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Glycomics profile analysis by MALDI TOF/MS in human CSF

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Protein glycosylation is important for human brain development and function. The majority of the >100 known subtypes presents with intellectual disability. To explore possible defects in protein glycosylation in the brain, we developed comprehensive glycomics analysis of N-glycome, O-glycome and free glycome by MALDI TOF/MS in cerebrospinal fluid (CSF). 0.4 ml CSF was filtered to separate free oligosaccharides from glycoprotein. N-glycans were released via PNGase F digestion and O-glycans were released separately by reductive beta-elimination reaction. After purified, glycans were permethylated and analyzed by MALDI TOF/MS. Thirty eight different N-glycan species, 85 free oligosaccharide and 25 O-glycan species were identified in 10 control CSF samples. Compared with plasma glycomics data, CSF has much more O-glycan species including O-mannosylated glycans and polysialylated O-glycans. Comparing 166 CSF samples from patients with undiagnosed neurological disease from the NIH Undiagnosed Diseases Program (UDP) with 10 control CSF samples, about 20 UDP patients have CSF glycomics profiles significantly deviated from the profiles of control CSF samples. Four of the UDP patients have known genetic disorders that alter protein glycosylation in human brain, including one patient with putative CAD deficiency, a defect in uridine biosynthesis. Interestingly, one of the known patients has a completely normal plasma glycomics profile and urine oligosaccharide profile, while both his CSF N and O-glycomics profiles are abnormal. Our results suggest that CSF glycomics analysis could be a useful tool to discover new diseases or disease mechanism.

Biography

Xueli Li has completed her PhD from Leipzig University, Germany. She is a Research Associate in The Michael JPalmieri Metabolic Laboratory, Children's Hospital of Philadelphia, USA. She has more than 5 publications in the area of Glycomics recently.

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