BIOGRAPHICAL SKETCH

NAME: Dierssen Sotos, Mara

eRA COMMONS USER NAME (credential, e.g., agency login): MARADIERSSEN

POSITION TITLE: Senior Group Leader at CRG ; Director of the Associated Unit for Behavioural Research (National Biotechnology Center-CSIC)

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YYYY	FIELD OF STUDY
University of Cantabria, Santander	MD	1985	Medicine
Hospital M. Valdecilla, Santander	Master Thesis	1986	Neuropharmacology
University of Cantabria, Santander	PhD	1989	Neuroscience
Autonomous University of Barcelona	Diplomate	1991	Radioactiv Inst. Supervisor
Autonomous University of Barcelona	Postdoctoral fellowship	1991-1994	Neuropharmacology

A. Personal Statement

The main focus of my laboratory is to understand how genetic perturbation in mental disorders modifies the way the brain integrates information. I have focused my research on Down syndrome and the main questions in the field remains. My work has been published in more than 160 peer-reviewed papers, with contributions to Nat Rev. Neurosci, Nature Medicine, Lancet Neuroogy, or PNAS (h index 46). I received several awards for her work in intellectual disability including Ramón Trias Fargas, Jaime Blanco, Trifermed Social Impact of Healthcare Award, or Sisley-Lejeune awards and the National Science Culture Award from the Generalitat de Catalunya. I am president of the Trisomy 21 Research Society, and past-president of the Spanish Society of Neuroscience, and the International Behavioral and Neural Genetics Society, and I served as executive committee member of the Federation of European Neuroscience Societies (FENS) and several committees of SfN. I am member of Editorial Boards (Genes Brain and Behavior, Frontiers in Behavioral Neuroscience, Amino Acids, Frontiers in Genetics among other) and have organized many international research conferences. I serve as evaluator of different Scientific Committees and Boards (ERC, Spanish National Evaluation Agency, Panel Expert for EU) and as associated editor of several journals. I am member of the Academia Europaea and of the European DANA Allianze for the Brain. I was Associated Professor of the University of Cantabria and Professor at the University Ramon Llull in Barcelona.

1. Ruiz-Mejias M, … **Dierssen M.** Overexpression of Dyrk1A, a Down syndrome candidate, decreases excitability and impairs gamma oscillations in prefrontal cortex. (2016) ***J Neurosci.*** 36: 3648-59 PMID: 27030752
2. **Dierssen M.** Down syndrome: the brain in trisomic mode. (2012) ***Nat Rev Neurosci.*** 13:844-58 PMID: 23165261
3. Martinez de Lagran M, …**Dierssen M.** Dyrk1A influences neuronal morphogenesis through regulation of cytoskeletal dynamics in mammalian cortical neurons (2012) ***Cereb Cortex.*** 22(12):2867-77 PMID: 22215728
4. **Dierssen M,** Benavides-Piccione R, Martínez-Cué C, Estivill X, Flórez J, Elston GN, DeFelipe J. Alterations of neocortical pyramidal cell phenotype in the Ts65Dn mouse model of Down syndrome: effects of environmental enrichment. (2003) ***Cereb Cortex*** 13:758-64 PMID: 12816891

B. Positions and Honors

Positions and Employment

1989 – 1990 Research fellow Freie Universität Berlin
1993 - 1997 Assistant Professor, Group leader, University of Cantabria
1997 - 2001 Senior scientist, Institute of Oncology Research-IRO, Barcelona
2002 - Senior Scientist, Centre for Genomic Regulation-CRG, Barcelona
2007 - Researcher of the Centre for Biomedical Research on Rare Diseases-CIBERER

Other Experience and Professional Memberships

2018 Distinguished member of the College of Medicine
2018 President Trisomy 21 Research Society 2016
2017 Distinguished Alumni University of Cantabria
2016 Chair Program Committee Trisomy 21 Research Society 2016
2013-2016 Founder member and Secretary General of the Trisomy 21 Research Society (www.t21rs.org)
2013-2015 President of the Spanish Neuroscience Society
2014 Member of the Academia Europaea
2014- Chair of the Woman in Neuroscience Committee of the Society for Neuroscience
2014- Member of the "Woman in Science" Commission of the Catalan Government
2013- Member of the Professional Development Committee of the Society for Neuroscience
2013- Member of the Rigor in Science Committee of the Society for Neuroscience
2010 - 2012 Executive Committee Member of FENS (Federation of European Neuroscience Societies)
2010 - Member of EDAB (European DANA Allianze for the Brain)
2010 - Committee Member of COSCE (Confederation of Spanish Science Societies)
2008 - Member of Barcelona Science Culture Council
2007 - 2009 Vice-president Spanish Society of Neuroscience (From 2005, member of Executive Committee)
2005 - Member of Barcelona Culture Institute Board of Directors
2003 - 2006 President International Behavioural and Neural Genetics Society
2002 - Member of the Council of FENS (Federation of European Neuroscience Societies)
Member of the Federation of European Neuroscience Societies, Federation of Spanish Science Societies, International Behavioural and Neural Genetics Society, European Dana Alliance for the Brain, European Brain and Behaviour Society, Confederation of Spanish Science Societies, Society for Neuroscience.

