



CURRICULUM VITAE (CVA)

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Part A. PERSONAL INFORMATION

CV date

07/03/2023

First name	María de la Luz		
Family name	Montesinos Gutiérrez		

(*) Mandatory

A.1. Current position

Position	Associate Professor		
Initial date	24/03/2008		
Institution	Universidad de Sevilla		
Department/Center	Fisiología Médica y Biofísica	Facultad de Medicina	
Country	Spain		
Key words	local translation, Down syndrome, mTOR, synaptic plasticity, memory		

A.2. Previous positions (research activity interruptions, art. 14.2.b))

Period	Position/Institution/Country/Interruption cause
2003 - 2008	“Ramón y Cajal” Researcher/Universidad de Sevilla/Spain
2002 - 2003	Researcher (Human Frontiers Science Programme)/Ecole Normale Supérieure-CNRS/France
2001-2002	Atachée Temporaire d'Enseignement et de Recherche)/Ecole Normale Supérieure-CNRS/France
2000-2001	Postdoctoral Researcher (Fondation pour la Recherche Médicale”)/Ecole Normale Supérieure-CNRS/France
1999-2000	CNRS Associated Researcher (CR3)/Ecole Normale Supérieure-CNRS/France
1997-1999	Postdoctoral EMBO Fellow/Ecole Normale Supérieure-CNRS/France
1993-1997	Predoctoral FPD (Regional Government of Andalusia) fellow/Instituto de Bioquímica Vegetal y Fotosíntesis (CSIC-Universidad Sevilla)/Spain

A.3. Education

PhD, Licensed, Graduate	University/Country	Year
DEGREE IN BIOLOGY	Universidad de Sevilla /Spain	1992
PhD in BIOLOGY	Universidad de Sevilla /Spain	1997

Part B. CV SUMMARY (max. 5000 characters, including spaces)



Since 2008 I am Associate Professor at the School of Medicine of the University of Seville. I am author of 27 indexed publications (Scopus). My H-index is 19. I have 1,0141 citations. During my scientific career I have participated in 26 research projects (in 19 of them as Principal investigator). I have supervised 4 Doctoral Thesis.

After conducting my doctoral work (1997) on amino acid transport in cyanobacteria (Instituto de Bioquímica Vegetal y Fotosíntesis, CSIC-Universidad de Sevilla, Spain), I focused my interest in the development of vertebrate CNS. I did a 6-years postdoc in the laboratory led by Alain Prochiantz (École Normale Supérieure, Paris). During that period (1997-2003) I was a Postdoctoral EMBO fellow (1997/99), Associate Researcher CR3 (funded by CNRS, 1999/2000), Postdoctoral fellow from FRM ("Foundation pour la Recherche Medicale", 2001/01), Assistant Professor (ATER) of Molecular and Cellular Genetics (2001/02), and Associate Researcher (funded by Human Frontier Science Program, 2002/03). In that period, I worked on the identification of homeoprotein-target genes and cofactors. Some of the results obtained were published in journals such as Nature Biotechnology, The Journal of Neuroscience, or Development.

I returned to Spain in 2003 as a "Cajal Program" Investigator, and I was associated to the laboratory of Rafael Fernández-Chacón (Universidad de Sevilla) for two years, working on synaptic proteins involved in neurodegeneration, and teaching at the School of Medicine. From this period, I would like to highlight our publication in Neuron, in collaboration with Thomas C. Südhof (Nobel Prize in Physiology 2013). By the end of 2005 I obtained some funding from the *Plan Nacional* (FIS) and the Jérôme Lejeune Foundation (France) to start a completely new line of research in the field of Down Syndrome (DS) in my University. In 2007 I obtained the *Habilitación Nacional para el Cuerpo de Profesores Titulares de Universidad* and I was positively evaluated by the I3 Program. As stated above, since March 2008, I am Associate Professor of Physiology at the School of Medicine (Universidad de Sevilla), where I regularly teach (Degrees of Medicine and Biomedicine; also teacher at the "Master Universitario en Investigación Biomédica"). Since December 2014, I am also Researcher affiliated to the Institute of Biomedicine in Seville (IBiS).

