
BIOGRAPHICAL SKETCH

Provide the following information.
Please follow this format.

FULL NAME Juan Larrain	CURRENT POSITION Associate Professor
Previous position: Assistant Professor (from year to year) 2002-2006	(From year) 2006

EDUCATION/TRAINING (Begin with baccalaureate or other professional education, such as physician, biochemist, etc. Include postdoctoral training)

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERR ED	FIELD OF STUDY
Catholic University of Chile, Chile.	BA	1988-1993	Biochemistry
Catholic University of Chile, Chile.	Ph.D.	1994-1998	Cell & Molecular Biology
Howard Hughes Medical Institute, University of California, Los Angeles, U.S.A.	PEW Postdoctoral Fellow.	1998-2000	Molecular Embryology

A. Brief description of your research (do not exceed 25 lines)

Our interest is to study the cellular and genetic mechanism of nervous system development and regeneration. For this we mainly used *Xenopus laevis* as a model organism with an approach based on cellular biology, biochemistry and genomics (through a very fruitful collaboration with Professor Francisco Melo at PUC). Regarding nervous system development we have described that Syndecan-4 is required for neural tube closure in *Xenopus* and mice embryos, through a mechanism that impinges in non-canonical Wnt signaling regulating protein stability of components of this pathway. This work has been published in journal including among others Nature Cell Biology, Development, The EMBO Journal, Developmental Biology and Journal of Biological Chemistry. For this work we have established collaboration with Professor Andrew Copp a world leader in neural tube malformations. In recent years we started a new research line aimed to develop *Xenopus laevis* as a unique model organism to study spinal cord regeneration taking advantage of the feasibility to perform comparative experiments in regenerative and non-regenerative stages. This decision has proved to be correct because now we have established our lab. as a worldwide leader in the use of *Xenopus* as a model system for spinal cord injury. We have demonstrated that hyaluronic acid is necessary for spinal cord regeneration, demonstrated the role of Sox2 in this process and performed a transcriptomic profiling analysis using state of the art deep sequencing techniques. All this work has been published in Development and Neural Development among other journals. Many new collaborations have been established with leaders on the field such as Hollis Cline (Scripps), Hazel Sive (MIT) and José Manuel García- Verdugo (Valencia). We have created and funded a school of scientist in developmental and regenerative biology that that have gone to places such as Stanford University, Cambridge University, University College London, Manchester University and St. Jude's Children Hospital as PhD and postdoctoral fellows and are starting to get positions at Chilean Universities.

B. Positions and Honors

B.1 Positions and Employment

- 2010-** Vice-President for Research, P. Universidad Católica de Chile
- 2009- 2011** Director, Millennium Nucleus in Regenerative Biology
- 2006-** Associate Professor, P. Universidad Católica de Chile
- 2005-2009** Chair, PhD Program in Cell & Molecular Biology, P. Universidad Católica de Chile
- 2002-2006** Assistant Professor, Faculty of Biological Sciences, P. Universidad Católica de Chile
- 2000-2002** Research Associate, Laboratory of Professor Edward M. De Robertis, Howard Hughes Medical Institute, University of California, Los Angeles, U.S.A.

B.2 Other Experience and Professional Memberships

- 2004-2006** Member of the Program: "Frontiers of Science" from the Chilean Academy of Science.
- 2006-2009** Member, Chilean Advisory Committee for the The Pew Programs in the Biomedical Sciences
- 2007-** Treasurer Latin-American Society for Developmental Biology
- 2008** Organizer International Symposium "From Developmental Biology to Tissue Regeneration"
- 2009-2011** Chair, Chilean Advisory Committee for the The Pew Programs in the Biomedical Sciences
- 2009** Member Study Group Biology II, FONDECYT, CONICYT
- 2010** Organizer V Latin-American Society for Developmental Biology
- 2010** Organizer International Course "Concepts and Model Organism in Regenerative Biology"

