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LETTER

# Congenital disorders of glycosylation: other causes of ichthyosis

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We read with interest the comprehensive review by Schmuth *et al*[1] on inherited ichthyoses/generalized Mendelian disorders of cornification. We would like to point out that some congenital disorders of glycosylation (CDG) present ichthyosis. Associations have been described for MPDU1-CDG (formerly CDG-If), DOLK-CDG (CDG-Im), SRD5A3-CDG (CDG-Iq) and PIGL-CDG (CHIME syndrome, Zunich neuroectodermal syndrome). MPDU1-CDG is a defect in the N-glycan assembly in the endoplasmic reticulum (ER). The four reported patients showed skin involvement (ichthyosis and/or erythroderma). Other features included psychomotor retardation, seizures, hypotonia, gastrointestinal problems, visual impairment, dwarfism and transient growth hormone deficiency. The MPDU1 protein is considered to be a chaperone favoring the efficient utilization of dolicholphosphoglucose and dolicholphosphomannose in glycosylation. A reduced level of the glycosylphosphatidylinositol (GPI)-anchor CD59 has been found in these patients suggesting that they have also a deficiency in GPI-anchor biosynthesis (see PIGL-CDG).[2,3] DOLK-CDG is a defect in dolichol kinase, the last step of the dolichol phosphate biosynthesis. It shows a clinical spectrum with at one end a non-syndromic dilated cardiomyopathy (reported in nine patients),[4] and at the other end a severe syndrome (reported in four patients) with ichthyosis, as well as dilated cardiomyopathy, epilepsy, microcephaly, visual impairment, hypoglycemia and death within the first 6 months.[5] SRD5A3-CDG is a defect in polyprenol reductase, involved in the biosynthesis of dolichol. This cerebro-cerebello-oculo-cutaneous syndrome has been described in some 15 patients. Its skin component consists of ichthyosis, erythroderma and/or dry skin.[6,7] PIGL-CDG or CHIME syndrome is characterized by *c*olobomas, congenital *h*eart defects, early-onset migratory *i*chthyosiform dermatosis, *m*ental retardation and *e*ar anomalies, besides other clinical manifestations. This is a defect in an ER-localized enzyme that catalyzes the second step of GPI-anchor biosynthesis, the de-*N*-acetylation of *N*-acetylglucosaminyl-phosphatidylinositol that occurs on the cytoplasmic side of the ER. It has been reported in eight patients.[8]

The two dolichol phosphate synthesis disorders and MPDU1-CDG can be picked up by serum transferrin isoelectrofocusing. Therefore, we strongly recommend to perform this test in any patient with syndromic ichthyosis or with a syndromic ichthyosis-like skin disorder.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

Jaak Jaeken*[,1], Daisy Rymen[1,2] and Gert Matthijs[2]
[1]*Center for Metabolic Disease, KULeuven, Leuven, Belgium;*
[2]*Center for Human Genetics, KULeuven, Leuven, Belgium*
*E-mail: jaak.jaeken@uzleuven.be*

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