Curriculum vitae, Elena Battaglioli

PRESENT POSITION

From 2023 Full Professor in Applied Biology (SSD BIO/13), Dept. Medical Biotechnology and Translational Medicine, University of Milan

EDUCATION

1993 Biology Degree (obtained *cum laude*), Dept. of Genetics and Microbiology, University of Milan

1993-1997 Graduate School in Cellular and Molecular Biology, University of Milan

1998-2002 Post doctorate, Howard Hughes Medical Institute, Dept. of Neurobiology & Behavior, SUNY at Stony Brook, NY

2002 Research Scientist, Dept of Neurobiology & Behavior, SUNY in Stony Brook, NY

2003-2004 Visiting Researcher, Protein Crystallography Group, University of Pavia

2004-2015 Assistant Professor in Applied Biology (SSD BIO/13), Dept. of Biology and Genetics for Medical Sciences, University of Milan

2015-2022 Associate Professor in Applied Biology (SSD BIO/13), Dept. Medical Biotechnology and Translational Medicine, University of Milan

January 2011-2019 Associate member of the CNR-Institute of Neuroscience

2010-2015 Adjunct Faculty to the Department of Integrative Biology at the University of Miami

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PERSONAL STATEMENT

My main scientific interest is to understand how the environment and experiences shape our behavior by affecting gene expression. Most of my contributions to science have led to a better understanding of the general epigenetic mechanisms involving transcription regulation, tissue specification and differentiation, especially related to the nervous system. In particular, during the last ten years, my lab has focused on the emerging field of Neuroepigenetics, clarifying epigenetic mechanisms of adaptive stress response in the brain. As a recognized scientist in the field of Neuroepigenetics, I was Principal Investigator of a research grant within the EPIGEN, Flagship Project, leading a multicentric unit focused on epigenetic mechanism of neuroplasticity and neuronal maturation (2012-2018). I was invited speaker at the ground-breaking Neuroepigenetic meetings organized by the EMBL Advanced Training Centre, Heidelberg (DE) (the first in Braga 2012, the last in Heidelberg-Virtual 2020). These meetings represent the state of the art reference of Neuroepigenetics, with contributions by the forefront scientists in the field. The ambitious goal of my research is now to explore genetic bases of the epigenetic drift of human stress-related brain disorders.

CONTRIBUTION TO SCIENCE

1997-2002 Since the beginning of my career, I have been interested in chromatin biology. During my PhD training in Italy, while studying regulatory elements driving tissue-specific expression of a neuronal gene, I followed the discovery by the laboratory of Gail Mandel of the neuronal silencer REST/NRSF, a master controller of excitability genes expressed only in the nervous system. In 1998, I had the possibility to join her HHMI laboratory at Stony Brook NY and there, together with a team of talented postdocs, I started unraveling the molecular mechanism that allows REST/NRSF to silence its targets. This was the exciting time when the chromatin field was flourishing. Mandel's lab linked for the first time, specific chromatin remodeling activities to neuronal gene silencing. In

particular, I demonstrated *in vivo* by chromatin immunoprecipitation that REST/NRSF is bound to its target promoters and is required to recruit its co-repressors. These discoveries, paved the way to the characterization of the histone code responsible for REST mediated, long-term neuronal gene repression.

2003-2016 While working in Mandel's lab, I isolated a protein (formerly known as KIAA0601, now named LSD1) involved in the function of the CoREST co-repressor complex that displayed a most fascinating feature. Based on amino acid sequence analysis, KIAA0601 appeared to belong to the flavin-class of amine oxidases, implying that this protein could function in the oxidation of an amine containing molecule, either as a metabolite or a chromatin protein. I therefore went to A. Mattevi's lab, an expert in the field of amino oxidases, with a challenging question: what is the enigmatic biochemical function of KIAA0601? At the end of 2004 I biochemically measured demethylase activity on a K4 di-methylated histone H3 peptide. The importance of this discovery was enormous since the existence of histone-demethylating enzymes was questioned till then, and with the discovery of LSD1 it was firmly established that histone methylation is a dynamic process. Although a group from Harvard published before us the same finding in December 2004, I considerably contributed to the field with several (16) publications centered on LSD1 biology. A recent significant contribution of our work is the implication of de novo loss of function *hLSD1/KDM1A* mutations in a new form of developmental disorder with intellectual disability, Cleft Palate, Psychomotor Retardation, and Distinctive Facial Features (CPRF) (OMIM: 616728).

2010-2023 Probably the most important discovery of my lab related to LSD1 biology is the identification of a neurospecific alternative splicing isoform, limited to mammals, which we named neuroLSD1. NeuroLSD1 represents an exceptional example of epigenetic enzyme specifically devoted to neurons. It can modulate its own activity in response to specific signals thanks to alternative splicing. Thus, NeuroLSD1 provides an epigenetic platform instrumental to neuronal plasticity. In particular, we showed that in response to stimuli, such as behavioral stress and epilepsy, LSD1 can transduce environmental inputs into changes in chromatin structure and gene transcription of a peculiar class of target genes, the Immediate Early Genes (IEGs). For these reasons LSD1 can now be considered a unique epigenetic factor able to shape mammalian behavior in an adaptive but also maladaptive manner. My group is now studying LSD1 in the context of epilepsy and anxiety and stress-related mental illness.