

Part A. PERSONAL INFORMATION		CV date	21/11/2022
First and Family name	Juan José Toledo Aral		
Social Security, Passport, ID number		Age	
Researcher codes	WoS Researcher ID	F-2613-2015	
	Open Researcher and Contributor ID (ORCID)	0000-0001-7512-7135	

A.1. Current position

Name of University/Institution	Universidad de Sevilla / Instituto de Biomedicina de Sevilla-IBiS		
Department	Departamento de Fisiología Médica y Biofísica / Neurociencias		
Address and Country	Av. Manuel Siurot s/n, 41013 Seville-Spain		
Phone number		E-mail	juanjo@us.es
Current position	Full Professor of Physiology	From	2005
Key words	GDNF, cell therapy, carotid body, Parkinson's disease, Covid-19		

A.2. Education

MD	University of Seville. Medical School	1988
PhD	University of Seville. Dept. Physiology	1993

A.3. JCR articles, h Index, thesis supervised...

Total JCR articles: 80

h index: 28

Total times cited: 4184

Thesis supervised: 6, and 2 in progress.

Patents: 2

Recognized research activity periods: 5 (1988-1994; 1995-2000; 2001-2006; 2007-2012; 2013-2018) and 1 research transfer (2001-2010)

Part B. CV SUMMARY

I obtained a Medical Degree at Seville Medical School of Seville University (1988). After finishing my MD, I did a PhD thesis on the electrophysiological properties and modulation of Na and K currents in septal guinea pig neurons under the direction of Drs. José López Barneo and Juan Ureña López in the Department of Medical Physiology and Biophysics of the University of Seville (1993).

Subsequently, I carried out a Postdoctoral stay until 1998 in the Department of Neurobiology and Behavior of the State University of New York at Stony Brook in the laboratory of Dr Gail Mandel studying the expression and structure of voltage dependent sodium channels and, in collaboration with Dr Simon Halegoua, the induction of these channels by neurotrophic factors. During this period my most personal and relevant contributions were the cloning of the first peripheral nervous system specific sodium channel and its involvement in nociception (Nav1.7) and the identification of a new signaling pathway triggered by the transient administration of NGF.

Later I returned to Spain as an Associate Professor at the Department of Medical Physiology and Biophysics of Seville University (1998) and, initially in collaboration with Dr. López-Barneo, I began to study the recently reported intrastriatal carotid body transplant in animal models of Parkinsonism. My contribution in this topic was to establish that the beneficial effect was trophic rather than the release of dopamine and to identify the high production of GDNF in the carotid body. I also collaborated in carrying out two clinical trials using autotransplantation of the carotid body in Parkinsonian patients with worse results than in animal research.

Since that time, I have dedicated my experimental efforts to translational research, trying to understand the mechanism by which carotid body transplants exert their beneficial effect. The



most important achievements have been to develop a chronic and systemic animal model where we have demonstrated that the effect is trophic and depends on the expression of GDNF by the carotid body. We have also developed a model of immunosuppression that has allowed xenotransplantation with human tissue. As the most relevant recent finding we have found that the expression of GDNF by the murine and human carotid body transplanted intrastrially, and in hypoxia, decreases with the age of the donor by hypermethylation of the GDNF promoter. The objective of my current research is to try to reverse this process of hypermethylation associated with aging with the idea of re-testing with greater guarantees of success the autotransplantation and/or allogeneic carotid body transplantation in Parkinsonian patients.

In addition to the research work I have also developed an intense academic-institutional work, where I would highlight the Direction of the Department of Medical Physiology and Biophysics of the US and the area of Neurosciences of the Institute of Biomedical Research of Seville-IBiS, the design and construction of the Biomedical Research Laboratory of HUVR and IBiS. I have also been actively implicated in national and regional evaluation agencies, both directing and participating in evaluation panels of Institutes, projects and human resources.

