

CURRICULUM VITAE INVESTIGATOR			
PERSONAL DATA			
Father's name Nuñez		Name Marco Tulio	
Birth date Jan 9, 1945	Age (at 15/07/2010) 65	Gender (M o F) M	Nationality(ies) Chilean
Title Biochemist		Academic Degree Biochemist	
Current position Full Professor	Institution (Department, Faculty, Institution) University of Chile, Faculty of Sciences		
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EDUCATION, ACADEMIC AND PROFESSIONAL EXPERIENCE			
University of Chile	B. Sc.	1969	Biochemistry
University of Chile	Biochemist	1971	Biochemistry
Massachusetts Institute of Technology, Biology Dept.	Postdoctoral Fellow	1974-7	Membrane Biochemistry
RESEARCH AND/OR PROFESSIONAL EXPERIENCE			
ACADEMIC EMPLOYMENT			
1973 - 1974	Instructor in Physiology, Faculty of Medicine, University of Chile		
1974 - 1977	Postdoctoral Fellow, Department of Biology, Massachusetts Institute of technology, Cambridge, MA, USA		
1978 - 1981	Principal Research Associate, Department of Medicine, Harvard Medical School		
1981 - 1985	Assistant Professor, Department of Medicine, Harvard Medical School		
1984 - 1994	Associate Professor, University of Chile		
1995	Full Professor, Universidad de Chile		
1995 - present	Director Laboratory of Iron and Biology of Aging, University of Chile.		
HONORS AND AWARDS			
1983 – 1985	Young Investigator Research Award, National Institute or Arthritis, Diabetes, Digestive and Kidney Diseases		
1991	Sabbatical Fellowship Fundación Andes, Louisiana State University		
1997	Presidential Chair in Science		
1998	Chancellor's Medal, University of Chile.		
2000	Visiting Scientist and External Evaluator, Okayama University, Okayama, Japan.		
1998 – 2002	Member of Study Group Biology 2, FONDECYT, Chile		
2003	Rector's Medal, University of Chile		
1999 – 2005	Senior Scientist Millennium Institute for Advanced Studies in Cell Biology and Biotechnology		
2009	Corresponding Member, Chilean Academy of Sciences		

ACADEMIC AND ADMINISTRATIVE SERVICE

- 1995 – 1996 Academic Director, Faculty of Sciences, University of Chile
1998 – 2000 Chairman, Department of Biology, Faculty of Sciences, University of Chile
2002 – 2004 Chairman PhD program on Molecular and Cell Biology and Neuroscience, Faculty of Sciences, University of Chile
2001 – present Member Institutional Evaluation Committee, University of Chile

GRADUATE STUDENTS

- Victoria Gaete V., Master in Physiology, Faculty of Science, University of Chile. Study of ionic and molecular factors involved in the acidification of endocytic vesicles. 1990.
- Miguel Arredondo Olguin, Master in Cell Biology, Faculty of Medicine, University of Chile. Interaction between Transferrin Receptor and HFE in the regulation of intracellular Fe content. 1997.
- Marco A. Garate M., PhD in Cell Biology, Faculty of Science, University of Chile. Ferritin, regulator of intestinal iron absorption. 1999.
- Miguel Arredondo Olguin, PhD in Molecular and Cellular Biology and Neuroscience, Faculty of Science, University of Chile. June, 2003. Interaction between Divalent Metal Transporter 1 (DMT1) and HFE: Implications for the regulation of intestinal iron absorption. 2002.
- Juan P. Muñoz Neculman, PhD in Molecular and Cellular Biology and Neuroscience, Faculty of Science, U. Chile). Ycdk5 p27 Involvement in the process of neuronal differentiation. Co-direction. 2004.
- Claudia Núñez Millacura, PhD, in Molecular and Cellular Biology and Neuroscience, Faculty of Science, University of Chile (in progress). Homeostasis of iron and iron-induced oxidative damage in neuroblastoma Neuro-2A cells. 2005.
- Fernando Ezquer R. Genetic modifications of intestinal iron transport: Opportunities in the treatment of hemochromatosis. PhD in Molecular and Cellular Biology and Neuroscience, Faculty of Science, University of Chile. Co-direction. 2006.
- Pablo Muñoz Carvajal. Oxidative pathway modulating ERK / MAPK-mediated iron and its effects on synaptic plasticity. PhD in Molecular and Cellular Biology and Neuroscience, Faculty of Science, University of Chile. 2006.
- Carolina Garri G. Characterization of endocytosis of ferritin from soybeans by cultured human enterocytes. Master in Biochemistry, Universidad Andrés Bello. 2007.
- Solange Le Blanc. Role of HCP1 and FLVCR in intestinal absorption and transepithelial transport of heme iron. Master in Biological Sciences, Faculty of Science, University of Chile. 2008.
- Elmer Antileo I. Determination of the degradative route of ferritin endocytosed by Caco-2 Master in Biological Sciences, Faculty of Science, University of Chile. 2008.
- Francisco Gomez Mardones. Characterization of neuritic degeneration in dopaminergic neurons induced by 1-methyl-4-phenylpyridin (MPP+) a model of Parkinson's disease. Master in Biological Sciences, Faculty of Science, University of Chile. 2010.
- Enrique Armijo Fuentes. Role of mitochondrial ferritin in the deregulation of cellular iron homeostasis in an experimental model of Parkinson's disease. Master in Biological Sciences, Faculty of Science, University of Chile. 2010.

