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Fruitfly fucosylation

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Abstract

A biocomputational study of the fruitfly genome reveals the presence of new genes putatively involved in fucosylation

Significance and context

Glycans - the oligosaccharide chains attached to many extracellular and membrane proteins and lipids - are of importance in a variety of biological processes. *N*-glycans are, for instance, involved in protein folding, glycosylated proteins have important roles in fertilization and pattern formation during embryogenesis, and in some instances *O*-glycans are involved in cellular signaling, often leading to the regulation of transcription and translation. Glycans often contain the sugar fucose as an essential component. The A, B, and O blood-group antigens, for instance, contain β1,2-fucosylated lactosamine, and fucosylated proteins are important for the normal development of an organism. Fucosylation requires GDP-L-fucose as a donor and also the presence of particular fucosyl transferases, which transfer the fucosyl residue from the donor to the acceptor molecule. GDP-L-fucose can be synthesized through a *de novo* pathway from GDP-mannose or through the salvage pathway from fucose. The removal of fucosylated glycans is mediated by fucosidases, and defects in both fucosylation and fucose removal lead to inherited disorders in humans, for example, fucosidosis, a recessive autosomal disorder characterized by an impaired lysosomal degradation of fucosylated glycans. Roos *et al*. carried out a biocomputational study on the genome of the model organism *Drosophila melanogaster* to characterize the metabolic pathways involving fucosylated glycans, which may contribute to a better understanding of similar processes in humans.

Key results

From their *in silico*study, Roos *et al*. identified two novel enzymes in *D. melanogaster*, similar to a GDP-mannose-4,6-dehydratase and a GDP-4-keto-6-deoxy-D-mannose epimerase/reductase, which are proposed to be involved in the synthesis of GDP-L-fucose. From this, they showed that, in *D. melanogaster*, GDP-L-fucose is formed solely through the *de novo* synthesis pathway, involving a GDP-mannose-4,6-dehydratase and a GDP-4-keto-6-deoxy-D-mannose epimerase/reductase. *D. melanogaster* most probably lacks the salvage pathway for synthesizing GDP-L-fucose, as no genes similar to the mammalian genes encoding fucokinase and fucose-1-phosphate guanylyltransferase could be found.

Study of the fruitfly genome further revealed the presence of genes for two novel fucosyltransferases (β1,3- and an β1,6-fucosyltransferase), two *O*-fucosyltransferases, proposed to be involved in the direct fucosylation of proteins at serine/threonine residues, and a fucosidase. Although β1,2-fucosyltransferases are present in some bacteria and mammals, no genes encoding these enzymes were found in *D. melanogaster*. On the basis of the study of the *D. melanogaster* genome sequence and homology searching, two new human fucosyltransferases - closely related to β1,3/ β1,4-fucosyltransferases - were identified.

Links

Information about the genome sequence of *D. melanogaster* is available at the Berkeley Drosophila Genome Project web page .

Conclusions

Roos *et al*. conclude that new members of protein families can be identified in one organism by their similarity to genes identified in other organisms.

Reporter's comments

Although expressed sequence tags are available for many of the glycan metabolism genes that Roos *et al.* discovered in *D. melanogaster*, suggesting that they are transcribed, their role in the production of fucosylated compounds still remains to be proved. The construction of precise knockouts and/or detailed biochemical studies and assays will be needed to confirm their proposed role. Such studies will be of importance in understanding these pathways in humans and thus in developing therapies for patients with defects in fucosylation metabolism.

Table of links

Journal of Biological Chemistry

Berkeley Drosophila Genome Project web page

References

1. Roos C, Kolmer M, Mattila P, Renkonen R: Composition of *Drosophila melanogaster* proteome involved in fucosylated glycan metabolism. J Biol Chem. 2002, 277: 3168-3175. 0021-9293

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