# PoLiMeR WP2_ ASC1: Glycogen Synthesis and GBE

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PoLiMeR

Polymers in the Liver - Metabolism and Regulation

MANCHESTER 1824

The University of Manchester

Manchester Institute of Biotechnology

# Glycogen metabolism & Glycogen Storage Diseases (GSDs)

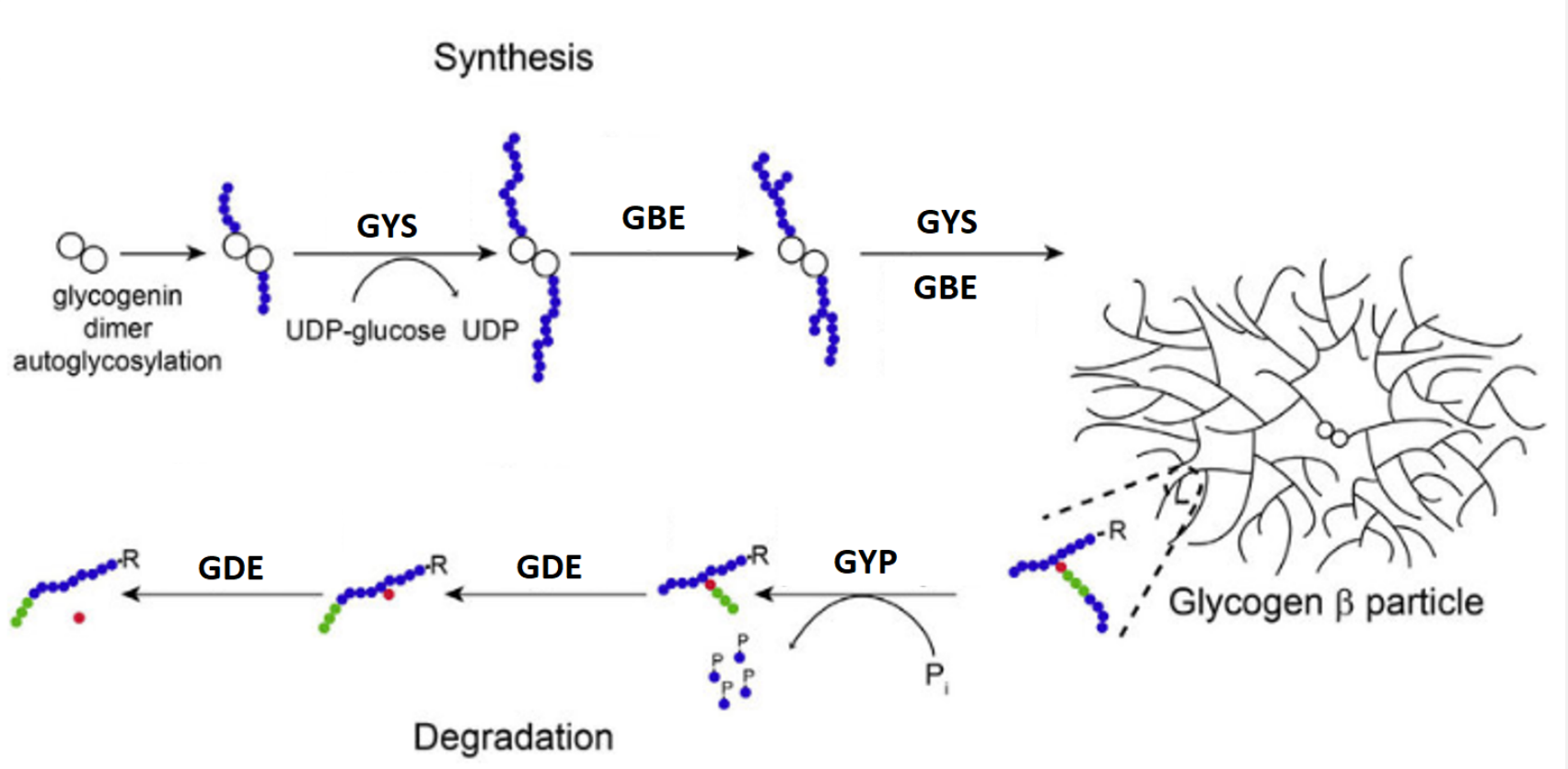
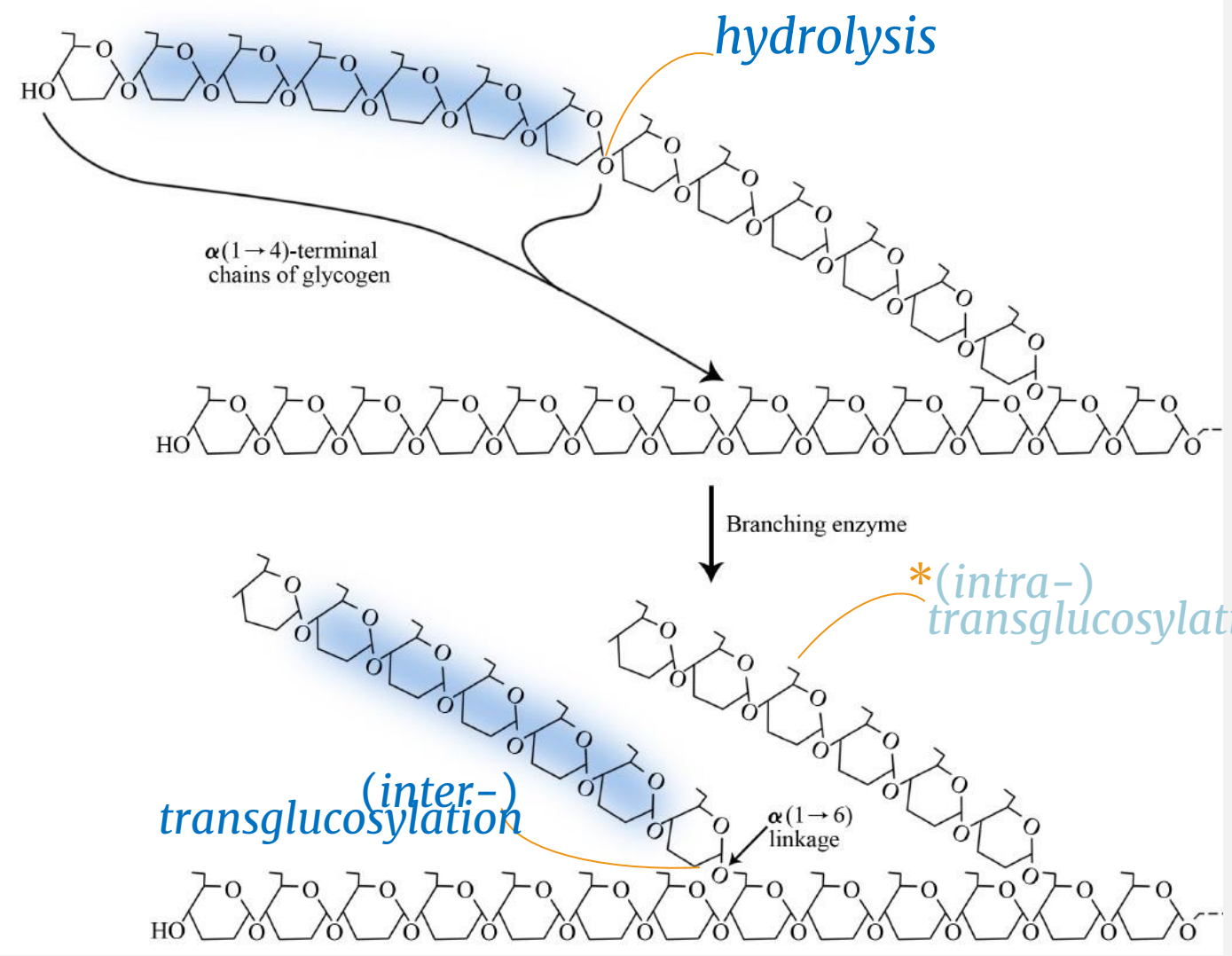