B.3 Honors

- 1993** "DIUC Research Fellowship" conceded by the Catholic University of Chile for the development of his undergraduate Thesis.
- 1993** Best graduate student of the 1988 Class in Biochemistry, Catholic University of Chile.
- 1994** "Fundación Andes" Ph.D. Fellowship.
- 1998** Pew Latin American Postdoctoral Fellow.
- 1999** Chilean Society for Cell Biology Award. Awarded for his Ph.D. thesis work.
- 1999** Chilean Academy of Science Award. Best National Ph.D. thesis in Biology.
- 2006** Young Scientist Prize from Bios-Chile and "Sociedad Chilena de Biología"
- 2007** TWAS ROLAC Young Scientist Award in Biological Sciences
- 2007** Affiliated member Third World Academy of Science (TWAS)
- 2008** Pius XI Gold Medal 2008, Pontifical Academy of Science

C. Peer-reviewed Publications

Most relevant to the current application (5 publications, please enclose PDF)

1. Muñoz, R., Moreno, M., Oliva, C., Orbenes, C., **Larraín, J.** (2006) Syndecan-4 regulates non-canonical Wnt signaling and is essential for convergent and extension movements in *Xenopus* embryos. *Nat. Cell Biol.* 8, 492-500.
2. Contreras, E.G., Gaete, M., Sánchez, N., Carrasco, H. and **Larraín, J.** (2009) Early requirement of Hyaluronan synthase activity for tail regeneration in *Xenopus* tadpoles *Development* 136, 2987-2996.
3. Escobedo, N., Contreras, O., Muñoz, R., Farías M., Carrasco, H., Hill C., Tran, U., Wessely O., Copp A.J. and **Larraín, J.** (2013) Syndecan 4 interacts with Vangl2 to regulate neural tube closure and planar cell polarity. *Development* 140, 3008-3017.
4. Gaete, M., Muñoz, R., Sánchez, N., Tampe, R., Moreno, M., Contreras, E., Lee-Liu, D. and **Larraín, J.** (2012) Spinal cord regeneration in *Xenopus* tadpoles proceeds through activation of Sox2 positive cells. *Neural Dev.* 7, 13.
5. Lee-Liu, D., Moreno, M., Almonacid, L.I., Tapia, V.S., Muñoz, R., von Marees, J., Gaete, M., Melo, F. and **Larraín, J.** (2014) Genome-wide expression profile of the response to spinal cord injury in *Xenopus laevis* reveals extensive differences between regenerative and non-regenerative stages. *Neural Dev.* 9, 12

Additional publications (in chronological order)

- 1.- Lobos, S., **Larrain, J.**, Salas, L., Cullen, D., and Vicuna, R. (1994). Isoenzymes of manganese-dependent peroxidase and laccase produced by the lignin-degrading basidiomycete *Ceriporiopsis subvermispora*. *Microbiology* 140, 2691-8.
- 2.- Salas, C., Lobos, S., **Larrain, J.**, Salas, L., Cullen, D., and Vicuna, R. (1995). Properties of laccase isoenzymes produced by the basidiomycete *Ceriporiopsis subvermispora*. *Biotechnol. Appl. Biochem.* 21, 323-33.
