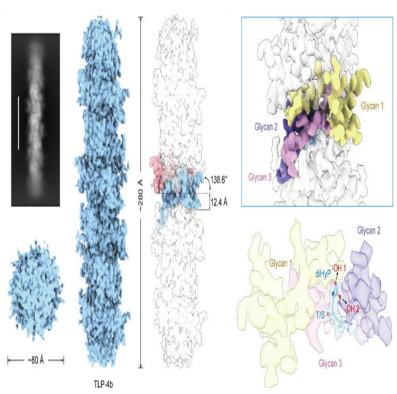

The 8-nm spaghetti: well-structured glycans coating linear tetrapeptide repeats

Description

The authors have developed a research strategy, called CryoSeek, to identify uncharacterized bio-entities from natural or endogenous resources using cryo-electron microscopy (cryo-EM). They report the discovery of a glycofibril whose primary molecular mass is attributed to a thick glycan backbone. The 3.3 Ã resolution cryo-EM reconstruction reveals that the only protein component of the glycofibril, which is approximately 8 nm in diameter, is a linear chain of tetrapeptide repeats. Each tetrapeptide repeat consists of a 3,4-dihydroxyproline (diHyp), a Ser or Thr, and two less conserved residues. Two and one glycan chains are O-linked to the diHyp and Ser/Thr residues, respectively.

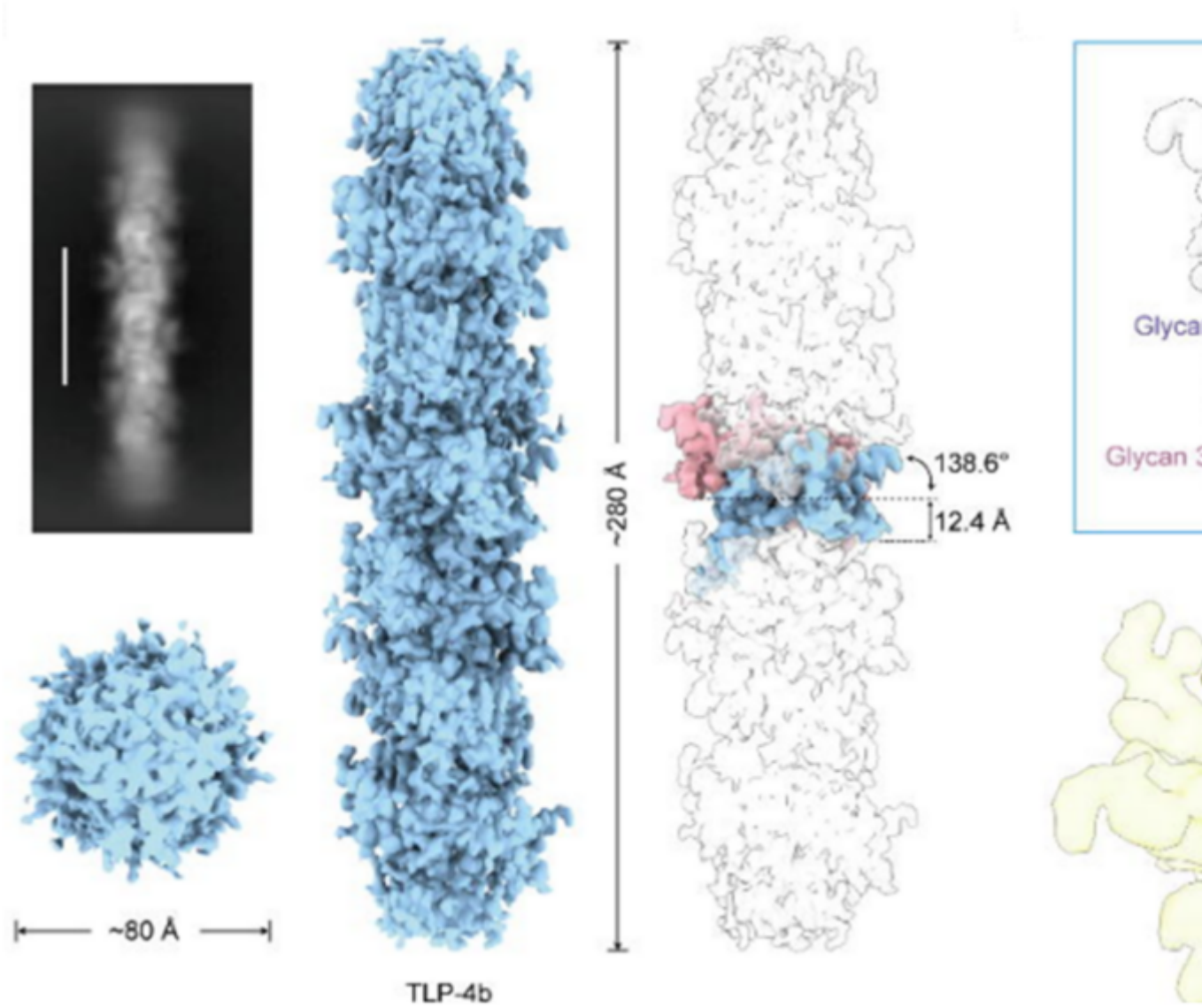

Figure: TLP-4b consists of linear tetrapeptide repeats coated with dense glycans. (A) High-resolution 3D reconstruction of TLP-4b with helical parameters. Left: Two perpendicular views of segmented TLP-4a and the corresponding 2D average. Right: Two adjacent asymmetric units. The two units are colored pink and light blue. The helical rise and twist for TLP-4b are 12.4 Ã and 138.6Â°, respectively. The overall resolution is 3.3 Ã . The EM map is contoured at 4.5 Ï?. (B) Three glycan branches of TLP-4b. *Upper*: Each helical repeat of TLP-4b has three branches of glycan densities linked to the central peptide. *Lower*: Glycan 1 and 2 are O-linked to a 3,4-dihydroxyproline (diHyp) residue, while the neighboring glycosylated residue can be a Thr/Ser. The EM map is contoured at 9 Ï?. All structural figures were prepared in ChimeraX.

The protein sequence pattern of this glycofibril is similar to that of the recently observed TLP-4, although the glycan chains are different. The authors rename the previously characterized glycofibril as TLP-4a and this one as TLP-4b. The present findings reveal the critical role of glycans in the structural folding of glycoconjugates and shed light on understanding the carbon/nitrogen ratio in biospheres.

Category

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