Speaker: Dr. Giovanni D'Angelo, Institute of Protein Biochemistry, Naples (I)

Title: Glycosphingolipid Metabolic Reprogramming Drives Neural Differentiation

Abstract:
Neural development is accomplished by differentiation events leading to metabolic reprogramming. Glycosphingolipid metabolism is reprogrammed during neural development with a switch from globo to ganglio-series glycosphingolipids production. Failure to execute the glycosphingolipid switch leads to neurodevelopmental disorders in humans, indicating that glycosphingolipids are key players in this process. Nevertheless, both the molecular mechanisms that control the glycosphingolipid switch and its function in neurodevelopment are poorly understood. Here, we describe a self-contained circuit that controls glycosphingolipid reprogramming and neural differentiation. We find that globo-series glycosphingolipids repress the epigenetic regulator of neuronal genes expression AUTS2. AUTS2 in turn, binds and activates the promoter of the first and rate limiting ganglioside producing enzyme GM3 synthase, thus fostering the synthesis of gangliosides. By this mechanism the globo-AUTS2 axis controls glycosphingolipid reprogramming and neural genes expression during neural differentiation, which involves this circuit in neurodevelopment and its defects in neuropathology.