Translational Medicine @ UniSa - ISSN 2239-9747 2019, Special Issue 1(31): 31

P11. DISEASE' MECHANISMS UNDERLYING THE NEUROPATHOLOGICAL PROGRESSION IN MUCOPOLYSACCHARIDOSIS IIIA

M. De Risi[1], M. Tufano[1], F.G. Alvino[1], S. Pulcrano[2], G.C. Bellenchi[2], A. Fraldi [1], M. Caiazzo[3],and E. De Leonibus[1,4]

[1]*Telethon Institute of Genetics and Medicine (TIGEM), Pozzuoli (Naples), Italy;*
[2]*Institute of Genetics and Biophysics, CNR, Naples, Italy;*
[3]*Utrecht Institute for Pharmaceutical Sciences (UIPS), Universiteitsweg, Utrecht, The Netherlands;*
[4]*Institute of Genetics and Biophysics (IGB), Naples and Institute of Cellular Biology and Neurobiology (IBCN), Monterotondo (Rome), National Research Council, Italy*

Mucopolysaccharidosis type IIIA (MPS-IIIA) is a neurodegenerative lysosomal storage disorder characterized by the deficiency of the enzyme sulfamidase. The pathology is characterized by different stages, each defined by a specific set of symptoms. The neurobiological mechanisms leading to these symptoms are still unknown. In the early phase, children with MPS-IIIA manifests with behavioural symptoms (BSs), including stereotypic and social behaviour dysfunctions; these symptoms are progressively substituted by the onset of dementia and motor impairment. Using an animal model of MPS-IIIA, we have identified endophenotypes of early and late stages of MPS-IIIA pathology, which are associated to dynamic changes in tyrosine hydroxylase (TH) expression, the dopamine (DA) synthesis-rating enzyme. This dynamic changes in TH expression are recapitulated in a cellular model of the pathology. These findings are important to define specific antipsychotic therapy for behavioral symptoms, and to understand the disease' mechanisms leading to DA dysfunctions in MPS-IIIA.