3. Urzua, U., Larrondo, L., Lobos, S., **Larrain, J.**, and Vicuna, R. (1995). Oxidation reactions catalyzed by manganese peroxidase isoenzymes from *Ceriporiopsis subvermispora*. *FEBS Lett.* 371, 132-6.
- 4.- Brandan, E., Carey, D.J., **Larrain, J.**, Melo, F., and Campos, A. (1996). Synthesis and processing of glypican during differentiation of skeletal muscle cells. *Eur. J. Cell Biol.* 71, 170-6.
- 5.- **Larrain, J.**, Cizmeci-Smith, G., Troncoso, V., Stahl, R.C., Carey, D.J., and Brandan, E. (1997). Syndecan-1 expression is down-regulated during myoblast terminal differentiation. Modulation by growth factors and retinoic acid. *J. Biol. Chem.* 272, 18418-24.
- 6.- **Larrain, J.**, Alvarez, J., Hassell, J.R., and Brandan, E. (1997). Expression of perlecan, a proteoglycan that binds myogenic inhibitory basic fibroblast growth factor, is down regulated during skeletal muscle differentiation. *Exp. Cell Res.* 234, 405-12.
- 7.- Brandan, E. and **Larrain, J.** (1998). Heparan Sulfate Proteoglycans during terminal skeletal muscle differentiation: possible functions and regulation of their expression. *Basic and Applied Myology* 8, 107-114.
- 8.- **Larrain, J.**, Carey, D.J., and Brandan, E. (1998). Syndecan-1 expression inhibits myoblast differentiation through a basic fibroblast growth factor-dependent mechanism. *J. Biol. Chem.* 273, 32288-96.
- 9.- **Larrain, J.**, Bachiller, D., Lu, B., Agius, E., Piccolo, S., and De Robertis, E.M. (2000) BMP-binding modules in chordin: a model for signalling regulation in the extracellular space. *Development* 127, 821-30.
- 10.- Oelgeschlager, M., **Larrain, J.**, Geissert, D., and De Robertis, E.M. (2000). The evolutionarily conserved BMP-binding protein Twisted gastrulation promotes BMP signalling. *Nature* 405, 757-63.
- 11.- De Robertis, E. M., **Larrain, J.**, Oelgeschlager, M., Wessely, O. (2000). The establishment of Spemann's organizer and patterning of the vertebrate embryo. *Nature Review Genetics* 1, 171-81.
- 12.- Coffinier, C., Tran, U., **Larrain, J.** and De Robertis, E.M. (2001) Neuralin is a novel Chordin-related molecule expresses in the mouse neural plate. *Mechanism of Development.* 100, 119-122.
- 13.- Riquelme, C., **Larrain, J.**, Schonherr, E., Henriquez, J.P., Kresse, H. and Brandan, E. (2001) Antisense inhibition of decorin in myoblasts decreases cell responsiveness to transforming growth factor beta and accelerates skeletal muscle differentiation. *J. Biol. Chem.* 276, 3589-3596.

