Protein glycosylation conserved from yeast to man. How a model organism helped to analyze severe human diseases.

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For many years the role of protein glycosylation had remained an enigma. For this most complex and costly type of protein modification only a few rare examples of functional implications had been reported. This was the more surprising, as the enzymatic machinery responsible for these modification has been conserved in evolution to a large extent from yeast to man. Since about ten years it is now well established that genetic defects in glycosyl transferases delivering specific sugars to N-linked saccharides of proteins, lead to severe, frequently lethal diseases of children (1). They are called "congenital disorders of glycosylation" (CDG). CDG turned out to be caused by defects in the assembly and processing of glycan chains. To a large extent the extensive knowledge of the pathway in yeast (2) has been instrumental to identify so far 18 subclasses of mutations (3). For another type of protein glycosylation, the so called O-mannosylation, a comparable development can be reported. The modification was originally considered to only occur in fungal cells, where the pathways and the responsible genes have been discovered (4). Subsequently a Drosophila mutant with an impaired cellular organisation of muscles and a gene defect in O-mannosylation was described (5), which laid the ground for uncovering the genetic cause for a number of again extremely severe, in this case neuromuscular diseases in humans (6, 7). It seems clear now that saccharides attached to proteins play a fundamental role in the correct embryonic and early postembryonic development for a great number of mammalian tissues and organs. To establish details of the corresponding signalling pathways will be a great challenge for future research. Possible functions of protein glycosylation for the unicellular organism *S.cerevisiae* will be discussed.

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