

PROGRESS REPORT

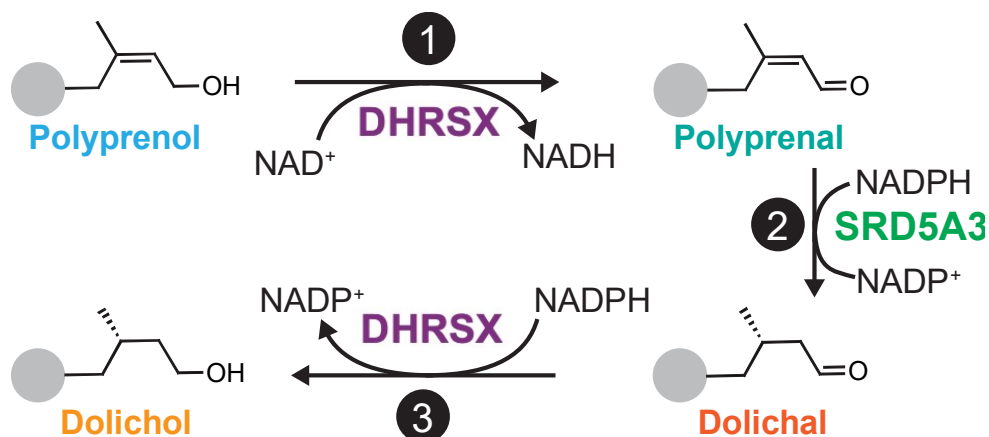
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Title: **DHRSX deficiency - A novel CDG and a new facet of dolichol metabolism?**

(a) Abstract

The study of Congenital Disorders of Glycosylation (CDG) and the identification of novel CDG gene loci has greatly contributed to our fundamental understanding of glycosylation. From our collection of unsolved cases we are still identifying new CDG genes, the most recent of these is *DHRSX*. Excitingly, this is the first truly recessive pseudo-autosomal inborn error of metabolism (DHRSX-CDG).

1. Objectives: To characterize the function of the DHRSX protein, and elucidate its role in glycosylation.
2. Methods: Cell and glycobiological experiments using cell models and yeast to identify metabolites and assay the profiles of lipid-linked oligosaccharides.
3. Results. We have shown that the DHRSX enzyme performs a critical role in the biosynthesis of the dolichol isoprenoid precursor, essential for formation of the lipid-linked oligosaccharide (LLO) and therefore N-glycosylation. This discovery has implications for human biochemistry, while the diagnostic odyssey ends for the DHRSX-CDG patients and their families.



The revised dolichol biosynthesis pathway (published in Wilson, Kentache, Althoff et al. Cell, May 30, 2024, S0092-8674(24)00467-7. Online ahead of print).