- 14.- De Robertis, E. M., Wessely, O., Oelgeschlager, M., Brizuela, B., Pera, E., **Larrain, J.**, Abreu, J. and Bachiller, D. (2001) Molecular mechanism of cell-cell signalling by Spemann's organizer. *Int. J. Dev. Biology* 45, 189-197.
- 15.- **Larrain, J.**, Oelgeschlager, M., Keptura, N.I., Reversade, B., Zakin, L. and De Robertis E.M. (2001) Proteolysis of Chordin as a switch for the dual activities of Twisted gastrulation on BMP. *Development* 128, 4439-4447.
- 16.- Garcia-Abreu, J., Coffinier, C., **Larrain, J.**, Oelgeschlager, M. and De Robertis, E.M. (2002) Chordin-like CR domains and the regulation of evolutionary conserved extracellular signaling systems. *Gene* 287, 39-47.
- 17.- **Larrain, J.**, Brown, C. and De Robertis, E. M. (2003) Integrin- α 3 mediates binding of Chordin to the cell surface and promotes its endocytosis. *EMBO Reports* 4, 813-18.
- 18.- Oelgeschläger, M., Reversade, B., **Larrain, J.**, Little, S., Mullins, M.C. and De Robertis, E. M. (2003) The pro-BMP activity of Twisted gastrulation is independent of BMP binding. *Development* 130, 4047-4056.
- 19.- Moreno, M., Muñoz, R., Aroca, F., Labarca, M., Brandan, E. and **Larraín, J.** (2005) Biglycan is a new extracellular component of the Chordin-BMP4 signalling pathway. *EMBO, J.* 24, 1397-1405.
- 20.- Carrasco, H., Olivares, G., Faunes, F., Oliva, C. and **Larraín, J.** (2005) Shh activity is negatively regulated by heparan sulphate proteoglycans. *J. Cell Biochem.* 96 831-838.
- 21.- Muñoz, R., Moreno, M., Oliva, C., Orbenes, C., **Larraín, J.** (2006) Syndecan-4 regulates non-canonical Wnt signaling and is essential for convergent and extension movements in *Xenopus* embryos. *Nat. Cell Biol.* 8, 492-500.
- 22.- Muñoz, R. and Larraín, J. (2006) xSyndecan-4 regulates gastrulation and neural tube closure in *Xenopus* embryos. *Scientific World Journal.* 6, 1298-301.
- 23.- Matthews, H.K., Marchant, L., Carmona-Fontaine, C., Kuriyama, S., **Larraín, J.**, Holt, M.R., Parsons, M. and Mayor, R. (2008) Directional migration of neural crest cell in vivo is regulated by syndecan-4 dependent Rac1 and non-canonical Wnt signalling-dependent RhoA. *Development* 135, 1771-1780.
- 24.- Olivares, G.H., Carrasco, H., Aroca, F., Carvallo, L., Segovia, F. and **Larraín, J.** (2009) Syndecan-1 regulates BMP signaling and dorso-ventral patterning during early *Xenopus* development Syndecan-1 regulates BMP signaling and dorso-ventral patterning during early *Xenopus* development *Dev. Biol.* 329, 338-349.
- 25.- Faunes, F., Sánchez, N., Castellanos, J., Vergara, I., Melo, F. and **Larraín, J.** (2009) Novel transcripts with differential dorsoventral expression in *Xenopus* gastrula identified by SAGE *Genome Biology* 10(2):R15.
- 26.- Contreras, E.G., Gaete, M., Sánchez, N., Carrasco, H. and **Larraín, J.** (2009) Early requirement of Hyaluronan synthase activity for tail regeneration in *Xenopus* tadpoles *Development* 136, 2987-2996.
- 27.- Carvallo, L., Muñoz, R., Bustos, F., Escobedo, N., **Larraín, J.** (2010) Wnt5a/11 induce ubiquitination and degradation of the focal adhesion receptor Syndecan4. *J. Biol. Chem.* 285, 29546-29555
- 28.- Palma, V., Carrasco, H., Reinchisi, G., Olivares, G., Faunes, F. and **Larraín, J.** (2011) Shh activity and localization is regulated by perlecan. *Biol. Res.* 44, 63-67.
- 29.- Faunes, F., Sánchez, N., Moreno, M., Olivares, G., Lee-Liu, D., Almonacid, L., Slater, A., Norambuena, T., Taft, R., Mattick, J., Melo, F. and **Larrain, J.** (2011) Regulated expression of transposable elements in neural tissues during *Xenopus* development. *PLoS One* 6, e22569.
- 30.- Faunes, F., Lee-Liu, D. and **Larrain, J.** (2011) Expression of DNA transposable elements during nervous system development: A discussion about its possible functions. *Mobile Genet. Elements* 1, 296-300.
- 31.- Faunes, F., Almonacid, L., Melo, F., and **Larrain, J.** (2012) Characterization of small RNAs in *X. tropicalis* gastrulae. *Genesis* (doi: 10.1002/dvg.22012)
- 32.- Gaete, M., Muñoz, R., Sánchez, N., Tampe, R., Moreno, M., Contreras, E., Lee-Liu, D. and **Larraín, J.** (2012) Spinal cord regeneration in *Xenopus* tadpoles proceeds through activation of Sox2 positive cells. *Neural Dev.* 7, 13.
- 33.- Escobedo, N., Contreras, O., Muñoz, R., Fariás M., Carrasco, H., Hill C., Tran, U., Wessely O., Copp A.J. and **Larraín, J.** (2013) Syndecan 4 interacts with Vangl2 to regulate neural tube closure and planar cell polarity. *Development* 140, 3008-3017.
- 34.- Lee-Liu, D., Edwards-Faret, G., Tapia, V. and **Larraín, J.** (2013) Spinal Cord Regeneration: Lessons for Mammals from Non-Mammalian Vertebrates *Genesis* 51, 529-44.