The team I lead has been the first to study local translation in the context of DS. We have focused primarily (but not exclusively) on the Akt-mTOR pathway, and have patented the ability of rapamycin, an mTOR inhibitor, to reverse important pathological aspects affected in a DS mouse model. Some of the results obtained have been published in journals such as The Journal of Neuroscience, Neurobiology of Disease, or Molecular Brain. From 2005 to date, we have had funding from the *Plan Nacional* (4 projects and 1 *Acción Integrada* with France), from private national and international foundations (1 project from Fundación Ramón Areces, Spain; 5 projects from the Fondation Jérôme Lejeune, France), as well as regional funding (2 Excellence Projects of the Andalusian Government).

I am evaluator at the ANEP (Agencia Nacional de Evaluación y Prospectiva, Spain) since 2008, and at CINECA (Ministero dell'Instruzione, dell'Università e della Ricerca, Italy) since 2012. I have been ad hoc evaluator for Fondation pour la Recherche Medicale (FRM, France), Medical Research Council (MRC, UK) and Fondazione Telethon (Italy). I belong to the Peer Review Board of the Journal of Visualized Experiments (JOVE) since 2011, and I also act as ad hoc referee for journals such as Brain Pathology, Neurobiology of Disease, Human Molecular Genetics, Journal of Neurochemistry, Journal of Biological Chemistry, Molecular and Cellular Neuroscience, Neuropharmacology, Neuroscience Letters, OMICs, PlosOne, Neural Plasticity, Journal of Neuroscience, Nature Communications, Experimental Neurology, Molecular Neurobiology, among others. I have been Executive Board Member of SENC (Sociedad Española de Neurociencia), Chair of the SENC Communication Committee, member of the FENS (Federation of European Neuroscience Societies) Communication Committee, and Chair of the Trisomy 21 Research Society (T21RS) Communication Work Group.



Part C. RELEVANT MERITS (sorted by typology)

C.1. Publications (see instructions)

- 1) **Scientific paper.** JJ. Casañas, ML. Montesinos (2022). Proteomic characterization of spinal cord synaptoneurosomes from Tg-SOD1/G93A mice supports a role for MNK1 and local translation in the early stages of amyotrophic lateral sclerosis. **Molecular and Cellular Neuroscience** 123:103792.
- 2) **Scientific paper.** JD. Urbano-Gámez, I. Benito, JJ. Casañas, ML. Montesinos (2021). Prenatal treatment with rapamycin restores enhanced hippocampal mGluR-LTD and mushroom spine size in a Down's syndrome mouse model. **Molecular Brain** 14(1):84.
- 3) **Scientific paper.** JJ. Casañas, M. González-Corrales, JD. Urbano-Gámez, A. Alves-Sampaio, JA. Troca-Marín, ML. Montesinos (2019). CPEB1 is overexpressed in neurons derived from Down syndrome iPSCs and in the hippocampus of the mouse model Ts1Cje. **Molecular and Cellular Neuroscience** 95:79-85.
- 4) **Scientific paper.** I. Benito, JJ. Casañas and ML. Montesinos (2018). Proteomic analysis of synaptoneurosomes highlights the relevant role of local translation in the hippocampus. **Proteomics** 18:e1800005.
- 5) **Scientific paper.** ML. Montesinos (2017). Local translation of the Down Syndrome Cell Adhesion Molecule (DSCAM) mRNA in the vertebrate central nervous system. **Journal of Neurogenetics** 31: 223-230.
- 6) **Scientific paper.** Y. Andrade-Talavera, I. Benito, JJ. Casañas, A. Rodríguez-Moreno and ML. Montesinos (2015). Rapamycin restores BDNF-LTP and the persistence of long-term memory in a model of Down's syndrome. **Neurobiology of Disease** 82: 516-525.
- 7) **Book chapter.** ML. Montesinos (2014). Roles for DSCAM and DSCAML1 in central nervous system development and disease. **Adv Neurobiol.** 8:249-270.
- 8) **Scientific paper.** JA. Troca-Marín, JJ. Casañas, I. Benito and ML. Montesinos (2014). The Akt-mTOR pathway in Down's syndrome: the potential use of rapamycin/rapalogs for treating cognitive deficits. **CNS Neurol Disord Drug Targets** 13:34-40.
- 9) **Scientific paper.** ML. Montesinos (2014). Pharmacological intervention for Down syndrome cognitive deficits: Emerging drug targets. **CNS Neurol Disord Drug Targets** 13: 6–7.
- 10) **Scientific paper.** JA. Troca-Marín, A. Alves-Sampaio and ML. Montesinos (2012). Deregulated mTOR-mediated translation in intellectual disability. **Progress in Neurobiology** 96:268-282.
- 11) **Scientific paper.** JA. Troca-Marín, A. Alves-Sampaio and ML. Montesinos (2011). An increase in basal BDNF provokes hyperactivation of the Akt-mammalian target of rapamycin pathway and deregulation of local dendritic translation in a mouse model of Down's syndrome. **The Journal of Neuroscience** 31: 9445-9455.