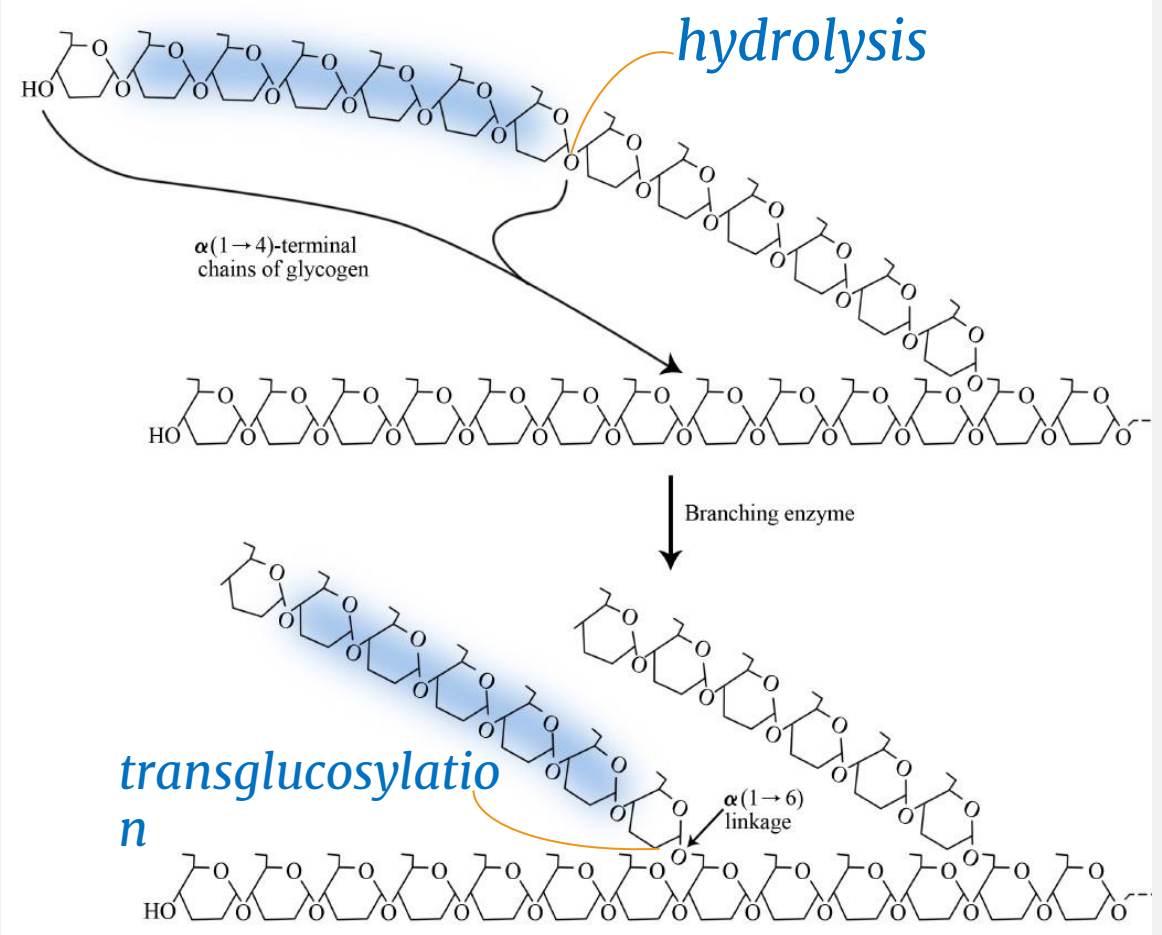

Image source: 10.1016/j.ebiom.2019.07.067

# Glycogen Branching Enzyme (GBE)



# Glycogen Branching Enzyme (GBE)

- Carbohydrate-Active enZyme (CAZy)
- GH13 family of glycosyl hydrolases
  subfamily 8 (eukaryotic)
  subfamily 9 (prokaryotic)
- Two reactions (*hydrolysis* & *transglucosylation)*
- Single active site
- Chromosome 3p12.3
- 16 exons, 702–a.a.



