

CURRICULUM VITAE

Name: Juan Carlos Sáez, Ph.D.
Birthday: February 2, 1956
Citizenship: Chilean.

DEGREES: -Ph.D. in Neuroscience, Albert Einstein Coll. Med., Yeshiva Univ., Bronx, N.Y. (1983-1986). Biochemist (equivalent to MS in Biochemistry), Univ. de Concepción, Concepción. Chile (1974-1979).

ACADEMIC POSITIONS:

Nov. 2004-present: Professor, Depto. Fisiología, Pontificia Univ. Católica de Chile, Santiago, Chile.

Sept. 2007-present. Visiting Professor, Dept. Neuroscience, Albert Einstein Coll. Medicine, Yeshiva Univ., Bronx, N.Y.

July 1994-Nov. 2004: Associate Professor, Depto. Fisiología, Pontificia Universidad Católica de Chile, Santiago, Chile.

Nov.1994-2007: Visiting Associate Professor, Dept. Neuroscience., Albert Einstein Coll. Med., Yeshiva Univ., Bronx, N.Y.

Feb. 1993-July 1994: Assistant Professor, Depto. Fisiología, Pontificia Univ. Católica de Chile, Santiago, Chile.

Dec. 1989-Feb. 1993: Assistant Professor, Dept. Neuroscience, Albert Einstein Coll. of Med., Yeshiva Univ., Bronx, N.Y.

Sept. 1987-Dec. 1989: Instructor, Dept. Neuroscience, Albert Einstein Coll. Med., Yeshiva Univ., Bronx, N.Y.

1986-1987: Post-doctoral fellow, Dept. Neuroscience., Albert Einstein Coll. Med., Yeshiva Univ., Bronx, N.Y.

Oct., 1979 - August, 1983: Instructor, Depto. Fisiología, Univ. de Concepción, Chile.

ADMINISTRATIVE POSITIONS:

January 2013-present: Committee member of the PhD program in Neuroscience. Pontificia Univ. Católica de Chile, Santiago, Chile.

March 2003-present: Director of the Ph.D. Program in Physiological Sciences. Pontificia Univ. Católica de Chile, Santiago, Chile.

2009-present. Subdirector of the Center for Neuroscience, Pontificia Universidad Católica de Chile.

AWARDS AND DISTINCTIONS:

-2014- Winner of the VII Concurso de Patentamiento UC. "Identificación, composiciones y usos terapéuticos de heterocíclicos bloqueadores de hemicanales formados por conexinas"

-2010, Winner of the II Competition of Intellectual Property, Pontificia Universidad Católica de Chile

-2008, Chilean **Scopus price** given by Elsevier Editorial. The Chilean Scientist with the highest productivity and impact in Pharmacology, Biochemistry, Genetics and Molecular Biology.

-1993, Glaxo Research Institute. Fellowship Award.

-1987, Grass Fellowship to work as independent Scientist at the Marine Biological Laboratory.

-1980, Best Thesis work of the year given by the Society of Pharmacists and Biochemists of Concepción.

MEMBERSHIP OF SCIENTIFIC SOCIETIES: 1. Latin American Biophysical Society (1985-

present). **2.** Biophysical Society (1990-1994). **3.** ASCB (1990-present). **4.** Chilean Society for Physiology (1994-present). **5.** Chilean Society for Biology (1994-present). **6.** Chilean Society for Cell Biology (1994-present). **7.** Chilean Society for Neuroscience (2003-present).

AD HOC EVALUATOR OF SCIENTIFIC JOURNALS:

Proceedings of the Academy of Science; Journal of Biological Chemistry; Journal of Cell Biology, Cardiovascular Research; Journal of Cell Physiology; American Journal of Physiology; Journal of Cell Science; Journal of Cell Biochemistry; Journal of Biological Chemistry; Journal of Immunology; FASEB J; BBA; BBRC; Journal of Neuroscience; Neuroscience; Journal of Neurochemistry; Glia; Journal of Neuroscience Research; Cell Calcium; Hepatology; Experimental Lung Res; Experimental Neurology.; Glia, Cell Adhesion and Communication; Journal of Cellular and Molecular Medicine; Journal of Experimental Medicine; Cardiovascular Research and Microvascular Res.

ORGANIZER OF SCIENTIFIC EVENTS

- 2015. Internationa Gap Junction Conference 2015 in Valparaiso-Chile.
- 2015. Workshop Biophysic of hemichannels and gap junction channels: A theoretical and practical training. Santiago Valparaiso, 2015.
- 2013. Symposium, co-organizer with Dr. AD Martinez: "Role and regulation of channels and hemichannels formed by connexin or pannexins in the nervous system" Reunión Annual de la Sociedad de Neurociencias de Chile, Valparaíso, 2013.
- 2013. Symposium, co-organizer with AD. Martinez: "Cell Membrane Channels Made by Connexins or Pannexins are Key Players in Genetic and Acquired Diseases" presented during the XXVII Annual Meeting of the Chilean Society for Cell Biology. November, Pucón, 2013.
- 2012. Workshop organizer: "Structure and function of connexin, pannexin and other cellular transporters. October 20-30, 2012, Valparaíso.
- 2012. Symposium organizer: "Intercellular communication via pannexin- and connexin-based channels in health and disease". Chilean meeting of the Society for Cell Biology. October, 2012.
- 2011. Symposium organizer. "Regulation of glial connexin channels: from the nucleus to the membrane". Chilean congress of the Society for Physiology.
- 2009. Mini Symposium Organizer. "El SIDA como una enfermedad neurodegenerative". Abril, 2009.
- 2006. Sympisium Organizer. "Gap junction hemichannels and mechanisms that regulate their functional state under physiological and pathological conditions" 2° Congress of the Chilean Society for Neuroscience, September, Curicó, Chile.
- 2006. Workshop Co-organizer with Dr. M. Villalón. "Regulation and function of free intracellular Ca^{2+} and intercellular Ca^{2+} waves", January, Santiago.
- 2003. Simposium Organizer. "Gap junction in the inflammatory response" del V Congreso Iberoamericano de Biofísica. Rio de Janeiro, Brasil.
- 2001. Workshop Organizer. "Chemical and electrical synapsis: theoretical and practical advances". Pontificia Univ. Católica de Chile, Santiago, Chile.
- 1995. Workshop Co-organizer with Dr. Ramón Latorre . "From Ion Channels to Cell-to-Cell Conversations". CECS, Santiago, Chile.

