Using recombinant glycogen synthase and structural biology techniques to understand therapeutic opportunities for APBD

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Glycogen branching enzyme 1 (GBE1) plays an essential role in glycogen biosynthesis, mutations of which lead to the heterogeneous early-onset glycogen storage disorder type IV (GSDIV) or the late-onset adult polyglucosan body disease (APBD). Our group has an ongoing interest in studying the catalytic and disease mechanism underlying the human glycogen biosynthetic machinery, which consists of the priming enzyme glycogenin (GYG1/2), the elongation enzyme glycogen synthase (GYS1/2), and the branching enzyme (GBE1).

My current study is aimed at validating two potential therapeutic avenues for APBD: pharmacological chaperoning for GBE1, and small molecule inhibition of GYS1. My presentation hence will consist of two parts:

- Characterization of the recombinant GBE1 mutant protein p.Y329S linked with APBD, and structure-guided design of a stabilizing peptide
- Effect of the small molecule guaiacol towards activity of recombinant glycogenin-glycogen synthase complex