

**TPR Repeat Domain of O-linked GlcNAc Transferase:
Similarities to Importin Alpha**

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Addition of N-acetylglucosamine (GlcNAc) is a ubiquitous form of intracellular glycosylation, catalyzed by the conserved O-linked GlcNAc transferase (OGT). OGT contains an N-terminal domain of tetratricopeptide (TPR) repeats that mediates the recognition of a broad range of target proteins. Nuclear pore complex components are major OGT targets, as OGT depletion by RNAi results in the loss of GlcNAc modification at the nuclear envelope. To gain insight into the mechanism of target recognition, we solved the crystal structure of the homodimeric TPR domain of human OGT, containing 11.5 TPR repeats[1]. The repeats form an elongated superhelix. The concave surface of the superhelix is lined by absolutely conserved asparagine residues, in a manner reminiscent of the peptide-binding site of importin α . Based on this structural similarity, we propose that OGT employs an analogous molecular mechanism to recognize its targets.

[1] Jinek M., Rehwinkel J., Lazarus B.D., Izaurralde E., Hanover J.A., Conti E., *Nat. Struct. Mol. Biol.*, 2004, **11**, 1001.

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