BIOGRAPHICAL SKETCH

NAME: Ilaria Meloni

POSITION TITLE: Associate professor, Medical Genetics, Department of Medical Biotechnologies, University of Siena

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Siena	M.S.	03/1999	Biology
University of Siena	PhD	2004	Mechanisms of Neurodegeneration, Neuroprotection and Neuroreparation in rare neurological diseases
University of Siena	Specialist	2007	Medical Genetics

A. Personal Statement

I'm a molecular geneticist and my main research interest is the molecular bases of X-linked forms of intellectual disability. In this context, I identified ACSL4, a new causative gene for X-linked intellectual disability. Subsequently, I focused on Rett Syndrome. In order to establish an innovative human cellular model for the study of the mechanisms underlying this pathology, I gained experience in genetic reprogramming and generated induced pluripotent stem cells (iPSCs = induced Pluripotent Stem Cells) from patients with mutations in the three genes associated with Rett syndrome: MECP2, CDKL5 and FOXG1. In recent years, I used these cells to study the molecular mechanisms of disease. I'm currently using this cellular model to evaluate the feasibility of gene editing via CRISPR/Cas9 as an approach for the correction of pathogenetic mutations in genes associated with Rett syndrome. I'm also continuing to pursue research on the molecular bases of RTT using both iPSCs for functional characterization and Next Generation Sequencing approach for the definition of the role of genetic baclkground. My work has led to the publication of 81 scientific papers in international journals with a total IF of 425,3726 (H index according to Scopus:32).

B. Positions, Scientific Appointments, and Honors

Institution	**Division/ Research group**	**Location**	**Position**	**From year**	**To year**
University of Siena	Medical Genetics Unit	Siena	Post-doctoral fellow	2004	2007
University of Leuven	VIB Laboratory of Neuronal Differentiation	Leuven	Visiting Fellow	2007	2008
University of Siena	Medical Genetics Unit	Siena	Post-doctoral fellow	2008	2009
University of Toronto	Developmental & Stem Cell Biology Program	Toronto	Visiting Fellow	2009	2010
University of Siena	Medical Genetics Unit	Siena	Post-doctoral fellow	2010	2016
Yale University School of Medicine	Child Study Center	New Haven	Laboratory Associate	2013	2013

University of Siena	Medical Genetics Unit	Siena	Senior Research Associate	2016	2019
University of Siena	Medical Genetics Unit	Siena	Associate Professor	2019	Today

C. Contributions to Science

I worked for some years on the identification of new causative genes for X-linked mental retardation and my work resulted in the identification and characterization of ACSL4 (Meloni I et al, Nat Genet 2002; Meloni I et al, Neuroscience 2009). Subsequently, I focused my research on Rett syndrome, with the aim to clarify the molecular mechanisms of disease and to verify whether mutations in the 3 genes presently associated to the disease (MECP2, CDKL5 and FOXG1) cause disease by alteration of similar/common pathways. To this aim, I acquired expertise in the technique of genetic reprogramming that allows deriving pluripotent stem cells, known as iPSCs (induced Pluripotent Stem Cells) directly from adult human fibroblasts. This human patient-specific cellular model has been fundamental to start a research focused at clarifying the molecular mechanisms of Rett syndrome and to verify whether similar mechanisms are involved following mutations in the 3 genes presently associated to the disease (Amenduni et al. Eur J Hum Genet. 2011; Livide G et al, Eur J Hum Genet. 2015; Patriarchi T, et al. Eur J Hum Genet. 2016). Since 2017 I'm focusing on CRISPR-based genome editing as an innovative therapy for Rett syndrome and associated disorders.

D. Relevant publications

1- Zappella M, Meloni I, Longo I, Canitano R, Hayek G, Rosaia L, Mari F, Renieri A. Study of MECP2 gene in Rett syndrome variants and autistic girls. **Am J Med Genet B Neuropsychiatr Genet**. 2003; 119 (1): 102-7.
2- Scala E, Ariani F, Mari F, Caselli R, Pescucci C, Longo I, Meloni I, Giachino D, Bruttini M, Hayek G, Zappella M, Renieri A. CDKL5/STK9 is mutated in Rett syndrome variant with infantile spasms. **J Med Genet**. 2005; 42(2):103−7.