- Carriel Carolina Burgos. Flow of iron between the cytosol and mitochondria. Implications for cellular iron homeostasis in neuronal cells. Master in Biological Sciences, Faculty of Science, University of Chile. 2011.
- Mena Natalia Jimenez. Effects of inhibition of complex I of mitochondrial iron homeostasis in an experimental model of Parkinson's disease. PhD in Molecular and Cellular Biology and Neuroscience, Faculty of Science, University of Chile. 2011.
- Alexis Humeres. Modification of the redox rate of the Calcium Channel / ryanodine receptor (RyR) by iron and reactive oxygen species. PhD in Biomedical Sciences, Faculty of Medicine, University of Chile. 2011.
- San Martin Carol R. Modification of mitochondrial dynamics by ROS and calcium release from RyR induced by iron and ADDLs. PhD in Biomedical Sciences, Faculty of Medicine, University of Chile. Co-direction. Ongoing.
- Carlos P. D. Alvarado Effect of Fe⁺² on the activation of NF-kB in human endometrial cells as a possible mechanism associated with the pathogenesis of endometriosis. PhD in Biomedical Sciences, Faculty of Medicine, University of Chile. Co-direction. Ongoing.
- Pamela Urrutia C. Inflammation and Hepcidin in the loss of iron homeostasis in neurodegenerative diseases. PhD in Molecular and Cellular Biology and Neuroscience, Faculty of Science, University of Chile. Ongoing.

MAIN PUBLICATIONS IN MEDIA WITH EDITORIAL COMMITTEE

Núñez, M.T., and Glass, J. 1983. The transferrin cycle and iron uptake in rabbit reticulocytes. Pulse studies using ⁵⁹Fe, ¹²⁵I-labeled transferrin. *J. Biol. Chem.* 258: 9676-9680.

Núñez, M.T., Cole, E.S., Glass, J. 1983. The reticulocyte plasma membrane pathway of iron uptake as determined by the mechanism of a,a'-dipyridyl inhibition. *J. Biol. Chem.* 258: 1146-1151.

Tsiftoglou, A.S., Núñez, M.T., Wong, W., Robinson, S.H. 1983. Dissociation of the iron transport and heme biosynthesis from commitment to terminal maturation of murine erythroleukemia cells. *Proc. Natl. Acad. Sci., U.S.A.*, 80: 7428-7532.

Núñez, M.T., Glass, J. 1985. Iron uptake in reticulocytes: inhibition mediated by the ionophores monensin and nigericin. *J. Biol. Chem.* 260: 14707-14711.

Choe, H-R., Moseley, S.T., Glass, J., Núñez, M.T. 1987. Rabbit reticulocyte coated vesicles carrying the transferrin-transferrin receptor complex. Purification and partial characterization. *Blood* 170: 1035-1039.

Núñez, M.T., Pinto, I., Glass, G. 1989. Assay and characteristics of the iron binding moiety of reticulocytes endocytic vesicles. *J. Memb. Biol.* 107: 129-136.

Núñez, M.T., Gaete, V., Watkins, J.A., Glass, J. 1990. Mobilization of iron from endocytic vesicles: the effect of acidification and reduction. *J. Biol. Chem.* 265: 6688-6692.

Núñez, M.T., Gaete, V., Escobar, A. 1990. Endocytic vesicles contain a calmodulin-activated Ca²⁺ pump. *Biochem. Biophys. Acta*, 1828: 21-24.