Honors

2018 Trébol Award (Down Spain)
2018 Distinguished member College of Medicine (Cantabria)
2018 Optmistas Comprometidos Award
2017 Trifermed Social Impact of Healthcare Award
2017 BigVang Medal
2016 Distinguished Alumni of the University of Cantabria
2016 Best Ideas Award for the clinical trial in Down syndrome
2015 Fundación Esteve Award
2014 David and Hillie Mahoney Award
2013 Ramón Trías Fargas Award
2011 Alicia Koplowitz Award
2010 Sisley-Lejeune Award
2008 Laura Iglesias award for women in science
2008 National Culture Award for Science
2002 and 2009 Jaime Blanco Award for Down syndrome research
2003 and 2008 Ramón Trias Fargas Award for Down syndrome research

Editorial activity

Editorial Board of Acta Neuropathologica; Amino Acids, Senior Editor Down Syndrome Research and Practice, Associate Editor BMC Neuroscience;Genes, Brain and Behaviour, Reviewer Editor Frontiers in Neurosciences, Frontiers Genetics of Complex Traits. *Reviewer "ad hoc" for more than 25 international journals* (Nature Neuroscience, Science, Journal of Neuroscience, PNAS, Human Molecular Genetics, Cerebral Cortex, Brain etc.)

C. Contributions to Science

1. Understanding the influence of neuronal architecture and connectivity disturbances on mesoscopic network activity and behavioral outcomes in intellectual disabilities and neurodegenerative disorders

We showed abnormal number, size or shape of dendrites and dendritic spines in Down syndrome (DS) mouse models, which correlate with learning and memory impairment (Cerebral Cortex, 2003). We reconstructed pyramidal neurons from the cerebral cortex and hippocampus; two regions involved in the DS cognitive

phenotypes, in basal conditions and after normalizing the genetic overexpression of candidate genes in trisomy (Cerebr. Cortex 2003; Brain Res., 2000). We could then proof the predictive validity of these findings in humans (J. Alzheimer's Disease 2017). Interestingly, either increasing or decreasing the number of dendritic spines (that act as neuronal connectors) will have detrimental effects on cognition (Neurobiol. Dis., 2005). The main question we addressed is what genetic disturbances in DS leading to dendritic wiring alterations are impeding the correct filling of this optimal target space. Building upon these results, we have developed morphological algorithms (L. Manubens in preparation) to explain experimental observations on the Ts65Dn mouse model of DS at the cellular level in terms of dendritic length, tortuosity and branching.

1. **Dierssen M,** … DeFelipe J (2003) ***Cerebr Cortex*** 13: 758-64. Alterations of neocortical pyramidal cell phenotype in the Ts65Dn mouse model of Down syndrome: effects of environmental enrichment.
2. Kurt MA, … **Dierssen M**, Davies DC (2004) ***Brain Res.*** 1022: 101-9. Deficits of neuronal density in CA1 and synaptic density in the dentate gyrus, CA3 and CA1, in a mouse model of Down syndrome.
3. Benavides-Piccione R, … **Dierssen M**. (2005) ***Neurobiol. Disease*** 20:115-122. Alterations in the phenotype of neocortical pyramidal cells in the DYRK1A+/- mouse.
4. Fenoll R, … **Dierssen M**, Novell-Alsina R, de la Torre R. (2017) **J Alzheimer's Dis**.;57(1):61-70 Anomalous White Matter Structure and the Effect of Age in Down Syndrome Patients.

2. Effect of deregulated gene expression on neuronal structure and connectivity in Down syndrome

The **dendritic arbor of a neuron is the outcome of the systems-level behavior of the network of genes and proteins** that underlie dendrite elongation and neurite outgrowth. Since branching is produced by changes in the cytoskeleton involving microtubules and actin filaments, proteins that alter cytoskeleton dynamics have a significant effect on dendritic branching. We established the causal involvement of the overexpression of Dyrk1A on dendrite stability and growth and on switching between neurite elongation and branching.

1. Martinez de Lagran M … **Dierssen M** (2012) ***Cerebral Cortex*** 22(12), 2867-77. Dyrk1A Influences Neuronal Morphogenesis Through Regulation of Cytoskeletal Dynamics in Mammalian Cortical Neurons
2. Carrasco P, Sahun I, … **Dierssen M**, Casals N. (2012) ***J Biol Chem***. 287(25):21224-32Ceramide levels regulated by carnitine palmitoyl transferase 1C control dendritic spine maturation and cognition.
3. Altafaj X, **Dierssen M,** et al. (2001) ***Hum. Mol. Genet.*** 10: 1915-23. Neurodevelopmental delay, motor abnormalities and cognitive deficits in transgenic mice overexpressing Dyrk1A (minibrain), a murine model of Down's syndrome.