REVIEW EDITOR

Frontiers in Neuroscience-Neuroenergetics
Frontiers in Physiology

PRESENTATIONS TO SCIENTIFIC MEETINGS

345 abstracts have been presented in different Chilean, South American and other International Meeting in USA, Canada, India, Japan, China and Europe.

PUBLICATIONS (ISI)

145. Harcha PA, Vargas A, Yi C, Koulakoff AA, Giaume C, **Sáez JC**. Hemichannels Are Required for Amyloid β -Peptide-Induced Degranulation and Are Activated in Brain Mast Cells of APP^{swe}/PS1^{dE9} Mice. *J Neurosci*. 2015 Jun 24;35(25):9526-38

144. **Sáez JC**, Cisterna BA, Vargas A, Cardozo CP. Regulation of pannexin and connexin channels and their functional role in skeletal muscles. *Cellular and Molecular Life Sciences*. (in press) (2015).

143. Orellana JA, Moraga-Amaro R, Díaz-Galarce R, Rojas S, Maturana CJ, Stehberg J, **Sáez JC**. Restraint stress increases hemichannel activity in hippocampal glial cells and neurons.

Front Cell Neurosci. 2015 Apr 2;9:102. doi: 10.3389/fncel.2015.00102. eCollection 2015.

142. Riquelme MA, Cea LC, Vega JL, Puebla C, Vargas AA, Shoji KF, Subiabre M, **Sáez JC**. Pannexin channels mediate the acquisition of myogenic commitment in C₂C₁₂ reserve cells promoted by P2 receptor activation. *Frontiers in Cell Dev Biol* 06 May 2015 doi: 10.3389/fcell.2015.00025

141. Salas D, Puebla C, Lampe PD, Lavandero S, **Sáez JC**. Role of Akt and Ca₂₊ on cell permeabilization via connexin43 hemichannels induced by metabolic inhibition. *Biochim Biophys Acta*. 2015 Mar 14. pii: S0925-4439(15)00068-X.

140. García I, Maripillán J, Jara O, Ceriani R, Palacios-Muñoz A, Ramachandran J, Olivero P, Perez-Acle T, González C, **Sáez JC**, Contreras JE, Martínez AD. Keratitis-Ichthyosis-Deafness syndrome-associated Cx26 mutants produce non-functional gap junctions but hyperactive hemichannels when co-expressed with wild type Cx43. *The Journal of Investigative Dermatology* Jan 27. doi: 10.1038/jid.2015.20. [Epub ahead of print].(2015).

139. Rovegno M, Soto PA, Sáez PJ, Naus C, **Sáez JC**, von Bernhardt R. ATP released via Connexin 43 hemichannels and P2 receptors mediate secondary cellular damage spread from the trauma zone to distal zones in astrocyte monolayers. *Glia* 63(7):1185-1199 2015.

138. Cisterna BA, Cardozo C, Sáez JC. Neuronal involvement in muscular atrophy. *Frontiers in Cell. Neurosci*. 2014 Dec 10;8:405. doi: 10.3389/fncel.2014.00405. eCollection 2014..

137. Ardiles AO, Flores-Muñoz C, Toro-Ayala G, Cárdenas AM, Palacios AG, Muñoz P, **Sáez JC**, Fuenzalida M, Martínez AD. Pannexin 1 regulates the bidirectional hippocampal synaptic plasticity in the adult mice. *Frontiers in Cell. Neurosci*. 2014 Oct 15;8:326. doi: 10.3389/fncel.2014.00326. eCollection 2014.

136. Figueroa V, Retamal MA, Cea LA, Salas JD, Vargas AA, Verdugo CA, Jara O, Martínez AD, **Sáez JC**. Gentamicin reversible blocks connexin hemichannels and does not affect gap junction channels. *Frontiers Cell. Neurosci*. 2014 Sep 4;8:265. doi: 10.3389/fncel.2014.00265. eCollection 2014.

134. Sáez P., Shoji KF, Aguirre A, **Sáez JC**. Regulation of hemichannels and gap junction channels by cytokines in antigen presenting cells. **Mediators of Inflammation** (in press) (2014).
133. Le HT, Sin WC, Lozinsky S, Bechberger J, Vega JL, Guo XQ, **Sáez JC**, Naus CC. Gap junction intercellular communication mediated by connexin43 in astrocytes is essential for their resistance to oxidative stress. **J Biol Chem**. 289:1345-1354 (2014).
132. Momboisse F, Olivares MJ, Baéz X, Guerra MJ, Flores-Muñoz C, **Sáez JC**, Martínez AD, Cárdenas AM. Pannexin 1 channels: new actors in the regulation of catecholamine release from adrenal chromaffin cells. **Frontiers Cell. Neurosci**. 2014 Sep 4;8:270. doi: 10.3389/fncel.2014.00270. eCollection 2014..
131. Araya-Secchi R, Kang S-G, Huynh T, Bernardin A, Martinez AD, **Sáez JC**, Pérez-Acle T, Zhou R. Characterization of a novel water pocket inside the human Cx26 hemi-channel structure. *Biophys. J.* (in press) (2014).
130. Retamal MA, Alcayaga J, Bultynck G, Leybaert L, Sáez PJ, Fernández R, LeónLE, **Sáez JC**. The opening of connexin and pannexin hemichannels increases the excitability of nodose ganglion sensory neurons. *Frontiers in Cellular Neurosci*. Jun 20;8:158. doi: 10.3389/fncel.2014.00158. eCollection 2014.
129. Cea LC, Riquelme MA, Vargas AA, Urrutia C, **Sáez JC**. Pannexin 1 channels in skeletal muscles. **Frontier in Membr. Physiol. Biophys.**. Apr 11;5:139. doi: 10.3389/fphys.2014.00139. eCollection 2014.
128. **Sáez JC**, Leybaert L. Hunting for connexin hemichannels. *FEBS Letters* 588: 1205-1211 (2014).
127. Shoji KF, Sáez PJ, Harcha PA, Aguila HL, **Sáez JC**. Pannexin1 channels act downstream of P2X₇ receptors in ATP-induced murine T cell death. **Channels** 8: 1-15 2014.
126. Hernández-Salinas R, Vielma AZ, Arismendi MN, Boric MP, Sáez JC, Velarde V. Boldine prevents renal alterations in diabetic rats. **J Diabetes Res**. 2013;2013:593672. doi: 10.1155/2013/593672. Epub 2013 Dec 12.
125. Orellana JA, **Sáez JC**, Bennett MVL, Berman JW, Morgello S, Eugenin EA. HIV increases the release of dickkopf-1 (DKK1) protein from human astrocytes by a Cx43 hemichannel-dependent mechanism. **J. Neurochem**. 128(5):752-763 (2014).
124. Giaume C, Leybaert L, Naus CC, **Sáez JC**. Connexin and pannexin hemichannels in brain glial cells: properties, pharmacology and roles. **Frontiers Pharmacol.**. 2013 Jul 17;4:88. doi: 10.3389/fphar.2013.00088. eCollection 2013.
123. Cea LC, Cisterna BA, Puebla C, Frank M, Figueroa XF, Cardozo C, Willecke K, Latorre R, **Sáez JC**. *De novo* expression of connexin hemichannels in denervated fast skeletal muscles leads to atrophy. **Proc. Natl. Acad. Sci. USA** 110:16229-16234 (2013).
122. Johnson RG, Sáez JC. We've Had Important Advances in the Connexin/Pannexin Field, Yet There Is Still Much to Do. **Neuropharmacology**. 2013 Aug 19. doi:pii: S0028-3908(13)00368-7.
121. Vega JL, Subiabre M, Figueroa F, Schalper KA, Osorio L, González Sáez JC. Role of gap junctions and hemichannels in parasitic infections. **BioMed Res Int**. 2013;2013:589130. doi: 10.1155/2013/589130.
120. Aguirre A, Maturana CJ, Harcha PA, Sáez JC. Possible Involvement of TLRs and Hemichannels in Stress-Induced CNS Dysfunction via Mastocytes, and Glia Activation. **Mediators Inflamm**. 2013;2013:893521. doi: 10.1155/2013/893521. Epub 2013 Jul 2.
119. Sáez PJ, Orellana JA, Vega-Riveros N, Figueroa VA, Hernández DE, Castro JF, Klein AD, Jiang JX, Zanolungo S, and **Sáez JC**. Disruption in Connexin-based Communication is Associated with Intracellular

