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Synchrotron radiation for preclinical research: investigation of tissue chemical change in mouse model of Pompe disease (glycogenosis type II) and assessment of gene therapy efficacy by using Infrared Micro spectroscopy with the synchrotron light.

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Pompe disease (glycogenosis type II) is an autosomal recessive disorder caused by the deficiency of the lysosomal enzyme acid alpha-glucosidase (GAA). The disease is characterized by lysosomal glycogen storage in heart and muscles, and manifests as a fatal cardiomyopathy in infantile form. Cardiac correction by enzyme replacement therapy (ERT) has recently prolonged the lifespan of these patients but ERT is not efficient to correct central nervous system (CNS). A gene therapy strategy using AAV vectors delivered to cerebrospinal fluid has been set up to restore GAA activity into the CNS. We demonstrate the use of Infrared Micro spectroscopy with synchrotron light as an innovative tool to map glycogen at the subcellular level in motor neurons (MNs) from spinal cord and cardiac fibers. Principal Component Analysis of infrared spectral data from MNs and cardiac fibers show that both treated and wild-type animals are merged in the same cluster whereas infrared spectra obtained from untreated Pompe mice are characterized by increase of the bands assigned to the carbohydrates of glycogen. This new analytical approach that allows a highly sensitive and resolutive direct probing of tissue glycogen is required to explore early biochemical change at a subcellular level and therefore to assess therapeutic efficiency for Pompe disease.

Keywords : Pompe disease, glycogen, Infrared Micro spectroscopy

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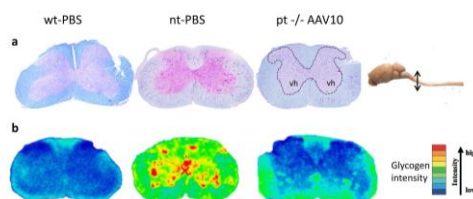


Figure 1 :a- Representative sections of cross-sectioned cervical spinal cord, paraffin embedding, PAS-luxol fast blue stain. The glycogen storage appears purple on a blue background, motor neuron of spinal cord are located in ventral horn (vh). b- Chemical imaging performed after the infrared chemical mapping showing the relative concentration of glycogen infrared spectra absorption acquired from cross-section cervical spinal cord of the dewaxed formalin fixed paraffin.