Department of Anatomy & Cell Biology Seminar Series

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Aberrant protein sialylation: pathophysiological factor common across diverse genetic diseases

Sialic acids (Sia), a family of negatively charged sugars with a nine-carbon backbone, are found in almost all living organisms. They are important components of glycan chains in glycoproteins and glycolipids and are involved in cellular communication, migration, adhesion, tumor cell metastases and infection processes. In mammalians, Sia are cleaved from sialoglycans by neuraminidases NEU1-4, followed by recycling of Sia in biosynthesis, or by their degradation into N-acetylmannosamine (ManNAc) and pyruvate by N-acetylneuraminate pyruvate lyase (NPL).

In my presentation, I will summarize emerging data that point to important roles of NEU1 and NPL in regulation of protein sialylation, crucial for adult myogenesis, synaptic transmission and kidney function. Our data demonstrate that NEU1 plays a major role in processing Sia residues of surface glycoproteins, altering their structure, activity and interaction patterns. In particular, it desialylates receptors for phagocytosis and inflammatory response on macrophages and activates them. In the kidney, desialylation by NEU1 plays a crucial role in processing and cellular trafficking of an endocytic reabsorption receptor, megalin prominently expressed in proximal convoluted tubules. Primary NEU1 deficiency in the mouse model of a lysosomal disease, sialidosis impairs megalin-mediated protein reabsorption leading to severe kidney dysfunction and proteinuria. In the group of neurological mucopolysaccharidoses, lysosomal storage diseases manifesting with accumulation of heparan sulphate, secondary deficiency of NEU1 results in hypersialylation of glycoproteins implicated in synaptogenesis crucially contributing to CNS pathology. In term, free Sia abundance in tissues and their availability for sialoglycoconjugate synthesis are controlled by NPL. NPL deficiency in mice causes drastic increase in Sia levels, aberrant sialylation of dystroglycan and mitochondrial LRP130 protein associated with reduction of skeletal muscle force and endurance, slower healing increased glycolysis, and partially impaired mitochondrial function. Together, our data provide evidence for the essential roles played by sialoglycome in multiple physiological and pathological processes.

Wednesday, May 1st, 2024
11:30am - 12:30pm

Hosted by: Carlos Morales, PhD

Room 1/12 - Strathcona Anatomy and Dentistry Building

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