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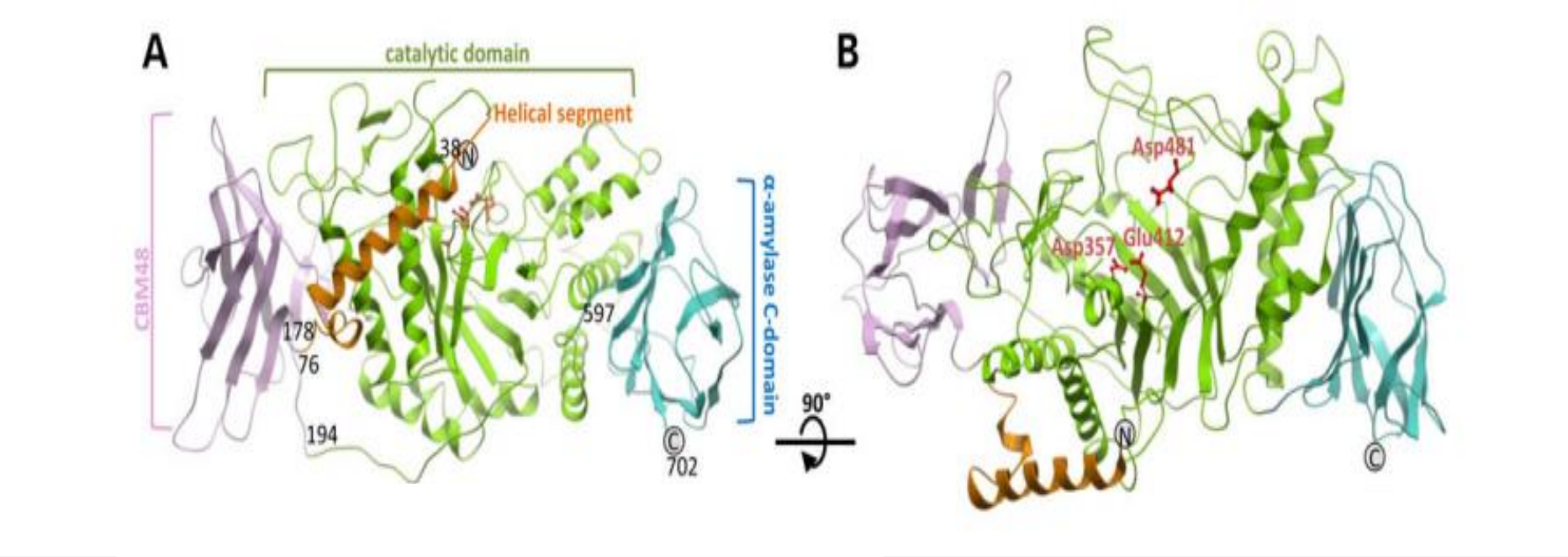


N-terminal helical segment (aa 43–75)
Carbohydrate-binding module 48 (CBM48; aa 76–183)
Central catalytic core (aa 184–600)
C-terminal amylase-like (aa 601–702)

Catalytic triad
Asp357-Glu412-Asp481



Wyatt W. Yue, *Human Molecular Genetics*, 2015, p 5667–5676, https://doi.org/10.1093/hmg/ddv280