Gaete, V., Glass, J., Núñez, M.T. 1991. Cl⁻, Na⁺, and H⁺ fluxes during the acidification of rabbit reticulocytes endocytic vesicles. *J. Bioenerg. Biomemb.* 23:147-160.

Watkins, J.A., Núñez, M.T. Gaete, V., Alvarez, O. y Glass, J. Kinetics of iron passage through sub-cellular compartments of rabbit reticulocytes. 1991; *J. Memb. Biol.* 119: 141-149.

Escobar, A., Gaete, V. y Núñez, M.T. 1991. An ascorbate transport system is involved in the reduction of transferrin-associated iron in endocytic vesicles. *Journal of Bioenerg. Biomemb.* 24: 227-233.

- Núñez, M.T., Escobar, A., Ahumada, A. y González, M. 1992. Sealed reticulocyte ghosts: An experimental model for the study of iron transport. *J. Biol. Chem.* 267:11490-11494.
- Watkins, J.A., Altazan, J.D., Elder, P., Li, C-Y., Núñez, M.T., Cui, X-X. y Glass, J. 1992. Kinetic characterization of reductant-dependent processes of iron mobilization from endocytic vesicles. *Biochemistry* 31: 5820-5830.
- González-Sepúlveda, M, y Núñez, M.T. 1994. Arginyl residues are involved in the transport of Fe²⁺ through the plasma membrane of the mammalian reticulocyte. *Journal of Membrane Biology* 41:225-230.
- Núñez, M.T., Alvarez, X., Smith, M., Tapia, V. y Glass, J. 1994. Role of redox systems on Fe³⁺ uptake by transformed intestinal epithelial (Caco-2) cells. *American Journal of Physiology (Cell Physiology)* 36: C1582-C1588.
- Tapia, V., Arredondo, M. y Núñez, M.T. 1996. Regulation of iron absorption by cultures epithelia (Caco-2) cells monolayers with varied iron status. *Am. J. Physiol.* 271 (Gastrointest. Liver Physiol. 34): G443-G447.
- Núñez, M.T., Tapia, V., and Arredondo, M. 1996. Intestinal epithelia (Caco-2) cells acquire iron through the basolateral endocytosis of transferrin. *J. Nutr.* 126: 2151-2158.
- Arredondo M, Orellana A, Garate MA, Nunez MT. Intracellular Iron Regulates Iron Absorption and IRP Activity in Intestinal Epithelial (Caco-2) Cells. 1997. *Am. J. Physiol.* 273 (Gastrointest. Liver Physiol. 36): G275-G280.
- Núñez, M.T., Núñez-Millacura, C., Beltrán, M., Tapia, V., and Alvarez, X. 1997. Apotransferrin and Holotransferrin Undergo Different Endocytic Cycles in Intestinal Epithelia (Caco-2) Cells. *J. Biol. Chem.* 272:19425-19428.
- Iturri, S., and Núñez, M.T. 1998. Effect of copper, cadmium, mercury, manganese and lead on Fe²⁺ and Fe³⁺ absorption in perfused mouse intestine. *Digestion* 59: 671-675.
- Muñoz, C., Ríos, E., López, M., Olivares, M., Schlesinger, L., and Núñez, M.T. 1999. Transferrin and iron salts modulate differently tumor necrosis factor- α secretion by cultured human monocytes. *Nutritional Research* 19:651-661.
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- Núñez, M.T., Gárate, M.A., Arredondo, M., Tapia, V. Y Muñoz, P. The cellular mechanisms of body iron homeostasis. *Biol. Res.*, 33: 133-142, 2000.
- Núñez, M.T., Tapia, V., Toyokumi, S., and Okada, S. 2001. Iron-induced oxidative damage in colon carcinoma (Caco-2) cells. *Free Rad. Res.* 34: 57-68.
- Arredondo, M., Muñoz, P., Mura, C., and Núñez, M.T. 2001. HFE negatively regulates apical iron uptake by intestinal epithelial (Caco-2) cells. *FASEB J.* 15:1276-1278.**
- Núñez, M.T., Osorio, A., Tapia, V., and Vergara, A. 2001. Iron upregulates calreticulin expression in intestinal epithelial Caco-2 cells. *J. Cell. Biochem.* 82: 660-665.
- Núñez-Millacura, C., Tapia, V., Muñoz, P., Maccioni, R.B. and Núñez, M.T. 2002. An oxidative stress-mediated positive-feedback iron uptake loop in neuronal cells. *Journal of Neurochemistry* 82: 240-248.**
- López, M., Ríos, E., Schlesinger, L., Olivares, L., Núñez, M.T. and Muñoz, C. 2003. Modulation of secretion and transcription of tumor necrosis factor by transferrin: effect of iron

status. *Brit. J. Haematol.* 120: 829-835.

