Begin-End page 127-156 ISBN Code 978-1-62100-288-8

Lizama C, Rojas-Benítez D, Antonelli M, Ludwig A, **Bustamante-Marín X.**, Brouwer-Visser J and Moreno RD “TACE/ADAM17 is involved in Germ Cells Apoptosis during rat Epermatogenesis” 2010 Aug;140 (2):305-17.

Yañez A., **Bustamante X.**, Bertinat R, Werner E, Rauch MC, Concha II, Reyes JG, Slebe JC. “Expression of key Substrate cycle Enzymes in rat Spermatogenic cells: fructose 1,6 bisphosphatase and 6 phosphofructose 1-kinase” J Cell Physiol. 2007 Sep;212 (3):807-16.

Signs of Death in Spermatocytes of Rat Testis, Glucosse as a Possible Modulator.
Marin X. B., Lizama C., Moreno RD. Placenta 2005, 27: A.1 - A.72.

Submitted Manuscripts

Bustamante-Marin X. M., Shapiro A., Sears P. R., Charng W-L. , Conrad D., Margaret L., Knowles M. R., Zariwala M. A. Ostrowski L. E. “Identification of Genetic Variants in CFAP221 as a Cause of Primary Ciliary Dyskinesia”. Journal of Human Genetics, Submission Date 25th Jul 19 10:05:40; Current Stage: Manuscript under consideration.

Bustamante-Marin X. M. , Horani A., Stoyanova M. , Charng W-L., Bottier M., Sears P. R., Daniels L. A., Bowen H., Conrad D., Knowles M. R., Ostrowski L. E., Zariwala Z., Dutcher S. K. "Mutation of CFAP57 causes primary ciliary dyskinesia by disrupting the asymmetric targeting of a subset of ciliary inner dynein arms". PNAS, Submission Date 29th Jul 19, Current Stage Under review.

Bustamante-Marin X., Marchal C., Piantadosi C. and Capel B. “Low oxygen availability during embryonic male germ cell development increases the incidence of testicular teratomas in *Dnd1^{Ter/+}* 129 SvJ mice”. *In preparation.*

PRESENTATIONS & POSTERS

Bustamante-Marin X. M., Yin W. N., Sears P. R., Werner M. E., Brotslaw E. J., Mitchell B. J., Jania C. M., Zeman K. L., Rogers T. D., Herring L. E., Refabért L., Thomas L., Amselem S., Escudier E., Legendre M., Grubb B. R., Knowles M. R., Zariwala M. A., Ostrowski L. E. "Lack of GAS2L2 Causes PCD by Impairing Cilia Orientation and Mucociliary Clearance". Gordon Research

Conference Cilia, Mucus & Mucociliary Interactions. Galveston, Lucca, Italy. February 17-22, 2019.

Bustamante-Marin X., Werner M. Zariwala M.A., Yin W., Sears P.R., Knowles M. R. and Ostrowski L. E. (Talk and Poster) "GAS2L2, a gene related to PCD, is required for proper ciliary function and orientation in human, mouse and *Xenopus*" Gordon Research Conference Cilia, Mucus & Mucociliary Interactions. Galveston, TX, USA. February 12-17, 2017.

Bustamante-Marin X., Zariwala M.A., Yin W., Sears P.R., Knowles M. R. and Ostrowski L. E. (Poster) "Characterization of GAS2L2, a gene associated with PCD with normal ciliary structure" PCD on the Move! Advances in Primary Ciliary Dyskinesia Research, Diagnosis & Care. Bloomington, MN, USA. August 26-28, 2015.

Bustamante-Marin X., Zariwala M.A., Yin W., Sears P.R., Knowles M. R. and Ostrowski L. E. (Poster) "Expression and localization of GAS2L2, a gene possibly associated with PCD" Gordon Research Conference Cilia, Mucus & Mucociliary Interactions Galveston, TX, USA. February 08-13, 2015.

Bustamante-Marin X., Marchal C., Piantadosi C. And Capel B. (Poster). Testicular teratoma development in *DND1* heterozygous mice. Society for the Study of Reproduction, Palais des congrès de Montréal, Montréal, Québec, Canada, July 22–26, 2013.

Bustamante-Marin X and Capel B. (Talk) Asymmetric Development of Spermatogenic Failure and Testicular Teratoma in 129 *Dnd1^{Ter/+}* mice; Deciphering the Causes. Cell Biology Seminar, Duke University, Durham NC, USA. February 2013.

Bustamante-Marin X and Capel B. (Poster) Gradual Loss of Germ Cells in *DND1* Heterozygous Mice. Triangle Consortium for Reproductive Biology, Duke University, Durham NC, USA. March 1-2, 2013.

Bustamante-Marin X. and Capel B. (Talk) Left/Right asymmetry in tumor development and spermatogenic failure in 129/SVJ *Dnd1^{Ter/+}* mice. Cell Biology Seminar, Duke University, Durham NC, USA. April 2012.