- Ca²⁺ Signal Alterations in Astrocytes from Niemann-Pick type C Mice. **PLOS One** (in press) 2013 Aug 15;8(8):e71361. doi: 10.1371/journal.pone.0071361. PMID:23977027 [PubMed - in process]
- 118.** Kozoriz MG, Lai S, Vega JL, Sáez JC, Sin WC, Bechberger JF, and Naus CC. Cerebral ischemic injury is enhanced in a model of oculodentodigital dysplasia. **Neuropharmacology** 2013 May 30. doi:pii: S0028-3908(13)00212-8.
- 117.** Sáez P.J., Shoji K.F., Retamal M.A., Harcha P.A., Ramírez G., Jiang J.X., von Bernhardt R. and Sáez J.C. ATP is required and advances cytokine-induced gap junction formation in microglia *in vitro*. **Mediators of Inflammation** 2013;2013:216402. Epub 2013 Apr 23.
- 116.** Figueroa X.F., Lillo M.A., Gaete P.S., Riquelme M. and Sáez J.C. Diffusion of nitric oxide across cell membranes of the vascular wall requires specific connexin-based channels. **Neuropharmacology** **75:471-478** (2013).
- 115.** Riquelme MA, Cea LA, Vega JL, Boric MP, Monyer H, Bennett MV, Frank M, Willecke K, Sáez J.C.. The extracellular ATP required for potentiation of the adult skeletal muscle contraction is released through pannexin 1 based channels. **Neuropharmacology** **75:594-603** (2013).
- 114.** Orellana J.A. Williams D.W., Sáez J.C., Berman J.W. and Eugeni E.A. Pannexin1 hemichannels are critical for HIV infection of human primary CD4⁺ T lymphocytes. **J. Leuk. Biol.** 94(3):399-407 (2013).
- 113.** Aguirre, A., Shoji, K.F., Sáez, J.C., Henríquez, M. and Quest, A.F.G. FasL-triggered death of Jurkat cells requires caspase 8-induced, ATP-dependent cross-talk between Fas and P2X₇ receptors. **J. Cell Physiol.** 228: 485-493 (2013).
- 112.** Bennett MV, Garré JM, Orellana JA, Bukauskas FF, Nedergaard M, Sáez JC. Connexin and pannexin hemichannels in inflammatory responses of glia and neurons. **Brain Res.** 1487:3-15 (2012).
- 112.** Fiori, M.C., Figueroa, V., Zoghbi, M.E., Saéz, J.C., Reuss, L. and Altenberg, G.A. Calcium transport through purified connexin 26 hemichannels. **J. Biol. Chem.** 287:40826-40834 (2012).
- 111.** Figueroa V., Sáez P.J., Salas J.D., Jara O., Martínez A.D., Sáez J.C. and Retamal M.A. Linoleic acid induces opening of connexin26 hemichannels through a PI3K/Akt/Ca²⁺-dependent pathway. **BBA-Biomembranes** 1828:1169-1179 (2012)
- 110.** Cea L.A., Riquelme M.A., Cisterna B., Puebla C., Vega J.L., Rovigno M. and Sáez J.C. Connexin- and pannexin-based channels in normal skeletal muscles and their possible role in muscle atrophy. **J. Membr. Biol.** 245: 423-436 (2012).
- 109.** Jara, O., Acuña, R., García, I., Miripillán, J., Figueroa, V., Sáez, J.V.C. Araya, R. Lagos, C. Pérez-Acle, T., Berthoud, V.M., Beyer, E.C and Martínez, A.D. Critical role of the first transmembrane domain of Cx26 in regulating oligomerization and function. **Mol. Biol. Cell** 23: 3299-3311 (2012).
- 108.** Stehberg J., Moraga-Amaro R., Salazar C., Becerra A., Echeverría C., Orellana J.A., Bultynck G., Leybaert L., Simon F., Sáez J.C. and Retamal M.A.. Release of gliotransmitters through astroglial connexin 43 hemichannels is necessary for fear memory consolidation in the basolateral amygdala.. **FASEB J.** 26: 3649-3657 (2012).
- 107.** Pérez-Armentaris E.M., Esparza-Aguilar, Coronel-Cruz C., Cruz-Miguel L., Pinzon-Estrada E., Racaño-Camacho E., Zacarias-Climaco G., Fernández P., Espinosa A.M., Becker I., Sáez J.C., Berumen J., Pérez-Palacios G. Connexins 26, 32 and 36 are expressed in a cell-specific manner at the end of the secondary transition of fetal mouse pancreas development and increase during fetal and perinatal life. **Anat. Rec. (Hoboken)** 295:980-990 (2012).
- 106.** Orellana JA, Sánchez HA, Schalper KA, Figueroa V, Sáez JC. Regulation of intercellular calcium signaling through calcium interactions with connexin-based channels. **Adv. Exp. Med. Biol.** 740:777-794 (2012).
- 105.** Eugeni E. A., Basilio D., Sáez J. C., Orellana Juan A., Raine C.S., Bukauskas F, Bennett M.V.L.

