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Título Profesional o Grado Académico (incluya el año de obtención):

**BIOQUÍMICO, UNIVERSIDAD DE CHILE, 1971**

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Estudios de Postgrado o Especialización (institución donde lo obtuvo y año de obtención):

**ENTRENAMIENTO POSTDOCTORAL BIOQUÍMICA DE MEMBRANAS, DEPARTMENT OF BIOLOGY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY (MIT), 1973-1976; INVESTIGADOR ASOCIADO DEPARTMENT OF MEDICINE HARVARD MEDICAL SCHOOL 1976-1982; ASSISTANT PROFESSOR HARVARD MEDICAL SCHOOL, 1982-1985.**

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Actividad Actual e Institución en la cual trabaja:

**PROFESOR TITULAR DE LA UNIVERSIDAD DE CHILE. DEPARTAMENTO DE BIOLOGÍA, FACULTAD DE CIENCIAS. MIEMBRO CORRESPONDIENTE DE LA ACADEMIA CHILENA DE CIENCIAS.**

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Reseña de su actividad laboral actual:

Estudio de los mecanismos celulares y moleculares involucrados en la absorción intestinal de hierro. Mecanismos moleculares que subyacen a la hemocromatosis hereditaria. Papel del hierro y del cobre en la producción de estrés oxidativo y envejecimiento celular.

**Docencia:** Pregrado: Coordinador, curso de Biología Celular; Profesor participante en otros cursos de las licenciaturas.

Postgrado: Profesor participante en curso troncal Biología Estructural y Molecular de la Célula; Coordinador curso electivo Estrés Oxidativo en Salud y Enfermedad: Bases Moleculares.

**PUBLICACIONES INDEXADAS:** (últimos 10 años).

1. Mazariegos, D.I., Pizarro, F., Olivares, M., Núñez, M.T. y Arredondo, M. 2004. The mechanisms for regulating absorption of Fe bis-glycine chelate and Fe-ascorbate in caco-2 cells are similar. *J. Nutr.* 134: 395-398. ISSN 0022-3166.
2. Zambrano, C., Egaña, J.T., Núñez, M.T., Maccioni, R.B. and Gonzalez-Billault, Ch. Oxidative stress promotes tau dephosphorylation in neuronal cells: the roles of cdk5 and PP1. *Free Radical Biology & Medicine* 2004;36: 1393-1402. ISSN 0891-5849.
3. Arredondo M, Cambiazo V, Tapia L, Gonzalez-Aguero M, Núñez MT, Uauy R, Gonzalez M. 2004. Copper overload affects copper and iron metabolism in Hep-G2 cells. *Am J Physiol Gastrointest Liver Physiol.* 287: G27-G32. ISSN 0193-1857.
4. Rodríguez, D.A., Moncada, C., Núñez, M.T., Lavanderos, S., Ponnappa, B.C. and Israel, Y. 2004. Ethanol increases tumor necrosis factor-alpha receptor-1 (TNF-R1) levels in hepatic, intestinal and cardiac cells. *Alcohol* 33: 9-15. ISSN 0741-8329.
5. 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. ISSN 0891-5849.
6. Morgan, C., Colombres, M., Núñez, M. T., Inestrosa, N. C. 2004. Structure and function of amyloid in Alzheimer's disease. *Progress in Neurobiology* 74: 323-349. ISSN 0301-0082.
7. 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. ISSN 1471-2202.
8. Ezquer, F., Nuñez, M.T. and Israel, Y. 2005. Antisense gene against the iron transporter DMT1 inhibits iron uptake in intestinal cells and shows RNAi and antisense effects. *Biochem. Pharmacol.* 69: 1559-1566. ISSN 0006-2952.
9. Arredondo, M., Núñez, M.T. 2005. Iron and copper metabolism. (Review). *Molecular Aspects of Medicine*, 26: 313-327. (Fondecyt 1040448). ISSN 0098-2997. (104 citations). (i.f. 10.27).
10. 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(1):11-19. ISSN 0022-3042.
11. Aguirre, P., Mena NP, Tapia V, Rojas A, Arredondo M and Núñez MT. (2006) Antioxidant responses of neuroblastoma cells to high iron supply. *Biological Research* 39: 103-104. ISSN 0716-9760.