Egaña, J.T., Zambrano, C., Núñez, M.T., González-Billault, C. and Maccioni, R.B. 2003. Iron-induced oxidative stress modify tau phosphorylation pattern in hippocell cultures. *Biometals* 16: 215-223.

Núñez, M.T., Núñez-Millacura, C., Tapia, V., Muñoz, P., Mazariegos, D., Arredondo, M., Muñoz, P., Mura, C. and Maccioni, R. 2003. Iron-activated iron uptake: a positive feed-back loop mediated by iron regulatory protein 1. *Biometals* 16: 83-90.

Arredondo, M., Muñoz, P., Mura, C.V. and Núñez, M.T. 2003. DMT1, a physiologically relevant apical Cu¹⁺ transporter of intestinal cells. *Am. J. Physiol. (Cell Physiol.)*, 284: C1525-C1530.

Arredondo M., Cambiazo V, Tapia L, González-Aquero M, Nuñez M.T, Uauy R., González M. (2004) Copper overload affects copper and iron metabolism in Hep-G2 cells. *J. Physiol Gastrointest Liver Physiol* 287: G27 – G32.

Zambrano, C., Egaña, J.T., Núñez, M.T., Maccioni, R.B. and Gonzalez-Billault, Ch. (2004) Decreased activity of cdk5 in hippocampal cells under oxidative stress is responsible for reduced tau phosphorylation, *Free Radical Biology & Medicine* 36: 1393-1402.

Núñez, M.T., Gallardo, V., Muñoz, P., Tapia, V., Esparza, A., Salazar, J. & Speisky, H. (2004) Progressive iron accumulation induces a biphasic change in the glutathione content of neuroblastoma cells. *Free Rad Biol & Med* 37: 953-960.

Inestrosa, N.C., Columbres, M., Núñez, M.T. and Morgan, C. (2004) Structure and function of amyloid in Alzheimer's disease. *Progress in Neurobiology* 74: 323-349.

Aguirre, P., Mena, N., Arredondo, M., Tapia, V. and Núñez, M.T. (2005) Iron homeostasis in neuronal cells: a role for SCL40. *BMC Neuroscience* 6, article 3.

Ezquer, F., Nuñez, M.T. and Israel, Y. (2005) Hemochromatosis: Antisense gene against the iron transporter DMT1 inhibits iron uptake in intestinal cells and shows RNAi and antisense effects. *Biochem. Pharmacol.* 69: 1559-1566.

Arredondo, M., Núñez, M.T.(2005) Iron and copper metabolism. (Review) *Molecular Aspects of Medicine* 26: 313-327.

Arredondo, M., Tapia, V., Muñoz, P., Aguirre, P., Rojas, A., Marzolo, M.P. and Núñez, M.T. (2006) Apical distribution of β 2-microglobulin is associated with inhibition of apical iron uptake in bHFE- intestinal epithelia cells. *Biometals* 19: 379-388.

Aracena P, Aguirre P, Muñoz P, Núñez MT. (2006) Iron and glutathione at the crossroad of redox metabolism in neurons. *Biological Research* 39:157-165.

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Salazar, J., Mena, N. and Núñez, M.T. (2006) Iron dyshomeostasis in an early stage model of Parkinson's disease. *Journal of Neural Transmition* 71(Suppl.): 205-213.

Mura, C.V., Delgado, R., Aguirre, P., Bacigalupo, J. and Nuñez, M.T. (2006) SHSY5Y neuroblastoma cells survival to iron challenge results in a quiescent and functional cell population. *Journal of Neurochemistry* 98:11-19.

Hidalgo C, Núñez MT. (2007) Calcium, iron and neuronal function. *IUBMB Life* 59(4-5): 280-285.

Aguirre, P., Valdés, P, Aracena-Parks, P. Tapia, V. and Núñez, M.T. (2007) Up-regulation of γ -glutamate-cysteine ligase as part of the long-term adaptation to iron accumulation in neuronal SH-SY5Y cells. *American Journal Cell Physiology*, **292**, C2197-C2203.

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Mena, NP., Esparza, A., Núñez, MT., Tapia, V. and Valdés, P.(2008) Heparin inhibits apical iron uptake in intestinal cells. *American Journal of Physiology-Gastrointestinal and Liver Physiol.* 294(1), G192-198.