and Berman J.W. The role of gap junction channels during physiologic and pathologic conditions of the human nervous system. **J. Neuroimmune Pharmacol.** 7:499-518 (2012).

104. Orellana, J.A., von Bernhardt R. Giaume C. and **Sáez J.C.** Glial hemichannels and their involvement in aging and neurodegenerative diseases. **Rev. Neurosci.** 23:163-177 (2012).

103. Schalper KA, Riquelme MA, Brañes MC, Martínez AD, Vega JL, Berthoud VM, Bennett MV, **Sáez J.C.** Modulation of gap junction channels and hemichannels by growth factors. **Mol. Biosyst.** 8:685-698 (2012).

102 Giaume C, Orellana JA, Abudara V, Sáez JC. Connexin-based channels in astrocytes: how to study their properties. **Methods Mol. Biol.** 814:283-303 (2012).

101. Koulakoff, A. Mei, X., Orellana, J.A., **Sáez, J.C.**, Giaume, C. Glial connexin expression and function in the context of Alzheimer's disease. **BBA – Biomembranes** 1818(8):2048-57 (2012).

100. Rovegno M, Soto PA, **Sáez J.C.**, von Bernhardt R. Biological mechanisms involved in the spread of traumatic brain damage. **Med Intensiva.** 36:37-44 (2012).

99. Orellana J. A., Sáez P. J., Cortés-Campos C., Elizondo R.J., Shoji K.F., Contreras-Duarte Susana, Figueroa V., Velarde V., Jiang J. X. Nualart F., **Sáez J.C.** and García M.A.. Glucose increases intracellular free Ca^{2+} in tanycytes via ATP released through connexin 43 hemichannels . **Glia** 60:53-68 (2012).

98. Orellana J.A., Díaz E., Schalper, K.A., Aníbal A. Vargas, Michael V. L. Bennett and **Sáez J.C.** Cation permeation through connexin 43 hemichannels is cooperative, competitive and saturable with parameters depending on the permeant species. **Biochem. Biophys. Res. Comm.** 409:603-609 (2011).

97. Orellana JA, Froger N, Ezan P, Jiang JX, Bennett MV, Naus CC, Giaume C, **Sáez J.C.** ATP and glutamate hemichannels mediate neuronal death through released via astroglial connexin 43 activation of pannexin 1 hemichannels. **J Neurochem.** 118:826-40 (2011).

96. Orellana J.A., Figueroa X.F., Sánchez H.A., Contreras-Duarte S., Velarde V., **Sáez J.C.** Hemichannels in the Neurovascular Unit and White Matter Under Normal and Inflamed Conditions. **CNS Neurol Disord Drug Targets.** 10:404-414 (2011).

95. Garré, J.M., Retamal, M.A., Cassina, P., Barbeito, L., Bukauskas, F.F., **Sáez, J.C.**, Bennett, M.V.L. and Abudara, V. FGF -1 induces ATP release from spinal astrocytes in culture and opens pannexin and connexin hemichannels. **Proc. Natl. Acad. Sci. USA** 107:22659-22664 (2010).

94 Schalper K.A., Lee S-C; Altenberg G.A., Nathanson M.H. and **Sáez J.C.** Connexin43 is a pH-gated plasma membrane calcium channel. **Am. J. Physiol.** 299:C1504-C1515. (2010).

93. **Sáez, J.C.**, Schalper, K. A., Retamal, M.A., Orellana, J.A, Shoji, K.F., and Bennett, M.V.L. Cell membrane permeabilization via connexin-hemichannels in living and dying cells. **Exp. Cell Res.** 316: 2377-2389 (2010).

92. Froger N., Orellana J.A., Amigou E., Kozoriz M.G., Naus C.C, **Sáez J.C.** and Giaume C. Inhibition of Cx43 hemichannels activated by pro-inflammatory treatment exhibited a neuroprotective effect against NMDA excitotoxicity. **Mol. Cell. Neurosci.** 45: 37-46 (2010).

91. Orellana, J.A., Hernández, D.E., Ezan, P., Velarde, V., Bennett, M.V.L. Giaume, C., and **Sáez, J.C.** Hypoxia in high glucose followed by reoxygenation in normal glucose reduces the viability of cortical astrocytes through increased permeability of connexin 43 hemichannels. **Glia** 58: 329-343 (2010).

90. Froger, N., Orellana, J.A., Ezan, P. Amigou, E., Sáez, J.C. and Giaume C. Cannabinoids prevent the opposite regulation of astroglial connexin43 hemichannels and gap junction channels induced by pro-inflammatory treatments. **J. Neurochem.** 111:1383-1397 (2009).

89. Buvinic S, Almarza G, Bustamante M, Casas M, López J, Riquelme M, Sáez JC, Huidobro-Toro JP, Jaimovich E. ATP released by electrical stimuli elicits calcium transients and gene expression in skeletal muscle. **J. Biol. Chem.** 284:34490-34505 (2009).

88. Sánchez H.A., Orellana J.A., Verselis V.K. and **Sáez J.C.** Metabolic inhibition increases the activity of connexin-32 hemichannels which are permeable to Ca^{2+} . **Am. J. Physiol.** 297:C665-78 (2009).

