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A Complex Between Beta-1,4-galactosyltransferase and Alpha-lactalbumin with its less Preferred Acceptor and Donor Substrates

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Beta-1,4-galactosyltransferase (beta1,4-Gal-T1) in the presence of manganese transfers galactose from uridine-diphospho-galactose (UDP-Gal) to the acceptor sugar N-acetylglucosamine (GlcNAc). In the mammary gland, during lactation, the acceptor sugar specificity of beta-1,4-Gal-T1 is modulated by alpha-lactalbumin in a way that it transfers galactose to glucose (Glc) but not to GlcNAc.

Earlier we have solved the crystal structure of the beta1,4-Gal-T1 and alpha-lactalbumin complex in the presence of the preferred and less preferred substrates. Further, in order to understand the sugar specificity of beta1,4-Gal-T1, the lactose synthase crystal structure has been solved in the presence of its less preferred acceptor substrates such as D-xylose and N-acetyl-mannosamine and donor substrates such as UDP-GalNAc, UDP-Man, and UDP-GalA. These crystal structures have been solved and refined to 2.2Å resolution. The structural information of the bound substrates to beta1,4-Gal-T1 rationalizes the substrate specificity of the enzyme, which arises from its molecular interactions with the substrates. These studies enable us to rationally alter beta1,4-Gal-T1 in such a way that it can transfer various other sugars from their UDP-derivatives to GlcNAc with higher efficiency.