3. Using computational neuronal network simulations to predict the effects of neuronal connectivity disturbances in brain disorders

One of the topics that recently emerged from our research is the classification of spontaneous neuronal network activity relative to the underlying connectivity. We studied various types of neural-based signals, such as EEG, local field potentials and intracellular synaptic potentials that exhibit a power-law frequency scaling structure. Since the oscillatory electrical activity is also dependent on the brain region and on the cognitive state (including cognitive disorders), we explored how the dynamics rely on the specificity of the network architecture (J Neurosci, 2016, 2013). Recently, we have studied the occurrence of propagating waves in cortical networks, using multiarray recording electrodes (J Neurosci, 2016). In this case, the propagating waves depend on the state of the network, explaining diverse results obtained in different preparations (awake or anesthetized). This translates into changes in functional connectivity detected in patients (Cortex, 2015).

1. Ruiz-Mejias M, … **Dierssen M.** ***Journal of Neuroscience*** (2016); 36(13): 3648-3777 Overexpression of Dyrk1A, a Down Syndrome Candidate, Decreases Excitability and Impairs Gamma Oscillations in the Prefrontal Cortex.
2. Pujol J… **Dierssen M,** de la Torre R. ***Cortex*** (2015); 64:148-56. Anomalous brain functional connectivity contributing to poor adaptive behavior in Down syndrome.
3. Santos M**, Dierssen M.** Hippocampal Hyperexcitability Underlies ***J Neurosci.*** (2013); 33(38): 15259-71, Enhanced Fear Memories in TgNTRK3, a Panic Disorder Mouse Model.
4. Del Pino I… **Dierssen M,** Canals S, Marín O, Rico B. ***Neuron*** (2013) 79(6):1152-68. Erbb4 deletion from fast-spiking interneurons causes schizophrenia-like phenotypes

4. Neurobiology and therapy for brain disorders

My group has contributed to the understanding of disorders such as panic disorder (J Neurosci, 2013, 2016), schizophrenia (Neuron 2013), and intellectual disability and has proposed hypothesis-driven therapies some of which went through the clinics (Lancet Neurology, 2016, Nature Medicine, 2013)

1. De la Torre R… **Dierssen M**. ***The Lancet Neurology***, (2016), 15(8):801-10 Safety and efficacy of the combination of cognitive training and epigallocatechin-3-gallate for cognitive improvement in adults with Down syndrome: a double-blind randomised controlled trial.
2. D'Amico D, … **Dierssen M.** ***Neuropsychopharmacol***. (2016) Infralimbic Neurotrophin-3 infusion rescues fear extinction impairment in a mouse model of pathological fear. PMCID:PMC5399232
3. Busquets-Garcia, M. … **M. Dierssen**, R. Maldonado, A. Ozaita, ***Nature Medicine,*** (2013); 9(5):603-7,
4. Targeting the endocannabinoid system in the treatment of fragile X syndrome.

Metrics:
Publications: 167 (https://www.ncbi.nlm.nih.gov/pubmed/?term=dierssen+m)
ORCID: 0000-0003-0853-6865
RESEARCHER ID: G-3552-2015
h-index: 46

D. Research Support
Ongoing Research Support
2020-2024 European Commission H2020 – SC1 Gene overdosage and comorbidities during the early lifetime in Down Syndrome GO-DS21. Role: Partner
2018-2020 European program JPND (Joint Program on Neurodegenerative Diseases) HEROES (tHE cRossroad Of dEmentia Syndromes).Role: Coordinator
2017-2019 SAF2016-79956-R. ReModelling BRAiN DevelopmenT in intellectual disability (REMBRANDT) *Ministry of Economy and Competitiveness* Role: PI
2017-2019 Marató TV3. Study Of New Molecular Targets In Preclinical Models Of Obesity. Role: co-PI
2017-2019 Consolidated Research Group. *Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR-SGR).* Role: PI
Completed research support (selected)
2013-2016 FOOD for THOUGHT: epigenomics of eating disorders. Era Net Neuron (EC) Role: PI
2014-2016 Estrategias terapéuticas para la recuperación cognitiva en la discapacidad intelectual *Plan Estatal Retos de la Sociedad – Ministerio de Economía y Competitividad*. Role: PI
2014-2016 *CDTI Investigación Industrial y Desarrollo Experimental de Alimentos Inteligentes* SMARTFOODS. Role: PI
2013-2015 Destabilizing FMR1 mRNA as a therapeutic strategy to treat FXTAS (SB/NF2013-0175n16649) Association Francaise contre les Myopathies (AFMTéléthon) Role: PI
2013-2016 Estrogen Receptors beta (ER-β) as Therapeutic Targets for the Improvement of Cognitive Performance in Fragile X FRAXA Foundation Role: PI
2013-2015 The role of Dyrk1A in Down syndrome obesity: mechanism and therapeutic approaches Jerome Lejeune Foundation Role: PI