Bioenergetic characterization of skin fibroblasts from patients with Congenital disorders of glycosylation

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Congenital disorders of glycosylation (CDG) are a fast growing group of rare inherited diseases caused by abnormal protein and lipid glycosylation. Recently published studies and our preliminary data indicated possible interconnection between glycosylation defects and mitochondrial function abnormalities.
Aim of this study was to analyze mitochondrial respiration and glycolysis in fibroblast cell lines from patients with Congenital disorders of glycosylation (specifically patients with: ALG8-CDG, PGM1-CDG, PMM2-CDG, Man1B1-CDG, RFT1-CDG, SLC10A7-CDG, ATP6AP1-CDG, NUS1-CDG) and compare them with control fibroblast cell lines. Measurements were performed by using Oxygraph-2k (Oroboros) and Seahorse XFe24 Bioanalyzer (Agilent).
Our preliminary results showed abnormal mitochondrial respiration in most of fibroblast cell lines from the patients with CDG with various respiration patterns in individual CDG type. Decreased Complex II dependent respiration on Oxygraph-2k and decreased oxidative phosphorylation value were found in fibroblasts derived from Man1B1-CDG patient. Slightly diminished basal respiration and decreased maximal respiration to nearly 50% in Man1B1-CDG line compared to controls on Seahorse Bioanalyzer was shown as well. Glycolytic function was decreased almost at all fibroblast cell lines from patients with CDG (except ATP6AP1-CDG) in comparison with the control cell lines.
These results indicate secondary functional abnormalities in mitochondria and glycolytic dysfunction due to a breakdown of the glycosylation pathway. The study of mitochondrial metabolism in congenital disorders of glycosylation may contribute to the elucidation of pathomechanisms in unclear metabolic diseases.

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