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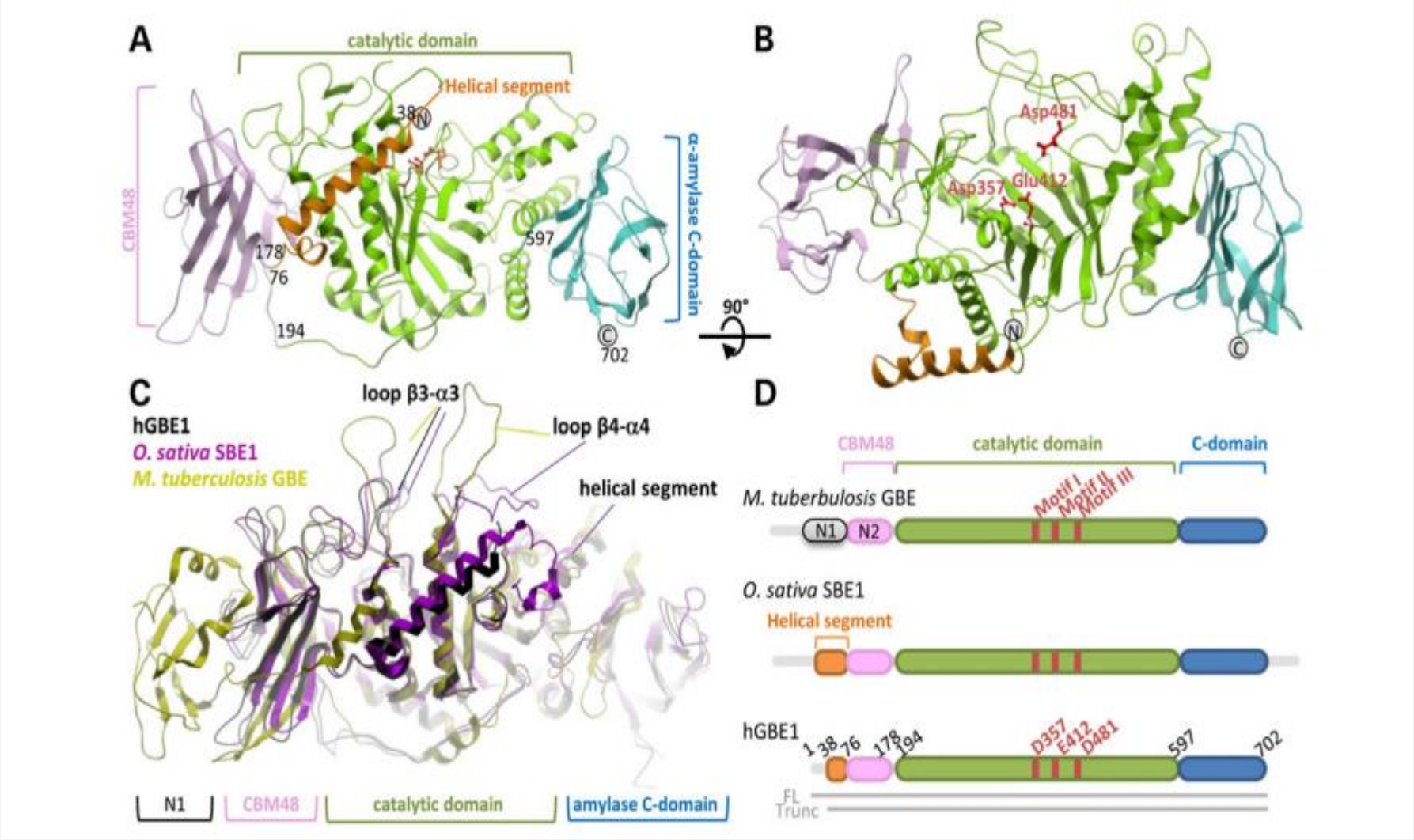