Bustamante Marin X and Blanche Capel (Poster). Spermatogenesis failure in *Dnd1* heterozygous mice. VI International Symposium on Vertebrate Sex Determination, Kona, Hawaii, USA. April 23-27, 2012.

Bustamante-Marin X, Cook, M and Capel, B. (Poster). Characterization of the Spermatogenesis in 129/SvJ *Dnd1^{Ter/+}* mice Gordon Research Conference Mammalian Gametogenesis & Embryogenesis Waterville Valley Resort Waterville Valley, NH., USA. August 21-26, 2011.

Bustamante – Marin X., Reyes J. G and Moreno R. D. (Poster) Glucose and Lactate modulate c-kit and Fas levels through ROS production in cultured rat spermatocytes.

Bustamante-Marín X, Quiroga C. Lavanderos S. Reyes J.G. and Moreno R.D.(Poster) “Lactate, Survival Factor in Spermatoocytes primary culture” LII Annual meeting Chilean Society of Biology, II Iberoamerican meeting of Physiological Sciences, XXIV Annual meeting of the Chilean Society of Physiology and 16^a Symposium on Ca⁺² Binding Proteins and Ca⁺² Functions in Health and Disease. Pucón, Chile. November 2009.

Bustamante-Marín X., Quiroga C., Lavanderos S., Reyes JG and Moreno R. (Talk) Lactate, survival factor of cultured rat spermatoocytes. XX Annual meeting Chilean Society of Reproduction and Development. La Serena, Chile, September 2009.

Bustamante-Marín X., Gutierrez J., Quest A. and Moreno R. D. (Poster) “Inhibition of protein kinase C (PKC) prevents death of spermatoocytes in culture. VIII meeting of the International Society of Andrology and Gametology. Pucon, Chile January 2009.

Bustamante-Marín X, Lagos R. and Moreno R.D (Poster) Apoptosis and Reactive Oxygen Species Induced by Glucose in Cultured of Rat Spermatoocytes.

Lagos-Cabre R, **Bustamante-Marín X** and Moreno R.D (Poster) p38 MAP Kinase is involved in Physiological and Stress Induced Germ Cell Apoptosis during Rat Spermatoogenesis.

XIX Annual meeting of the Chilean Society of Reproduction and Development. Chillan, Chile September 2008.

Bustamante-Marín X. and Moreno R.D. (Talk) Apoptosis and Reactive Oxygen Species Induced by Glucose in Cultured Rat Spermatoocytes. XI Annual Symposium of de Frontiers in Reproduction Woods Hole, USA, June 2008.

Bustamante-Marín X. and Moreno R.D. (Poster) Lactate and Glucose, control Apoptosis of Rat Spermatoocytes. XVIII Annual meeting of the Chilean Society of Reproduction and Development. Chillan, Chile September 2007.

Lagos-Cabre R, **Bustamante-Marín X** and Moreno R.D. (Poster) p38 MAP Kinase is involved in Physiological and Stress Induced Apoptosis in male Germ Cell during the First Round of Spermatoogenesis in the Rat International Workshop, Chillan, Chile, November 2007.

Bustamante-Marín X. and Moreno R. D. (Poster) Differential effects of Lactate and Glucose on Rat Spermatoocyte Viability. V meeting of the International Society of Andrology and Gametology. Santiago, Chile. January 2009.

Bustamante-Marín X. Lizama C. and Moreno R. D. Signs of Death in Spermatoocytes of the rat Testis: Glucose as a Possible Modulator. XIX Annual meeting of the Chilean Society of Physiology Santiago, Chile. August 2005.

Bustamante-Marín X. and Reyes JG (Poster) Activity of 6 Phosphofructose 2-kinase, Fructose-1,6-bisphosphatase and Fructose-2,6-bisphosphatase. XXI National Meeting of Biochemistry students. Valdivia, Chile. August 2004.

TEACHING & MENTORING EXPERIENCE

- **Teacher's Assistant** for Dr. Brenda Temple, Fall 2018
 - University of North Carolina at Chapel Hill
 - Biochemistry-107
- **Teacher** March to August 2010
 - Universidad de Antofagasta Chile
 - Embryology
- **Teacher** March to July 2009
 - University Católica Silva Henríquez.
 - Biological bases of Neuroscience
- **Teacher** March 2007 - December 2008
 - Universidad Andrés Bello.
 - Seminars of Neurophysiology
- **Teaching Assistant** for Dr. Ricardo Moreno, March to December 2006
 - Pontificia Universidad Católica de Chile
 - Animal Reproduction
- **Laboratory Teaching Assistant** for Dr Gareth Owen, March to December 2006
 - Pontificia Universidad Católica de Chile
 - Molecular and Cell Biology

PROFESIONAL DEVELOPMENT

- **University of North Carolina at Chapel Hill, August 2019**
Epidemiology: The Basic Science of Public Health.
- **University of California, May 2018**
Academic English, Writing.
- **Duke University, June 2014**
Dr. Julie Reynolds
Assessments of honors theses as part of the NSF grant "*Understanding the Role of Writing in Promoting Learning and Engagement for Diverse Undergraduate Thesis Writers*".