San Martin, C., Theil, E., Garri, C., Pizarro, F., Walter, T. and Núñez, M.T. (2008) Caco-2 Intestinal Epithelial Cells Absorb Soybean Ferritin by μ_2 (AP2)-Dependent Endocytosis^{1,2}. *J Nutr. Biochemical, Molecular and Genetics Mechanisms*, 138, 659-666.

Salazar, J., Mena, M., Hunot, S., Prigent, A., Alvarez-Fischer, D., Arredondo, A., Duyckaerts, Ch., Sazdovitch, V., Zhao, L., Garrick, L.M., Nuñez, M.T., Garrick, D.M., Raisman-Vozari, R., and Hirsch, E.C. (2008) Divalent metal transporter 1 (DMT1) contributes to neurodegeneration in animal models of Parkinson's disease. *Proc. Natl. Acad. Sci. USA* 105(47), 18578-18583.

Borquez, D., Valdés, P. and Núñez, M.T. (2008) Iron Toxicity: a Critical Review on its Role in Parkinson's Disease. In: *Neurodegenerative Diseases: From Molecular Concepts to Therapeutic Targets* (N. Inestrosa, editor), Nova Science Publishers, Inc., Hauppauge, New York. 189-204

Barbeito, A. G., Garringer, H. J., Baraibar, M.A., Gao, X., Arredondo, M., Núñez, M.T., Smith, M.A, Ghetti, B., Vidal, R. (2009) Abnormal iron metabolism and oxidative stress in mice expressing a mutant form of the ferritin light polypeptide gene. *Journal of Neurochemistry* 109(4):1067-1078.

Haeger, P., Alvarez, A., Leal, N., Adasme, T., Núñez, M.T. and Hidalgo, C. Epub (2009) Increased Hippocampal Expression of the Divalent Metal Transporter 1 (DMT1) mRNA Variants 1B and +IRE and DMT1 Protein after NMDA-Receptor Stimulation or Spatial Memory training. *Neurotox Res.* 17 (3), 238-247.

Muñoz, J.P., Chiong, M., Garcia, L., Troncoso, R., Toro, B., Pedrozo, Z., Diaz-Elizondo, J., Salas, D., Parra, V., Nuñez, MT., Hidalgo, C. and Lavandero, S. (2010) Iron induces protection and necrosis in cultured cardiomyocytes: role of reactive oxygen species and nitric oxide. *Free Radic Biol Med.* 48, 526-534.

Núñez, M.T., Tapia, V., Rojas, A., Aguirre, P., Gómez, F., Sandoval, D., Armijo, E., Nualart, F. (2010) Iron supply determines apical/basolateral membrane distribution of intestinal iron transporters DMT1 and ferroportin 1. *Am J Physiol Cell Physiol.* 298, C477-485.

Núñez, M.T. (2010) Regulatory Mechanisms of Intestinal Iron Absorption - Uncovering of a Fast-Response Mechanism Based on DMT1 and Ferroportin Endocytosis (Review). *Biofactors*, 36, 88-97.

Salgado, J.C., Olivera, A., Gerdtzen, Z.P., Tapia, V., Theil, E.C., Conca, C., and Núñez, M.T. (2010) Mathematical Modelling of the Dynamic Storage of Iron in Ferritin. *BMC Systems Biology* 4:147.

Gómez, F.J., Aguirre, P., Gonzalez-Billault, C. and Núñez, M.T. (2011) Iron mediates neuritic tree collapse in mesencephalic neurons treated with 1-methyl-4-phenylpyridinium (MPP+). *J Neural Transm.* 2011.118(3):421-31.

Muñoz, P., Humeres, A., Elgueta, C., Kirkwood, A., Hidalgo, C., Núñez, M.T. (2011) Iron Mediates N-Methyl-D-aspartate Receptor-dependent Stimulation of Calcium-induced Pathways and Hippocampal Synaptic Plasticity. *Journal of Biological Chemistry*, 286, 13383-13392.

Núñez, M.T., Olivares, M. 2011. Nutritional Aspects of Iron Metabolism. In: *Biochemical*

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Natalia P. Mena, N.P., Bulteau, A.L., Salazar, J., Hirsch, E. and Núñez, M.T. 2011. Effect of mitochondrial complex I inhibition on Fe-S cluster protein activity. *Biochem. Biophys. Res. Comm.* 409(2):241-246.