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Cryo-EM structure of the yeast oligosaccharyltransferase complex gives insight into N-linked protein glycosylation

N-linked glycosylation is a complex post-translational protein modification that plays a role in diverse biological processes, e.g. in host-pathogen interaction, in cell-cell communication and during protein quality control. The central enzyme in the N-glycosylation pathway is the oligosaccharyltransferase (OST), which catalyzes the transfer of a pre-assembled lipid-linked oligosaccharide onto an asparagine side chain of peptide substrates. In prokaryotes, a single-subunit OST enzyme carries out this reaction. Eukaryotes, in contrast, encode multi-subunit OST complexes. To uncover the function of the additional subunits, their structures and their assembly into the complex, we determined the structure of the yeast octa-subunit OST (Wild, Kowal, Eyring et al., Science, 2018). Our single-particle cryo-EM structure at 3.3 Å resolution reveals that the STT3 subunit harbors the catalytic center, which faces away from the other subunits, thereby allowing unhindered access to the lipid-linked oligosaccharide and peptide substrates. The non-catalytic subunits form a rigid scaffold providing additional binding surfaces for substrate recognition and for potential protein interaction partners. Of note, our high-resolution OST structure fits well into a previously published cryo-electron tomography map of the mammalian OST-translocon-ribosome complex. The docking analyses reveal an orientation of the OST complex with its catalytic site facing the translocon. This architecture allows OST to efficiently glycosylate native peptide chains entering the ER through the translocon.

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