87. Elgueta, R., Tobar, J.A., Shoji, K.F., De Calisto, J., Kalergis, A.M., Bono, M.R., Roseblatt, M. and **Sáez, J.C.** Gap junctions at the dendritic cell-T cell Interface are key elements for antigen-dependent T cells activation. **J. Immunol.** 183:277-284 (2009).
86. Schalper, K.A., Orellana, J.A., Berthoud, V.M. and **Sáez, J.C.** Dysfunctions of the diffusional membrane pathways mediated by hemichannels in inherited and acquired human diseases. **Current Opinion in Pharmacology** 7:486-505 (2009).
85. Orellana, J.A., Sáez, P.J., Shoji, K.F., Schalper, K.A., Palacios-Prado, N., Velarde, V., Giaume, C., Bennett, M.V.L. and **Sáez, J.C.** Modulation of brain hemichannels and gap junction channels by pro-inflammatory agents and their possible role in neuro-degeneration. **Antioxidants & Redox Signaling** 11: 369-99 (2009).
84. Loreto P. Véliz, González F.G., Duling B.R., **Sáez J.C.**, Boric M.P. Functional role of gap junctions in cytokine-induced leukocyte adhesion and transmigration *in vivo*. *Am. J. Physiol.* 295:H1056-H1066 (2008).
83. Schalper, K.A., Palacios-Prado, N. Orellana, J.A., Sáez, J.C. Currently used methods for identification and characterization of hemichannels. **Cell Commun Adhes.** 15:207-218 (2008).
82. Schalper, K.A., Palacios-Prado, N., Retamal, M.A., Shoji, K.F., Martínez A.D. and **Sáez, J.C.** The connexin hemichannel composition determines the FGF-1-induced membrane permeability and free $[Ca^{2+}]_i$ responses. **Mol. Biol. Cell.** 19: 3501–3513 (2008).
81. **Sáez, J.C.** Astrocytes as connexin-dependent signaling cells for local blood flow regulation. **Am J Physiol.** 294:H586-H587 (2008).
80. Retamal, M.A., Froger, N., Palacios-Prado, N., Ezan, P., Sáez, P. J., **Sáez, J.C.** and Giaume, C. Cx43 hemichannels and gap junction channels in astrocytes are oppositely regulated by pro-inflammatory cytokines released from activated microglia. **J. Neurosci.** 27: 13781-13792 (2007).
79. Eugenin E.A., González, H.E., Sánchez, H.A., Brañes, M.C., **Sáez, J.C.** Inflammatory conditions induce gap junctional communication between rat Kupffer cells both *in vivo* and *in vitro*. **Cell. Immunol.** 247:103-110 (2007).
78. Retamal, M.A., Schalper, K.A., Shoji, K.J., Orellana, J.A., Bennett, M.V.L. and **Sáez, J.C.** Possible involvement of different connexin43 domains in plasma membrane permeabilization induced by ischemia-reperfusion. **J. Membr. Biol.** 218:49-63 (2007).
77. Retamal, M.A., Schalper, K.A., Shoji, K.F., Bukauskas, F.F., Bennett, M.V.L. and **Sáez, J.C.** Opening of connexin 43 hemichannels is increased by lowering intracellular redox potential. **Proc. Natl. Acad. Sci. USA** 104: 8322-8327 (2007).
76. Mendoza-Naranjo A., Sáez P.J., Johansson C.C., Ramírez M., Mandaković D., Pereda C., López M.N., Kiessling R., **Sáez J.C.**, Salazar-Onfray F. Functional gap junctions facilitate melanoma antigen transfer and cross-presentation between human dendritic cells. **J. Immunol.** 178: 6949-6957 (2007).
75. Corvalán, L., Araya, R., Brañes, M.C., Sáez, P.J., Kalergis, A.M. Tobar, J.A., Theis, M. Willecke, K., and **Sáez, J.C.** Injury of skeletal muscle and specific cytokines induce the expression of gap junction channels in mouse dendritic cells. **J. Cell. Physiol.** 211: 649-660 (2007).
74. Orellana, J. A., Palacios-Prado, N. and **Sáez, J.C.** Chlorpromazine reduces the intercellular communication via gap junctions in mammalian cells. **Toxicol. Appl. Pharmacol.** 213: 187-197 (2006).
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13. Spray, D.C., Sáez, J.C., Hertzberg, E.L. and Dermietzel, R. Gap Junctions in Liver: Composition, Function and Regulation. In: The Liver: Biology and Pathobiology (Eds, I.M. Arias, W.B. Jakoby, H. Popper, D. Schachter and D.A. Shafritz), Raven Press Ltd., New York, Third edition, 951-967 (1994).

12. Spray, D.C., Bai, S., Burk, R.D. and Sáez, J.C. Regulation and Function of Liver Gap Junctions and their Genes. In: Progress in Liver Diseases (Boyer, J.L. and Ockner, R.K., eds.) W.B. Saunders Co. vol. 12. pp. 1-18 (1994).

11. Sáez, J.C., V.M. Berthoud, A.P. Moreno and Spray D.C. Gap junctions: Multiplicity of controls in differentiated and undifferentiated cells and possible functional implications. In: Advances in Second Messenger and Phosphoprotein Research (Shenolikar, S. and Nairn, A.C., eds.) Vol. 27. Raven Press, New York., pp. 257-262 (1993).

10. Sáez, J.C., Nairn, A.C., Czernik, A.J., Spray, D.C. and Hertzberg, E.L. Rat heart connexin43: regulation by phosphorylation in heart. Gap Junctions. In: Progress in Cell Research (Hall, J.E., Zampighi, G.A. and Davis, R.M., eds.), Elsevier Science Publishers. vol. 39, pp. 263-269 (1993).

9. Berthoud, V.M., Ledbetter, M.L.S., Hertzberg, E.L. and Sáez, J.C. Regulation of gap junctions by cell contact and phosphorylation in MDCK cells. Gap Junctions. In: Progress in Cell Research (Hall, J.E., Zampighi, G.A. and Davis, R.M., eds.), vol. 3. Elsevier Science Publishers. pp. 257-262 (1993).

8. Sáez, J.C. and Spray, D.C. Cell Junctions. In: Encyclopedia of Human Biology. Academic Press, Inc. Pp.267-278 (1991).

7. Sáez, J.C., Bennett, M.V.L. and Spray, D.C. Hepatocyte gap junctions: Metabolic regulation and possible

role in liver metabolism. In: Transduction in Biological Systems. (Hidalgo, C., Bacigalupo, J. Jaimovich, E. and Vergara, J., eds.) Plenum. Publ. Co., NY. pp. 231-243 (1990).

