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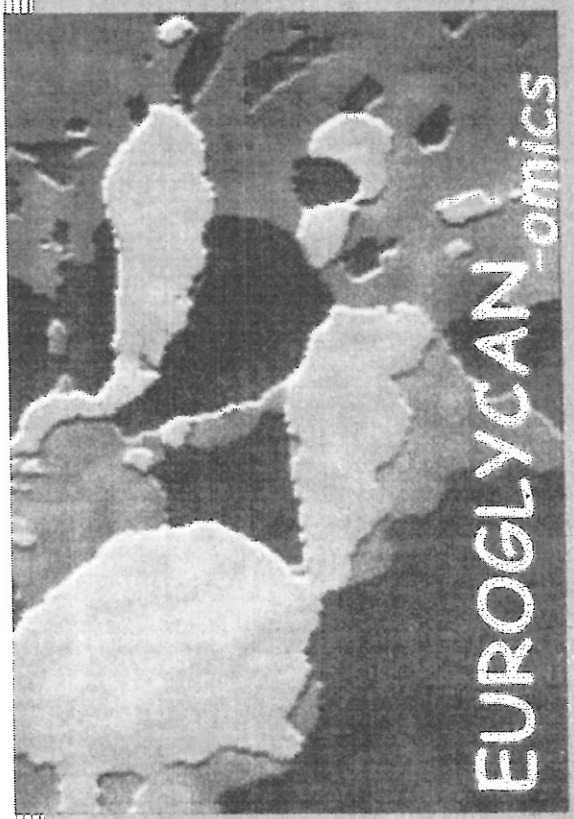
on

Congenital Disorders of Glycosylation and related disorders



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GlcNAc2Man5-7 N-glycan accumulation in serum of Slovak ALG12-CDG patient

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ALG12-CDG is a rare inherited metabolic disease, caused by a defect in alpha-mannosyltransferase 8, encoded by the ALG12 gene. To date, only fifteen patients have been diagnosed with ALG12-CDG globally. Due to the clinical and biochemical abnormalities observed in a newborn Slovak patient, IEF of transferrin was performed and significant hypoglycosylation typical of CDG I was observed. MALDI TOF/TOF analysis of unmodified, permethylated and 13C stable-isotope labelled serum N-glycans, after their enzymatic release, isolation and fractionation by non-porous graphitized carbon SPE, was performed. In the patient sample, the relative intensities of signals corresponding to GlcNAc2Man5-7 were 1.4-1.8 fold greater than that of the negative control. Relative intensity of GlcNAc2Man8 was 8-fold lower than that of GlcNAc2Man9, and GlcNAc2Man9Glc1 appeared to be absent from the N-glycoprofile of the patient. Thus, the N-glycan synthesis pathway of the patient was likely disrupted at the point in which the eighth mannose residue is added to GlcNAc2Man7, when attached to a dolicholphosphate carrier at the endoplasmic reticulum membrane. Sequencing analysis of the coding regions of the ALG12 gene of the patient revealed a novel homozygous substitution c.1439 T > C p.(Leu480Pro).

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