3- Mari F, Caselli R, Russo S, Cogliati F, Ariani F, Longo I, Bruttini M, Meloni I, Pescucci C, Schurfeld K, Toti P, Tassini M, La rizza L, Hayek G, Zappella M, Renieri A. "Germline mosaicism in Rett sindrome identified by prenatal diagnosis". **Clin Genet**. 2005; 67(3):258-60.
4- Ariani F, Hayek G, Rondinella D, Artuso R, Mencarelli MA, Spanhol−Rosseto A, Pollazzon M, Buoni S, Spiga O, Ricciardi S, Meloni I, Longo I, Mari F, Broccoli V, Zappella M, Renieri A. FOXG1 is responsible for the congenital variant of Rett syndrome. **Am J Hum Genet**. 2008; 83(1):89−93.
5- Meloni I, Parri V, De Filippis R, Ariani F, Artuso R, Bruttini M, Katzaki E, Longo I, Mari F, Bellan C, Dotti CG, Renieri A. The XLMR gene ACSL4 plays a role in dendritic spine architecture. **Neuroscience**. 2009; 159 (2): 657-69.

6- Amenduni M, De Filippis R, Cheung AY, Disciglio V, Epistolato MC, Ariani F,Mari F, Mencarelli MA, Hayek Y, Renieri A, Ellis J, Meloni I. iPS cells to model CDKL5-related disorders. **Eur J Hum Genet**. 2011;19(12):1246-55.

7- Livide G, Patriarchi T, Amenduni M, Amabile S, Yasui D, Calcagno E, Lo Rizzo C, De Falco G, Ulivieri C, Ariani F, Mari F, Mencarelli MA, Hell JW, Renieri A, Meloni I. GluD1 is a common altered player in neuronal differentiation from both MECP2-mutated and CDKL5-mutated iPS cells. **Eur J Hum Genet**. 2015; 23(2): 195-201.

8- Frullanti E, Amabile S, Lolli MG, Bartolini A, Livide G, Landucci E, Mari F, Vaccarino FM, Ariani F, Massimino L, Renieri A, Meloni I. Altered expression of neuropeptides in FoxG1-null heterozygous mutant mice. **Eur J Hum Genet**. 2016; 24(2): 252-7.

9- Pecorelli A, Belmonte G, Meloni I, Cervellati F, Gardi C, Sticozzi C, De Felice C, Signorini C, Cortelazzo A, Leoncini S, Ciccoli L, Renieri A, Jay Forman H, Hayek J, Valacchi G. Alteration of serum lipid profile, SRB1 loss, and impaired Nrf2 activation in CDKL5 disorder. **Free Radic Biol Med**. 2015; 86: 156-165.

10- Patriarchi T, Amabile S, Frullanti E, Landucci E, Lo Rizzo C, Ariani F, Costa M, Olimpico F, W Hell J, M Vaccarino F, Renieri A, Meloni I. Imbalance of excitatory/inhibitory synaptic protein expression in iPSCderived neurons from FOXG1+/- patients and in foxg1+/- mice. **Eur J Hum Genet**. 2016; 24(6): 871-80.

11- Landucci E, Brindisi M, Bianciardi L, Catania LM, Daga S, Croci S, Frullanti E, Fallerini C, Butini S, Brogi S, Furini S, Melani R, Molinaro A, Lorenzetti FC, Imperatore V, Amabile S, Mariani J, Mari F, Ariani F, Pizzorusso T, Pinto AM, Vaccarino FM, Renieri A, Campiani G, Meloni I. iPSC-derived neurons profiling reveals GABAergic circuit disruption and acetylated α-tubulin defect which improves after iHDAC6 treatment in Rett syndrome. **Exp Cell Res**. 2018; 368(2): 225-235.

12- Gao Y, Irvine EE, Eleftheriadou I, Jimenez Naranjo C, Hearn-Yeates F, Bosch L, Murdoch L, Czerniak A, Glegola JA, Meloni I, Renieri A, Kinali M & Mazarakis ND. Gene replacement ameliorates deficits in mouse and human models of CDKL5 disorder. **Brain** 2020; 143(3):811-832.

13- Croci S, Carriero ML, Capitani K, Daga S, Donati F, Frullanti E, Lamacchia V, Tita R, Giliberti A, Valentino F, Benetti E, Ciabattini A, Furini S, Lo Rizzo C, Pinto AM, Conticello SG, Renieri A, Meloni I. High Rate of HDR in gene editing of T158M MECP2 mutational hotspot. **Eur J Hum Genet.** 2020; 28(9):1231-1242.

14- Croci S, Carriero ML, Capitani K, Daga S, Donati F, Papa FT, Frullanti E, Lopergolo D, Lamacchia V, Tita R, Giliberti A, Benetti E, Niccheri F, Furini S, Lo Rizzo C, Conticello SG, Renieri A, Meloni I. AAV-mediated *FOXG1* gene editing in human Rett primary cells. **Eur J Hum Genet.** 2020; 28(10):1446-1458.

15- Musi CA, Castaldo AM, Valsecchi AE, Cimini S, Morello N, Pizzo R, Renieri A, Meloni I, Bonati M, Giustetto M, Borsello T. JNK signaling provides a novel therapeutic target for Rett syndrome. **BMC Biol**. 2021;19(1):256.