6. Spray, D.C., Sáez, J.C. and Hertzberg, E.L. Junctions between hepatocytes: Structural and regulatory factors. In: The Liver: Biology and Pathobiology (Eds, I.M. Arias, W.B. Jakoby, H. Popper, D. Schachter and D.A. Shafritz), Raven Press Ltd., New York, Second edition, pp. 851-866 (1988).

5. Spray, D.C. and Sáez, J.C. Agents that regulate gap junctional conductance: Sites of action and specificities. In: Biochemical Regulation of Intercellular Communication. Advances in Modern Environmental Toxicology (Series Editor, Vol.XIV, M.A.Mehlman) pp. 1-27 (1988).

4. Spray, D.C., Sáez, J.C. Burt, J.M., Wantanabe, T., Reid, L.M., Hertzberg, E.L. and Bennett, M.V.L. Gap junctional conductance: multiple sites of regulation. In: Gap junctions. (Modern Cell Biology. (Series Editor Vol. 7, B. Satir) (eds., E.L. Hertzberg and R.G. Johnson) Alan R. Liss., NY, pp.-227-244 (1988).

3. Bennett, M.V.L., Sáez, J.C. and Spray, D.C. Multiplicity of controls of gap junctional communication. *Puerto Rico Health Sci. J.* 7, 126-132 (1988)

2. Fujita, M., Spray, D.C., Choi, H., Sáez, J., Jefferson, D.M., Hertzberg, E., Rosenberg, L.C. and Reid, L.M. Extracellular matrix regulation of cell-cell communication and tissue specific gene expression in primary liver cultures. In: Cellular Endocrinology: Hormonal Control of Embryonic and

Cellular Differentiation. Prog. Clin. Biol. Research. Alan R. Liss, Inc. pp. 333-360 (1986).

1. Kessler, J.A., Spray, D.C., **Sáez, J.C.** and Bennett, M.V.L. Development and regulation of electrotonic coupling between cultured sympathetic neurons. In: Gap Junctions, (Eds., M.V.L. Bennett and D.C. Spray) Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, pp. 231-240 (1985).

SCIENTIFIC LECTURES (INVITED)

49 lectures in different Chilean Universities and Research Institute, Institutions of USA (Yale University, UMDNJ, John Hopkins School of Medicine, NIH, Albert Einstein College of Medicine, University of Chicago and Mayo Clinic) in Mexico (UNAM), Spain (Instituto Ramón y Cajal and Hospital Ramón y Cajal), Brazil (Universidade de Sao Paulo and Instituto de Biofísica de Rio de Janeiro), France (Unité INSERM-Laboratoire de Neurobiologie Pharmacologique, Collège de France), Uruguay (Universidad de la República de Uruguay), Mexico (UNAM), Chile (Universidad de Chile, Universidad de Concepción, Universidad Austral de Chile, Universidad de Santiago de Chile). Univ. de Chile en Valparaíso, Univ. Católica de Valparaíso. Universidad de Chile. Jichi Medical School, Japan; Gunma University, Japan; University of San Antonio, Texas Tech in Lubbock. Down State University, Brooklyn, NY, USA. University of British Columbia, Canada. University of Leuven, Belgium. Barcelona University.

Inaugural Conferences

-Opening lecture of the Academic year. Graduate program in Physiology and Neuroscience. University of Sevilla, Spain, **Descubriendo los hemicanales y sus funciones en el sistema nervioso y tejidos periférico (September 2014).**

-Opening of the Academic Year. Graduate programs of the Faculty of Cell Biology, Universidad de Concepción. **“Una Opinión Personal sobre el Posgrado desde la Vocación al Compromiso País” (March 30, 2012).**

- Opening of the Academic Year. Graduate programs of the Faculty of Health Sciences at the Universidad de Antofagasta. **"La vocación: una experiencia personal en busca de un aporte al servicio del país" (May 9, 2013).**

MENTOR OF UNDERGRADUATE THESIS

- **2013-2014 Angelica Benvenuto**

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- **2011. (Co-mentor with Dr. Xavier Figueroa)** Mauricio A. Lillo. Biochemist, PUC. Involvement hemichannels formed by connexins or pannexins in NO transport across the plasma membrane in the vascular wall.

- **2009.** Anibal Vargas. Lic. Biología, PUC. Characterization of antimycin A as inhibitor of hemichannels formed by connexins.

- **2007-2009. (Co-mentor with Dr. Sergio Lavandero).** Daniela P. Salas. Biochemist, Universidad de Chile. Hemichannels formed by connexins in volume regulation in cardiomyocytes exposed to hypotonic stress.

- **2009.** Paola Soto. Biologist, PUC. Study on channels formed by connexin32 in a cell line derived from oligodendrocytes.

- **2008.** Marlene Arismendi, Industrial Chemist, UTEM, Purification and biological activity of compounds derived from Boldo on channels formed by connexins.

- **2008.** Diego Hernández, Biologist, PUC. Regulation of astroglial and neuronal channels formed by connexins in neurodegenerative processes.
- **2009.** Natalia Vega, Biochemist, PUC. Regulation of cell membrane permeability by phosphorylation of hemichannels formed by connexin43 via protein kinase C (PKC).
- **2008.** Paloma Harcha, Biologist, PUC. D2SC1 cells express functional hemichannels formed by pannexina1.
- **2006.** Ariel Orellana. Biologist, PUC. Acquisition of myogenic commitment of reserve C₂C₁₂ cells requires activation of P2X receptors.
- **2006.** Pablo J. Sáez, Biologist, PUC. ATP and TNF- α induce formation gap junction channels in microglia.
- **2006.** Kenji Shoji, Biologist, PUC. The redox sensor of hemichannels formed by connexin43 is located in the carboxyl terminus of the protein subunit.
- **2005.** Juan Andrés Orellana, Biologist, PUC. Chlorpromazine inhibits the intercellular communication mediated by gap junctions in Gn-11 cells and astrocytes.
- **2005.** Constanza J. Cortés, Biologist, PUC. Opening of Cx43 hemichannels in mediated by oxidative mechanisms in astrocytes”.
- **2005.** Nicolás Palacios, Biologist, PUC. Modulation of the functional state of connexin-based channels by sexual hormones and tamoxifen in a cells line derived from human breast cancer.
- **2002-2003.** Manuel Riquelme-Biochemist, PUC. P2X receptors and connexin-based channels are needed for acquisition of myogenic commitment.
- **1998-1999.** Patricio Orio-Biochemist, Universidad de Chile. Molecular characterization and function gap junctions Express by Peripherals human lymphocytes.
- **1997.** Alejandro Sepúlveda-Biochemist, Univ. Austral de Chile. Gap junctions between antigen presenting cells and T cells: characterization and regulation of connexins.
- **1997.** Eliseo Eugenio-Biochemist, Univ. Austral de Chile. Regulation of glycogen stores by norepinephrine in rat pineal gland: role of gap junctions.
- **1994-1995.** Francisco Scheiing- Biochemist, Universidad Católica de Valparaíso. Effect of leptocarpin on gap junctions of epithelial cell lines.
- **1996.** Erwin Strahsburger-Biochemist, Univ. Austral de Chile. Regulation of gap junctional Communications in astroglial cells of the pineal gland.

