Glycans as integrators of genes and environment – an often-ignored layer of biological complexity

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Glycosylation is an essential posttranslational modification generated by a complex biosynthetic pathway comprising hundreds of glycosyltransferases, glycosidases, transcriptional factors, ion channels and other proteins. This process results in the creation of branched oligosaccharide chains, called glycans, which become integral part of proteins and significantly contribute to their structure and function. Nearly all proteins invented after the appearance of multicellular life are glycosylated and glycans are glycans are functionally relevant for nearly all processes at the multicellular level. Since glycans are created without the genetic template, alternative glycosylation creates an additional layer of structural complexity by combining genetic variability with past and present environmental factors. Individual variability in glycome composition is very large, but glycosylation of an individual protein seems to be under strong genetic influence, with the heritability of the (for example) IgG glycome being up to 80%. Structural details of the attached glycans are of great physiological significance and many pathological conditions are associated with various types of glycan changes. Since the onset of genome wide association studies (GWAS), thousands of genetic loci have been associated with different diseases and traits. However, in the last few years, and particularly after recent publication of the results from the ENCODE project, it is becoming increasingly clear that GWAS studies are only a beginning of the understanding of complex human diseases. Hypotheses generated in these studies have to be put in the context of complex biology of life and a more elaborate approach that combines different 'omics phenotypes is needed to understand disease mechanisms and perform patient stratification that transcends genomics. Glycomics, as by far the most complex epiproteomic modification, has an immense potential in this respect, which is only beginning to be investigated.

Selected publications

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