- 35.- Astudillo, P., Carrasco, H. and **Larraín, J.** (2014) Syndecan-4 inhibits Wnt/ β -catenin signaling through regulation of Low-Density Lipoprotein receptor-related protein (LRP6) and R-Spondin 3. *Int. J. Biochem. Cell Biol.* 46, 103-112.
- 36.- Astudillo, P. and **Larrain, J.** Wnt signaling and cell-matrix adhesion. (2014) *Current Molecular Medicine* 14, 209-220.
- 37.- Lee-Liu, D., Moreno, M., Almonacid, L.I., Tapia, V.S., Muñoz, R., von Marees, J., Gaete, M., Melo, F. and **Larraín, J.** (2014) Genome-wide expression profile of the response to spinal cord injury in *Xenopus laevis* reveals extensive differences between regenerative and non-regenerative stages. *Neural Dev.* 9, 12
- 38.- Muñoz R, Edwards-Faret G, Moreno M, Zuñiga N, Cline H, Larraín J. (2015) Regeneration of *Xenopus laevis* spinal cord requires Sox2/3 expressing cells. *Developmental Biology*. In press

Books, Chapters

- 1.- Lee-Liu, D., Faunes, D., Almonacid, L., Melo, F. and **Larrain, J.** (2012) Transcriptomics Using next Generation Sequencing Technologies. *Methods Mol. Biol.* 917, 293-317.
- 2.- Moreno, M., Tapia, K. and **Larrain, J.** (2014) Neural regeneration in *Xenopus* tadpoles during metamorphosis. *Xenopus development*. Life Sciences Book, Wiley-Blackwell (in press)

D. Research Support as PI (last ten years)

1. Funding Agency FONDECYT/CONICYT 3/15/2014-3/14/2017
1141162 Larrain (PI)
Title: Role of Stat3 signaling in spinal cord regeneration
Goal of the funded grant: To study the role of JAK/STAT signaling in spinal cord regeneration in *Xenopus*
2. Funding Agency ICGEB, Trieste Italy 3/15/2014-3/14/2017
CRP/CHI13-01 Larrain (PI)
Title: Role of Sox2+ ependymal cells in spinal cord regeneration in *Xenopus*
Goal of the funded grant: Characterize the activation and fate of sox2 cells in response to injury
3. Funding Agency Millenium Scientific Initiative 2014-2016
RC12003 Larrain (Senior Scientist)
Title: Millenium Nucleus for Regenerative Biology
Goal of the funded grant: To establish *Xenopus* as a model system to study the cellular and genetic mechanism of spinal cord regeneration
4. Funding Agency CONICYT 2013-2017
PFB12/2007 Larrain (Senior Scientist)
Title: Center for Aging and Regeneration
Goal of the funded grant: To establish *Xenopus* as a model system to study the cellular and genetic mechanism of spinal cord regeneration
5. Funding Agency Millenium Scientific Initiative 2011-2013
RC12003 Larrain (Director)
Title: Millenium Nucleus for Regenerative Biology
Goal of the funded grant: To establish *Xenopus* as a model system to study the cellular and genetic mechanism of spinal cord regeneration
6. Funding Agency FONDECYT/CONICYT 3/15/2010-3/14/2013
1100471 Larrain (PI)
Title: Function of Syndecan-4 and beta 1 integrin in Wnt signaling and early vertebrate development

Thesis title: Función de las células GFAP+ en la regeneración de la médula espinal de *Xenopus laevis*

Name: Pablo Astudillo 2013
Program: Biología Celular Molecular, PUC
Thesis title: Función de Sindecán-4 y Fibronectina en la Regulación de la vía WNT/ β -Catenina

Name: Noelia Escobedo 2012
Program: Biología Celular Molecular, PUC
Thesis title: "Expression and function of Syndecan-4 during mouse development"

Name: Marcia Gaete 2010
Program: Ciencias Médicas, U. de Chile
Thesis title: Función de SOX2 en la regeneración de la médula espinal de *Xenopus laevis*

Name: Rosana Muñoz 2009
Program: Biología Celular Molecular, PUC
Thesis title: La vía de señalización Wnt/PCP regula los niveles de xSindecán 4 en el mesodermo dorsal del embrión de *Xenopus laevis*

Name: Fernando Faunes 2009
Program: Biología Celular Molecular, PUC
Thesis title: Identificación de nuevos genes involucrados en el establecimiento del patrón dorso-ventral de *Xenopus* mediante SAGE.

Name: Gonzalo Olivares 2008
Program: Biología Celular Molecular, PUC
Thesis title: xSindecán-1 participa en el establecimiento del eje dorso-ventral en embriones de *Xenopus laevis* modulando la señalización por BMP4 a través de un mecanismo dependiente de chordin.

Name: Mauricio Moreno 2006
Program: Biología Celular Molecular, PUC
Thesis title: Biglicán es un nuevo antagonista extracelular en la vía de señalización chordin-BMP4 en embriones de *Xenopus laevis*.

Postdocs

Cecilia López, Argentinian 2009-2011

Loreto Carvallo Chilean 2007-2009