

IMPRS on Multiscale Biosystems

Title: Structural and functional characterization of human glycogen debranching enzyme (GDE) using x-ray crystallography and Cryo-EM

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Project description: Glycogen is the most important fast accessible energy storage found in bacteria up to humans. Similar to starch, glycogen is a glucose homopolymer with α -1,4 linkages and additional α -1,6 branching points, which are occurring on average on every 12th residue (Fig. 1).

The efficient release of Glucose and thereby energy, needs the continuous remodeling of glycogen to resolve the branching points, which prevent efficient breakdown. This is done by the glycogen debranching enzyme (GDE) in humans. Human GDE is a two domain protein combining α -1,4 and α -1,6 hydrolytic activity in one enzyme (Fig. 1). Improper function of GDE leads to severe diseases for example glycogen storage disorder 3. Despite its critical role in

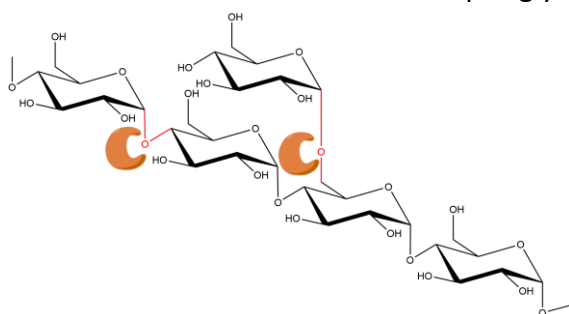


Figure 1: Principal primary structural arrangement of glycogen. The two linkages to be cleaved by GDE are coloured with red and the enzyme is indicated as cartoon shape in brown.

glycogen metabolism, structural and functional data are still scarce, hampering further progress in that field. Within this project **you will establish a system for the production of the human GDE recombinantly in *E. coli***. The enzyme and variants thereof for structural and functional studies using **x-ray crystallography, Cryo-EM and other biophysical techniques**. Furthermore, with a combination of different substrate analogues and structural analysis you will unravel the role of the disease causing mutations on the functional pattern of GDE and its two distinct activities. With the help of automated glycan assembly, bespoke substrate analogs will be used by you to shed light on the potential cooperativity between the two domains of GDE.

Required background: Candidates should have a background in biochemistry and techniques for protein expression and purification. Additionally, knowledge in x-ray crystallography or Cryo-EM may be useful.

Paper to read before the interview: Adeva-Andany MM. *et al.*, Glycogen metabolism in humans, *Biochimica et Biophysica Acta Clinical.*, (5), 85-100, 2016

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<http://www.mpikg.mpg.de/5892723/carbohydrates-structure-and-function>

<http://www.bcp.fu-berlin.de/en/chemie/biochemie/research-groups/wahl-group/index.html>