12. Ezquer, F., Núñez, M.T., Rojas, A. Asenjo, J. and Israel, Y. 2006. Hereditary hemochromatosis: an opportunity for gene therapy. *Biological Research* 39: 113-124. (Fondecyt 1040448). ISSN 0716-9760.
13. Mena NP, Esparza, AL and Núñez MT. (2006) Regulation of transepithelial transport of iron by hepcidin. *Biological Research* 39: 191-193. ISSN 0716-9760.
14. Aracena, P., Aguirre, P., Muñoz, P. and Núñez, M.T. 2006. Iron and glutathione at the crossroad of redox metabolism in neurons. *Biological Research* 39: 157-165. ISSN 0716-9760.
15. Mazariegos DI, Cabantchik, IZ, Cassels BK and Núñez MT. (2006). Characterization of mitochondrial iron uptake in HepG2 cells. *Biological Research* 39: 199-201. ISSN 0716-9760.
16. Arredondo, M., Martinez, R., Núñez, M.T., Ruz, M., and Olivares, M. 2006. Inhibition of iron and copper uptake by iron, copper and zinc.. *Biological Research* 39: 191-193. ISSN 0716-9760.
17. Muñoz P, Zavala G, Castillo K, Aguirre P, Hidalgo C, and Núñez MT. (2006) Effect of iron on the activation of the MAPK/ERK pathway in PC12 neuroblastoma cells. *Biological Research* 39: 189-190. ISSN 0716-9760.
18. Arredondo, M., Tapia, V., Muñoz, P., Aguirre, P., Rojas, A., Marzolo, M.P. and Núñez, M.T. 2006. Apical distribution of HFE- $\alpha$ 2-microglobulin is associated with inhibition of apical iron uptake in intestinal epithelia cells. *Biometals* 19: 379-388. ISSN 0966-0844.
19. Salazar, J., Mena, N. and Núñez, M.T. 2006. Iron dyshomeostasis in an early stage model of Parkinson's disease. *J. Neural Transmition* 71(Suppl.): 205-213. ISSN 0303-6995.
20. Hidalgo, C., Carrasco, A., Muñoz, P. and Núñez, M.T. 2007. A role for reactive oxygen/nitrogen species and iron on neuronal synaptic plasticity. *Antioxidants and Redox Signalling* 9: 245-255. ISSN 1523-0864.
21. Hidalgo C, Núñez MT. Calcium, iron and neuronal function. 2007. *IUBMB Life*. 59(4-5): 280-285.
22. Aguirre, P., Valdés, P., Aracena-Parks, P. and Núñez, M.T. 2007. Up-regulation of glutathione and gamma-glutamyl-cysteine ligase is part of the long-term adaptation to iron accumulation in neuronal SH-SY5Y cells. *Am J Physiol Cell Physiol*. 292:C2197-C2203. ISSN 0363-6143.
23. Mena NP, Esparza A, Núñez MT. 2008. Hepcidin inhibits apical iron uptake in intestinal cells. *American Journal of Physiology-Gastrointestinal and Liver Physiol*. 294(1):G192-198. (Fondecyt 1070840). ISSN 0193-1857.
24. 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 mu2 (AP2)-dependent endocytosis. *J Nutr*. 138:659-666. ISSN 1541-6100.
25. Salazar, J., Mena, M., Hunot, S., Prigent, A., Alvarez-Fischer, D., Arredondo, A., Duyckaerts, C., 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 parkinsonian syndromes. *Proc. Natl. Acad. Sci. USA* 105(47):18578-83. ISSN 1091-6490.
26. 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. *J Neurochem*. 109(4):1067-1078. ISSN 1471-4159.

27. Muñoz, J.P., Alcaino, H., Díaz-Elizondo, J., Olea, C., Chiong, M., Pedrozo, Z., Núñez, M.T., 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(4):526-34. ISSN 1873-4596.
28. 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. *Am J Physiol Cell Physiol.* 298(3):C477-85. (Fondecyt 1070840).
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30. Núñez, M.T. 2010. Regulatory Mechanisms of Intestinal Iron Absorption - Uncovering of a Fast-Response Mechanism Based on DMT1 and Ferroportin Endocytosis (Review). *Biofactors* 2010;36(2):88-97. (Fondecyt 1070840). ISSN 1872-8081.
31. 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.* 118(3):421-31. ISSN 1435-1463.
32. 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. ISSN 1752-0509.
33. Muñoz-Carvajal, P., Humeres, A., Kirkwood, A., Hidalgo, C. and Núñez, M.T. 2011. Iron mediates N-methyl-D-aspartate receptor-dependent stimulation of calcium-induced pathways and hippocampal synaptic plasticity. *J. Biol. Chem.* 286(15):13382-92. ISSN 1083-351X.
34. 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):241-6. ISSN 1090-2104.
35. García-Beltrán, O., Mena, N., Pérez, E.G., Cassels, B.K., Nuñez, M.T., Werlinger, P., Zavala, D., Aliaga, M.E., Pavez, P. 2011. The development of a fluorescence turn-on sensor for cysteine, glutathione and other biothiols. A kinetic study. *Tetrahedron Letters* 52:6606-6609. ISSN 0040-4039.
36. Aguirre, P., Urrutia, P, Tapia, V., Segura-Aguilar, J. and Núñez, M.T. 2012. The dopamine metabolite aminochrome inhibits mitochondrial complex I and modifies the expression of iron transporters DMT1 and FPN1. *BioMetals*, 25(4): 795-803. ISSN 1572-8773.
37. Núñez MT, Urrutia P, Mena NP, Aguirre P, Tapia V and Salazar J. 2012. Iron Toxicity in Neurodegeneration. *BioMetals* 25(4):761-776. ISSN 0966-0844. ISSN 1572-8773.
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39. SanMartín, C.D., Paula-Lima, A.C., Hidalgo, C. and Núñez, M.T. 2012. Sub-lethal levels of amyloid b-peptide oligomers decrease non-transferrin-bound iron uptake and do not potentiate iron toxicity in primary hippocampal neurons. *Biomaterials* 25(4):805-813. Print ISSN 0966-0844. ISSN 1572-8773.