Part C. RELEVANT MERITS

C.1. Publications

1. Full protection from SARS-CoV-2 brain infection and damage in susceptible transgenic mice conferred by MVA-CoV2-S vaccine candidate. Villadiego J, García-Arriaza J, Ramírez-Lorca R, García-Swinburn R, Cabello-Rivera D, Rosales-Nieves AE, Álvarez-Vergara MI, Cala-Fernández F, García-Roldán E, López-Ogáyar JL, Zamora C, Astorgano D, Albericio G, Pérez⁴ P, Muñoz-Cabello AM, Pascual A, Esteban M, López-Barneo J, **Toledo-Aral JJ**. *Nature Neuroscience*. In press.
2. Gadomski S, Fielding C, García-García A, Korn C, Ashraf S, Villadiego J, del Toro R, Domingues O, Skepper JM, Michel T, Zimmer J, Sendtner R, Dillon S, Poole K, Holdsworth G, Sendtner M, **Toledo-Aral JJ**, De Bari C, McCaskie AW, Robey PG, Méndez-Ferrer S. A cholinergic neuroskeletal interface promotes bone formation during postnatal growth and exercise. *Cell Stem Cell*. 2022. 29:1-17.
3. Carola G, Malagarriga D, Calatayud C, Pons-Espinal M, Blasco-Agell L, Richaud-Patin Y, Fernandez-Carasa I, Baruffi V, Beltramone S, Molina E, Dell'Era P, **Toledo-Aral JJ**, Tolosa E, Muotri AR, Garcia Ojalvo J, Soriano J, Raya A, Consiglio A. Parkinson's disease patient-specific neuronal networks carrying the LRRK2 G2019S mutation unveil early functional alterations that predate neurodegeneration. *NPJ Parkinsons Dis*. 2021;7:55.
4. Villadiego J, Ramírez-Lorca R, Cala F, Labandeira-García JL, Esteban M, **Toledo-Aral JJ**, López-Barneo J. Is carotid body infection responsible for silent hypoxemia in COVID-19 patients?. *Function*. 2021. Vol 2, Issue 1, zqaa032.
5. Sánchez-Guijo F, García-Olmo D, Prósper F, Martínez S, Zapata A, Fernández-Avilés F, **Toledo-Aral JJ**, Torres M, Fariñas I, Badimón L, Labandeira-García JL, García-Sancho J, Moraleda JM. Spanish Cell Therapy Network (TerCel): 15 years of successful collaborative translational research. *Cytotherapy*. 2020. 22:1-5.
6. AQP1 and AQP4 Contribution to Cerebrospinal Fluid Homeostasis. Trillo-Contreras JL, **Toledo-Aral JJ**, Echevarría M, Villadiego J. *Cells*. 2019 Feb 24;8(2). pii: E197



7. Dual cholinergic signals regulate daily migration of hematopoietic stem cells and leukocytes. García-García A, Korn C, García-Fernández M, Domingues O, Villadiego J, Martín-Pérez D, Isern J, Bejarano-García JA, Zimmer J, Pérez-Simón JA, **Toledo-Aral JJ**, Michel T, Airaksinen MS, Méndez-Ferrer S. *Blood*. 2019 Jan 17;133(3):224-236.
8. Trillo-Contreras JL, Ramírez-Lorca R, Hiraldo-González L, Sánchez-Gomar I, Galán-Cobo A, Suárez-Luna N, Sánchez de Rojas-de Pedro E, **Toledo-Aral JJ**, Villadiego J, Echevarría M. Combined effects of aquaporin-4 and hypoxia produce age-related hydrocephalus. *Biochim Biophys Acta Mol Basis Dis*. 2018; 1864: 3515-3526.
9. Long-term immunosuppression for CNS mouse xenotransplantation: Effects on nigrostriatal neurodegeneration and neuroprotective carotid body cell therapy. Villadiego J, Romo-Madero S, García-Swinburn R, Suárez-Luna N, Bermejo-Navas A, Echevarría M, **Toledo-Aral JJ**. *Xenotransplantation*. 2018 Nov;25(6):e12410.
10. Immunization with α -synuclein/Grp94 reshapes peripheral immunity and suppresses microgliosis in a chronic Parkinsonism model. Villadiego J, Labrador-Garrido A, Franco JM, Leal-Lasarte M, De Genst EJ, Dobson CM, Pozo D, **Toledo-Aral JJ**[#], Roodveldt C. *Glia*. 2018 Jan;66(1):191-205. [#]*Co-corresponding Author*
11. Synaptic Regulator α -Synuclein in Dopaminergic Fibers Is Essentially Required for the Maintenance of Subependymal Neural Stem Cells. Perez-Villalba A, Sirerol-Piquer MS, Belenguer G, Soriano-Cantón R, Muñoz-Manchado AB, Villadiego J, Alarcón-Arís D, Soria FN, Dehay B, Bezard E, Vila M, Bortolozzi A, **Toledo-Aral JJ**, Pérez-Sánchez F, Fariñas I. *J Neurosci*. 2018 Jan 24;38(4):814-825
12. Chronic and progressive Parkinson's disease MPTP model in adult and aged mice. Muñoz-Manchado AB, Villadiego J, Romo-Madero S, Suárez-Luna N, Bermejo-Navas A, Rodríguez-Gómez JA, Garrido-Gil P, Labandeira-García JL, Echevarría M, López-Barneo J, **Toledo-Aral JJ**. *J Neurochem*. 2016 Jan;136(2):373-87.
13. Effects of Rho Kinase Inhibitors on Grafts of Dopaminergic Cell Precursors in a Rat Model of Parkinson's Disease. Rodriguez-Pallares J, Rodriguez-Perez AI, Muñoz A, Parga JA, **Toledo-Aral JJ**, Labandeira-García JL. *Stem Cells Transl Med*. 2016 Jun;5(6):804-15.
14. Direct confocal acquisition of fluorescence from X-gal staining on thick tissue sections. Levitsky KL, **Toledo-Aral JJ**, López-Barneo J, Villadiego J. *Sci Rep*. 2013 Oct 14;3:2937.
15. Cellular properties and chemosensory responses of the human carotid body. Ortega-Sáenz P, Pardal R, Levitsky K, Villadiego J, Muñoz-Manchado AB, Durán R, Bonilla-Henao V, Arias-Mayenco I, Sobrino V, Ordóñez A, Oliver M, **Toledo-Aral JJ**, López-Barneo J. *J Physiol*. 2013 Dec 15;591(24):6157-73.