MENTOR OF GRADUATE THESIS

Paloma Harcha

- **2011-present.** Bruno Cisterna. Doctor Ciencias Fisiológicas, PUC. "Role of connexin hemichannels in muscle atrophy induced by denervation".
- **2012-present.** Elsa Fritz, (Co-tutor, Dr. Jorge Campusano) Doctor Ciencias Fisiológicas, PUC. "Rol de las inexas en el comportamiento coordinado por el ciclo circadiano de *Drosophila melanogaster*".
- **2013-present.** Gonzalo Gomez, Doctor Ciencias Fisiológicas, PUC. "La vía RhoA/ROCK regula la actividad de los hemicanales y canales de uniones en hendidura formados por Cx43 en el daño renal por Angiotensina II.
- **2013-present.** Dusan Recordon, Doctor Ciencias Fisiológicas, PUC. "Señalización purinérgica en el proceso de imitación vasculogénica".
- **2009-present.** Carola Marturana, Doctor Ciencias Fisiológicas, PUC. "PARTICIPACIÓN DE LOS HEMICANALES FORMADOS POR PANEXINA 1 DE OLIGODENDROCITOS, EN LA AMIELINIZACIÓN DURANTE EL ESTRÉS PRENATAL".
- **2011-present** Anibal Vargas, Doctor Ciencias Fisiológicas, PUC. "Participación de

Hemicanales formados por Conexinas en atrofia muscular inducida por caquexia".

- **2009-present. Paloma Hacha, Doctor Ciencias Fisiológicas, PUC. "PARTICIPACIÓN DE LOS HEMICANALES EN LA DEGRANULACIÓN MEDIADA POR INMUNOGLOBULINA E EN MASTOCITOS MURINOS"**

2012-2014. Carolina Urrutia- Activation of hemichannels formed by connexins promotes Ca^{2+} influx, oxidative stress and cell death, which is prevented by antioxidant agents that block hemichannels". Master in Science: Free Radicals and Biomedicine". University of Valparaíso.

- **2009-2013.** Maximiliano Rovegno. **(Co-Tutor con Dra. Rommy von Benhardi)**. "Activación inflamatoria en astrocitos inducida por el ATP liberado vía hemicanales formados por conexina, en un modelo de estudio *in vitro* del traumatismo encefalo - craneano (TEC). Doctorado en Ciencias Médicas, PUC.
- **2009-2013.** Raúl Lagos Cabré. **(Co-tutoria con el Dr. Ricardo Moreno)**. "La modulación de proteínas de la familia ADAM por xenoestrógenos induce apoptosis en células germinales masculinas". Doctorado en Ciencias Fisiológicas, PUCC.
- **2009-presente.** Daniela Salas. **(Co-tutoría con el Dr. Sergio Lavandero)**. "Regulación de la Cx43 cardiaca por insulina". Doctorado en Bioquímica, Universidad de Chile.
- **2008-2012.** Pablo J. Sáez. Candidato a Doctor Ciencias Fisiológicas, PUC. Regulación y función de los hemicanales y uniones en hendidura en la interacción de las células dendríticas y los linfocitos T.
- **2009-2012.** Vania Figueroa. **(Co-Tutor con el Dr. Agustín Martínez)**. Activación de hemicanales formados por hCx26 y hPx1, en condiciones fisiológicas y patológicas y su posible rol en la etiopatogénea de la sordera. Doctorado en Neurociencias, Universidad de Valparaíso.
- **2008-2012.** Luis A. Cea. Doctor Ciencias Fisiológicas, PUC. La actividad muscular controla los niveles de las conexinas 39, 43 y 45 en músculo esquelético de rata.
- **2008-2011.** Kenji Shoji. Doctor Ciencias Fisiológicas, PUC. Los linfocitos T presentan hemicanales formados por Px1 acoplados a los receptores P2X₇ y median la muerte linfocitaria iniciada por ATP extracelular.
- **2008-presente.** Romina Hernández (Co-tutor con Dra. M.V. Velarde). Candidato a Doctor Ciencias Fisiológicas, PUC. Efecto de boldina en nefropatía diabética de ratas.
- **2008-2010.** Juan A. Orellana. Doctor en Ciencias Biológicas, mención Ciencias Fisiológicas, PUC. Papel y regulación de canales astrogiales formados por conexina43 en la muerte neuronal inducida por hipoxia en alta glucosa: potenciación por agentes neurodegenerativos,
- **2005-2010.** Manuel A. Riquelme. Doctor en Ciencias Biológicas, mención Ciencias Fisiológicas, PUC. Papel de los hemicanales formados por la Panexina1 y del ATP extracelular durante la adquisición del compromiso miogénico y la potenciación de la contracción muscular esquelética adulta.
- **2003-2008.** Carolina Gatica de la Puente. Doctor en Ciencias Biológicas, mención Ciencias Fisiológicas, PUC. Papel de los hemicanales y canales de uniones en hendidura, en la diferenciación neuronal y en la adquisición de compromiso miogénico en líneas celulares.
- **2005-2008.** Helmuth Sánchez. Doctor en Ciencias Biológicas, mención Ciencias Fisiológicas, PUC. Participación de canales formados por conexina32 en respuestas celulares de dos modelos de isquemia-reperfusion *in-vitro*.
- **2007-2008.** Kurt A. Schalper. Doctor en Ciencias Médicas, PUC. Modulación funcional de hemicanales formados por conexinas por estímulos de distinta naturaleza.
- **2003-2005.** Mauricio Retamal. Doctor en Ciencias Biológicas, mención Ciencias Fisiológicas. PUC. Los Hemicanales formados por conexina43son sensibles a cambios en el potencial redox.
- **2003-2005. (Co-Director con la Dra. V. Abudara)** Mauricio Garré. Efectos del factor fibroblástico FGF-1 sobre la comunicación intercelular a través de uniones en hendidura en el fenotipo reactivo neurotóxico de astrocitos espinales. Maestría en Biología, opción Neurociencias. PEDECIBA, Uruguay.