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41. García-Beltrán, O., Mena, N.P., Berríos, T.A., Castro, E.A., Cassels, B.K., Núñez, M.T. and Aliaga, M.E. 2012. A selective fluorescent probe for the detection of mercury (II) in aqueous media and its applications in living cells. *Tetrahedron Letters* 53:6598–6601. ISSN 0040-4039.
42. Antileo, E., Garri, C., Tapia, V., Chiang, M., Lavandero, S., Nualart, F., Muñoz, J.P., Fernández, J. and Núñez, M.T. 2013. Exogenous ferritin is endocytosed and degraded via autophagosomes and lysosomes in intestinal epithelial (Caco-2) cells. *Am J Physiol Gastrointest Liver Physiol*. 304(7):G655-61. ISSN 1522-1547.
43. Urrutia, P., Aguirre, P., Esparza, A., Tapia, V., Mena, N.P., Arredondo, M., González-Billault, C. and Núñez, M.T. Inflammation alters the expression of DMT1, FPN1 and hepcidin, and it causes iron accumulation in central nervous system cells. 2013. *J Neurochem*. 26(4):541-9. ISSN 1471-4159.
44. García-Beltrán, O., Mena, N.P., Yañez, O., Caballero, J., Vargas, V., Nuñez, M.T., Cassels, B.K. Design, synthesis and cellular dynamics studies in membranes of a new coumarin-based "turn-off" fluorescent probe selective for Fe<sup>2+</sup>. *European Journal of Medical chemistry*. 67:60-63. ISSN 1471-4159.

#### **PROYECTOS DE INVESTIGACIÓN:** (últimos 10 años)

1. 2002-2004 Liberación de calcio mediada por canales receptores de ryanodina en músculo esquelético y neuronas. Estudios en vesículas y células. FONDECYT 1020967. Co-investigador.
2. 2004-2007 Mecanismos celulares de regulación de la absorción intestinal del hierro". FONDECYT 1040448. Investigador Responsable.
3. 2005-2008 Ferritina, una potencial tercera vía de absorción de hierro: estudios celulares y de biodisponibilidad en humanos. FONDECYT 1050068. Co-Investigador
4. 2006-2011 Instituto Milenio en Dinámica Celular y Biotecnología. ICM-P05-001-F.
5. Key Scientist y Sub-Director.
6. 2007-2008 Proyecto colaborativo CONICYT-INSERM "Desbalance Oxidativo en la Enfermedad de Parkinson". Investigador Responsable
7. 2007-2010 Posicionamiento de los transportadores DMT1 y ferroportina en la membrana apical y basolateral y la regulación de la absorción intestinal de hierro. FONDECYT 1070840. Investigador Responsable
8. 2007-2008 Desbalance oxidativo en la enfermedad de Parkinson. Proyecto de colaboración INSERM-CONICYT. Investigador Chileno Responsable.
9. 2009-2012 On the contribution of iron transporters DMT1, Zip14 and ferroportin
10. to the pathological progression in an animal model of Alzheimer's
11. disease. FONDECYT 1100599. Investigador Responsable.
12. 2010-2011 Metabolismo del hierro mitocondrial en la enfermedad de Parkinson. Proyecto colaborativo CONICYT-INSERM. Investigador Responsable Chileno.

13. 2011-2012 Hecpidin as a mediator of Neuroinflammation in Parkinson's Disease, Alzheimer's Disease and Multiple Sclerosis. Proyecto colaborativo CONICYT-INSERM. Investigador Responsable Chileno.
14. 2012-2015 Research Ring on oxidative stress in the nervous system. Physiological and pathological aspects. PIA-CONICYT ACT1114 Investigator Proicipal
15. .2013-2017 Disruption of the oxidative stress-iron accumulation cycle as a strategy for decreasing dopaminergic neuron death in experimental models of Parkinson's disease- FONDECYT 1130068.

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