16. Neuroprotective and reparative effects of carotid body grafts in a chronic MPTP model of Parkinson's disease. Muñoz-Manchado AB, Villadiego J, Suárez-Luna N, Bermejo-Navas A, Garrido-Gil P, Labandeira-García JL, Echevarría M, López-Barneo J, **Toledo-Aral JJ**. Neurobiol Aging. 2013 Mar;34(3):902-15.

C.2. Research projects and grants as PI

“Terapia celular en la enfermedad de Parkinson”
Consejería de Innovación, Ciencia y Empresa. Junta de Andalucía.
2009-2012 309.923 €

“Estudio del trasplante de células de cuerpo carotídeo en un modelo crónico de parkinsonismo en ratón”
Instituto de Salud Carlos III (FIS 09).
2010-2012 142.175 €

"Improving Translational Research Potential at the Institute of Biomedicine of Seville"
(ITRIBIS)
Co-leader of Work Package 1 - PROJECT MANAGEMENT.
European Commission (FP7-REGPOT-2012-2013-1/ITRIBIS/316151)
2013-2016 4.218.197 € (Budget for the whole Institute)

Red Temática de Investigación Cooperativa “Terapia Celular”
Instituto de Salud Carlos III (RD12/0019/0033)
2013-2016 152.960 €

Título: Uso de cuerpo carotídeo en terapia celular en la enfermedad de Parkinson
Entidad financiadora: Instituto de Salud Carlos III (PI12/02574).
2013-2018 109.505 €

“Terapia celular en la enfermedad de Parkinson”
Consejería de Innovación, Ciencia y Empresa. Junta de Andalucía (P12-CTS-2739)
2014-2019 191.875 €

“Desarrollo de una terapia para el tratamiento de variantes genéticas de alfa-sinucleína en la enfermedad de Parkinson”
MINECO (RTC-2015-3309-1) en colaboración con nLife Therapeutics
2015-2018 383.106 €

Red Temática de Investigación Cooperativa “Terapia Celular”
Instituto de Salud Carlos III (RD16/0011/0025)
2017-2022 284.999 €

“Envejecimiento y Regulación de la Expresión de GDNF en el Cuerpo Carotídeo: Relevancia Neuroprotectora”
Ministerio de Ciencia e Innovación. (PID2019-105995RB-I00) · Cuantía: 167.0706,00 €
2020 – 2023 167.706 €

“Aging dependent regulation of carotid body GDNF expresión: relevance in antiparkinsonian cell therapy”
Consejería de Economía, Conocimiento, Empresas y Universidad. (US-1380891)
2022-2023 90.000 €



C.4. Patents

1. Process for detecting X-gal precipitate or other opaque precipitates by means of confocal microscopy. Levitsky K, Villadiego J, **Toledo-Aral JJ**, López-Barneo J. International PCT: WO 2013/001113.

1. Stem cells derived from the carotid body and uses thereof. Pardal R, Ortega P, Durán R, Bonilla V, López-Barneo J, Ordoñez, **Toledo-Aral JJ**. PCT/EP2008/060192, extended 12/02/2010

C.5. Institutional responsibilities

2001 – 2005	Design and construction, Biomedical Research Laboratory-HUVR
2006 – 2011	Design and construction, Institute of Biomedicine of Seville – IBiS
2011 – present	Neuroscience Area Chair, Institute of Biomedicine of Seville – IBiS
2013 – present	Chair, Dept Physiology, Med School, Univ of Seville.
2001 – present	Chair and member of evaluation committees of national and regional agencies for Research centers, projects and human resources.