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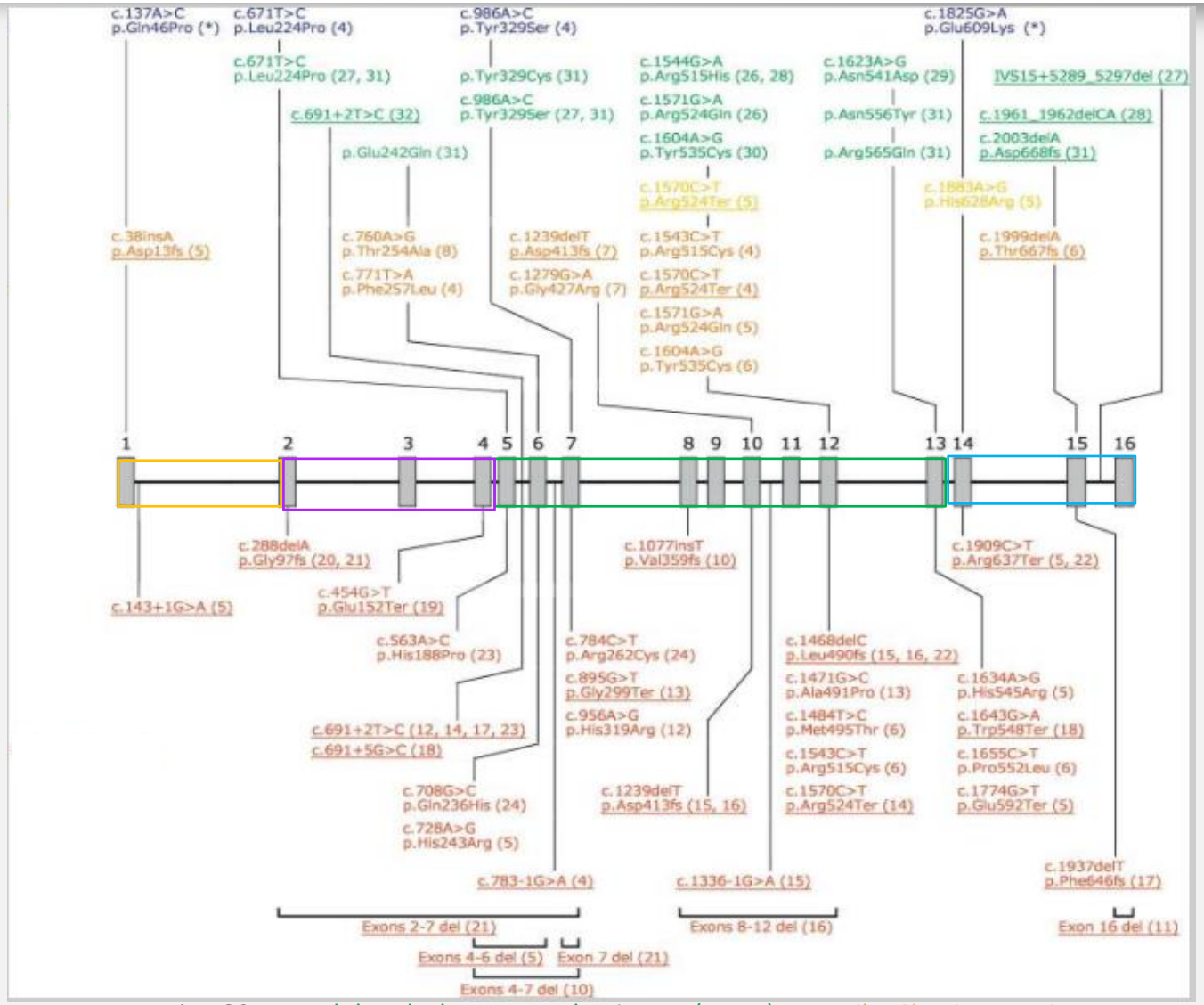
# GBE mutations