C.2. Congress

- 1) M.L. Montesinos. Deregulated mTOR-mediated translation in different intellectual disabilities. 32nd ECNP (European College of Neuropsychopharmacology) Congress. 2019. Denmark. Invited talk.
- 2) J.J. Casañas; I. Benito; M.L. Montesinos. Proteomic characterization of synaptoneurosomes from a Trisomy 21 mouse model provides clues to explain the benefits of rapamycin on synaptic plasticity. 11th FENS Forum of Neuroscience. FENS. 2018. Germany. Poster.
- 3) J.J. Casañas; B. Galán-Rodríguez; A. Alves-Sampaio; J.A. Troca-Marín; M.L. Montesinos. Dendritic function of alpha-CaMKII is impaired in a mouse model of Down's syndrome. 10th FENS Forum of Neuroscience. FENS. 2016. Denmark. Poster.
- 4) M.L. Montesinos. Local translation, plasticity and memory in trisomy 21: a therapeutic opportunity for rapamycin? XXXVIII Congreso de la Sociedad Española de Bioquímica y Biología Molecular. SEBBM. 2015. Spain. Invited talk.
- 5) M.L. Montesinos; Y. Andrade-Talavera; I. Benito; J.J. Casañas; A. Rodríguez-Moreno. Rapamycin reverses plasticity and memory deficits of Ts1Cje mice. Trisomy 21 Research Society: Changing Paradigms in Down Syndrome. Trisomy 21 Research Society. 2015. France. Poster.
- 6) M.L. Montesinos. mTOR-dependent plasticity and memory in Trisomy 21. 16th National Congress of the Spanish Society of Neuroscience (SEBBM). SENC. 2015. Spain. Invited talk.



- 7) M.L. Montesinos. BDNF levels and deregulation of local translation in Down's syndrome. Mechanisms of neurotrophic factors in health and disease. Ramon Areces International Symposium. Fundación Ramón Areces. **2013**. Spain. Invited talk.
- 8) J.J. Casañas; A. Alves-Sampaio; J.A. Troca-Marín; M.L. Montesinos. Synaptic levels of localized mRNAs are broadly affected in a mouse model of Down's syndrome. 10th International Conference on Intracellular RNA localization and localized translation. **2013**. Canada. Poster.
- 9) J.A. Troca-Marín; A. Alves-Sampaio; I. Benito; J.J. Casañas; B. Northrop; M.L. Montesinos. Akt-mTOR deregulation in Down's syndrome. Jacques-Monod conference - Mechanisms of Intellectual Disability from genes to treatment. **2012**. France. Oral communication.
- 10) J.A. Troca-Marín; J.J. Casañas; I. Benito; B.N. Sharp; M. Bertrand; F. Stella; M.L. Montesinos. mTOR signaling in Down's syndrome intellectual disability. Synaptic Basis of Disease (Synbad). **2012**. Switzerland. Poster.