- **2001-2005. (Co-Director con el Dr. M. Boric)** Loreto P. Véliz. Doctor en Ciencias Biológicas, mención Ciencias Fisiológicas, PUC. Expresión y función de las uniones en hendidura entre leucocitos y células endoteliales durante la inflamación.
- **1999-2003.** Sra. Liliana Corvalán. Doctor en Ciencias Biológicas, mención Ciencias Fisiológicas, PUC. “Uniones en hendidura en contactos entre células dendríticas y entre células dendríticas y linfocitos T”.
- **1999-2003.** Dr. Jorge Contreras. Doctor en Ciencias Biológicas, mención Ciencias Fisiológicas, PUC. “Propiedades biofísicas y mecanismos de acción de los hemicanales formados por la conexina 43: posible participación en la muerte celular inducida por isquemia”.
- **1999-2004.** Roberto Araya. Doctor en Ciencias Biológicas, mención Ciencias Fisiológicas, PUC. Papel de los receptores purinérgicos y de las uniones en hendidura en el proceso de diferenciación del músculo esquelético.
- **1998-2001.** Dr. Eliseo A. Eugenín. Doctor en Ciencias Biológicas, mención Ciencias Fisiológicas, PUC. “Uniones en hendidura (UH) entre macrófagos: identificación de conexinas, regulación de su expresión y su función en procesos metabólicos y celulares”.
- **1997-2000.** Dr. María C. Brañes. Doctor en Ciencias Biológicas, mención, Biología Celular y Molecular. PUC. “Los neutrófilos y las células endoteliales forman uniones en hendidura homo y heterocelulares reguladas por factores proinflamatorios”.
- **1996-1998.** Dr. Hernán González. Doctor en Ciencias Médicas. PUC. “Efecto de la endotoxemia sobre las uniones en hendidura del hígado de la rata”.
- **1996-1999.** Dr. Agustín Martínez. Doctor en Ciencias Biológicas, mención Ciencias Fisiológicas. PUC. “Regulación *in vitro* de las uniones en hendidura de células gliales en respuesta a condiciones que desencadenan un proceso inflamatorio y a mediadores de la respuesta inflamatoria”.
- **1989-1992.** Dr. Viviana M. Berthoud, Ph.D. in Sciences. “Regulation of Gap Junctions”. Department of Neuroscience, Albert Einstein College of Medicine, Nueva York, E.E.U.U.

Mentor of Postdoctoral fellows

Dr. Rosalba Escamilla. Role of hemichannels in oligodendrocytes of neuroinflammatory diseases.(2014-present).

Dr. Carlos Puebla. Role of hemichannels in membrane transport and regulation by PUFAs. (2011-present).

Dr. Adam Aguirre. Regulation of hemichannels in brain cells by viral infections (2012-present)

Dr. Jose L. Vega. Regulation of hemichannels by protein phosphorylation (2011-2013).

Dr. Luis A. Cea. Regulation and function of hemichannels in diseases of skeletal muscles (2012-2013)

Dr. Juan A. Orellana. Role of hemichannels in HIV infections (2010-2011).

Dr. Mauricio Retamal Regulation of connexin based channels by inflammatory conditions (2006-2007).

PREVIOUS FUNDING

Continuously funded by NIH (1988-1996).

Continuously funded by Fondecyt (1993-present).

INSERM-CONICYT (2007-2008).

Current Funding

FONDECYT Regular 1150291 (Principal Investigator) (2015-2019). “Neuronal derived factor(s) and mechanism(s) that repress the expression of nonselective ion channels in normal adult skeletal muscles”

Millenium Institute, Centro Interdisciplinario de Neurociencias de Valparaíso. P09-022-F (2011-2016) Associate Investigator.

Proyecto Anillo ACT71 (2010-2013) (Director). Pro-inflammatory conditions increase the cell membrane permeability through pathways that offer new therapeutic target for human diseases.

Proyecto Fondecyt Regular 1100850 (2010-2014) (co-investigator). Coordination of microvascular function by long distance endothelial cell signaling based on connexin-mediated communication and voltage-dependent vasodilator mechanisms”.

Proyecto Fondecyt Regular 1111033 (2011-2014).(Principal Investigator).
“Role and regulation of hemichannels in functional responses of inactive, active, and acutely cachexic adult skeletal muscles”.

Proyecto Fondecyt Regular 1090573 (2009-2012). (Co-investigator) Pathogenic mechanism of connexin26 mutations involved in syndromic and non-syndromic deafness.

Proyecto Fondecyt Regular 1110778 (2011-2014). (Co-Investigator). Involvement of tace/adam17 and pannexin hemichannels in xenoestrogens induced apoptosis in mammalian spermatogenesis

Nucleo Milenio Inmunología e inmunoterapia. P04/030F (2006-2008) aprobada la renovación (2009-2011) (Co-investigador).

Millenium Institute (P09-022-F), Centro Interdisciplinario de Neurociencias de Valparaíso (2011-2016) (Co-Investigador).

DAAD-CONICYT (2010-2011) Biological functions of connexin45 and pannexin1 hemichannels for contraction and inflammatory response of skeletal muscles in mice.

National Institute of Neurological Disorders and Stroke (2008-2012) (Co-investigator)
Project Title: Cx43 Hemichannels: Gating Modification and Functions

FONDEF D07I1086 (2008-2013) (Principal Investigator). Improving molecular inhibitors of hemichannels for their use as anti-inflammatory compounds in human diseases.

ECOS-CONYCT, (2011-2013). Role of Glial Hemichannels in neurodegenerative processes: application to Alzheimer’s disease.