C.3. Research projects

- 1) Reference: #2004_2020B. Title: Role of SOD1 in hippocampal long-term depression and its relevance for altered plasticity in Trisomy 21. PI: María Luz Montesinos (Universidad de Sevilla). Funding agency: Fondation Jérôme Lejeune (France). Duration: 15/02/2021-15/02/2023. Funding: 40.000 €
- 2) Reference: SAF2015-65032-R. Title: Señalización mGluR1/5-mTOR y traducción local de APP en modelos de síndrome de Down. Potencial terapéutico de la rapamicina. PI: María Luz Montesinos (Universidad de Sevilla). Funding agency: MINECO. Proyectos de I+D+I (Retos). Convocatoria 2015. Duration: 01/01/2016-31/12/2018. Funding: 145.200 €
- 3) Reference: P12-CTS-1818. Title: Desregulación de mTOR y déficit cognitivo. PI: María Luz Montesinos (Universidad de Sevilla). Funding agency: Junta de Andalucía. Consejería de Innovación, Ciencia y Empresa. Incentivos a Proyectos de Investigación de Excelencia. Convocatoria 2012. Duration: 30/01/2014-01/08/2018. Funding: 192.919 €
- 4) Reference: no reference. Title: Maladie d'Alzheimer dans la trisomie 21: rôle de la traduction locale de l'ARNm APP. PI: María Luz Montesinos (Universidad de Sevilla). Funding agency: Fondation Jérôme Lejeune (France). Duration: 21/07/2014-21/01/2018. Funding: 40.000 €
- 5) Reference: PI11/00507. Title: Fisiopatología neuronal del síndrome de Down: hipótesis del bucle de retroalimentación positiva glutamatérgico y traslación del modelo animal a la patología humana. PI: María Luz Montesinos (Universidad de Sevilla). Funding agency: Instituto de Salud Carlos III. Ministerio de Economía y Competitividad. Convocatoria 2011. Duration: 01/01/2012-30/09/2015. Funding: 96.300 €
- 6) Reference: no reference. Title: Potentiel de la rapamycine pour le traitement des déficiences cognitives de la trisomie 21. PI: María Luz Montesinos (Universidad de Sevilla). Funding agency: Fondation Jérôme Lejeune (France). Duration: 21/07/2011-20/07/2013 Funding: 33.600 €
- 7) Reference: P09-CTS-4610. Title: Transporte y traducción local de mRNAs dendríticos en patologías neuronales. PI: María Luz Montesinos (Universidad de Sevilla). Funding agency: Junta de Andalucía. Consejería de Innovación, Ciencia y Empresa. Incentivos a Proyectos de Investigación de Excelencia. Convocatoria 2009. Duration: 03/02/2010-02/01/2014. Funding: 178.671 €
- 8) Reference: PI08/1401. Title: Papel de la traducción local de DSCAM y otros genes del cromosoma 21 en los defectos dendríticos asociados al síndrome de Down. PI: María Luz Montesinos (Universidad de Sevilla). Funding agency: Instituto de Salud Carlos III. Ministerio de Ciencia e Innovación. Convocatoria 2008. Duration: 01/01/2009-31/12/2011. Funding: 143.627 €

C.4. Contracts, technological or transfer merits

Patents

Title: "Uso de la rapamicina y otros inhibidores de la vía mTOR para el tratamiento del síndrome de Down"

Authors: ML Montesinos, JA Troca-Marín, A Alves-Sampaio

Date: 24/06/2010

Patent number: P201000840 (Spain)