## 54 Mutations

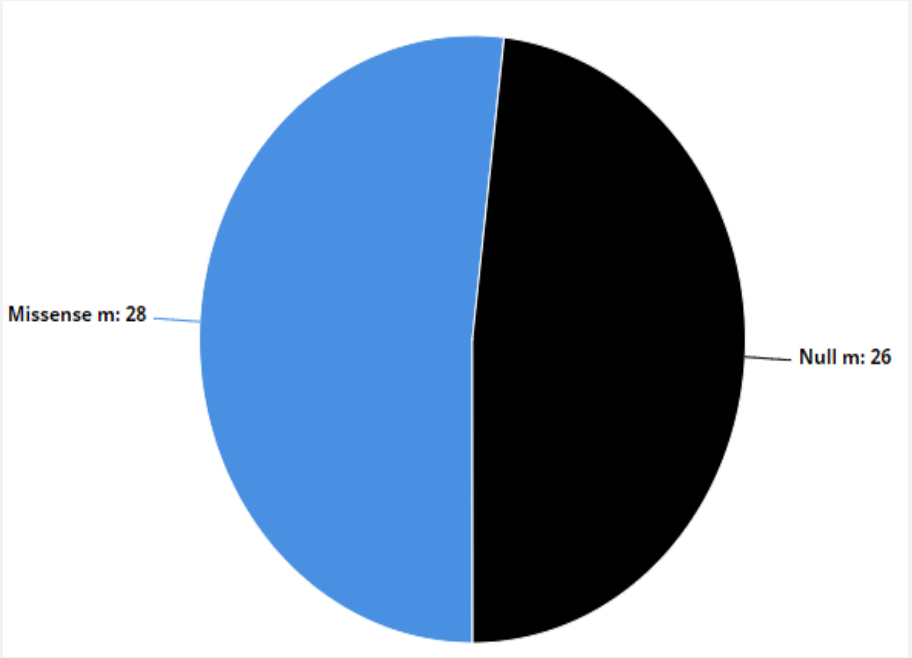



Non progressive GSD IV, Adult Polyglucosan Body Disease (APBD), Juvenile, Classic Hepatic Form
Neonatal neuromuscular forms

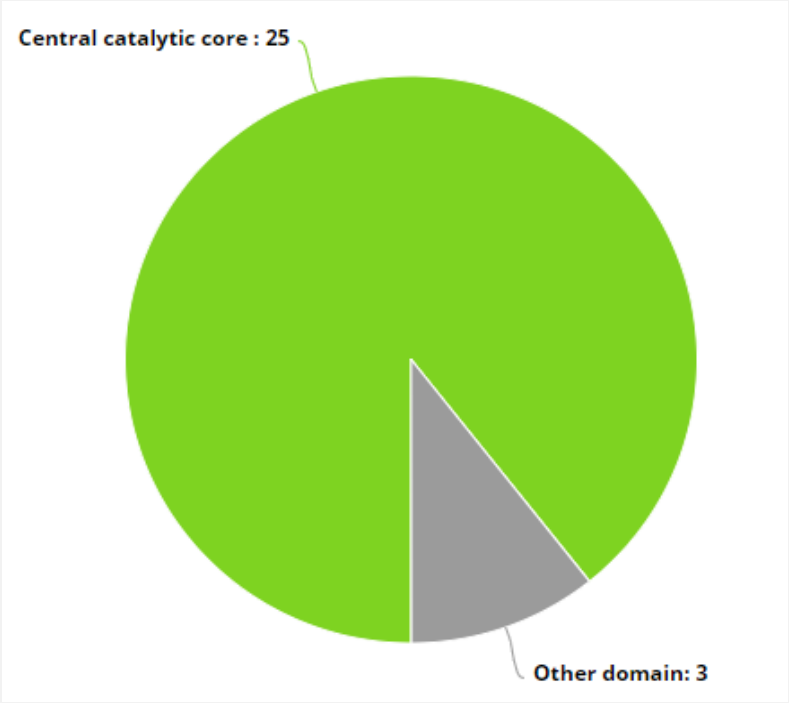


Iijima, H., Kurosawa, K., & Adachi, M. (2018). Molecular genetics and metabolism reports, 17, 31-37. https://doi.org/10.1016/j.ymgmr.2018.09.001

# GBE mutations

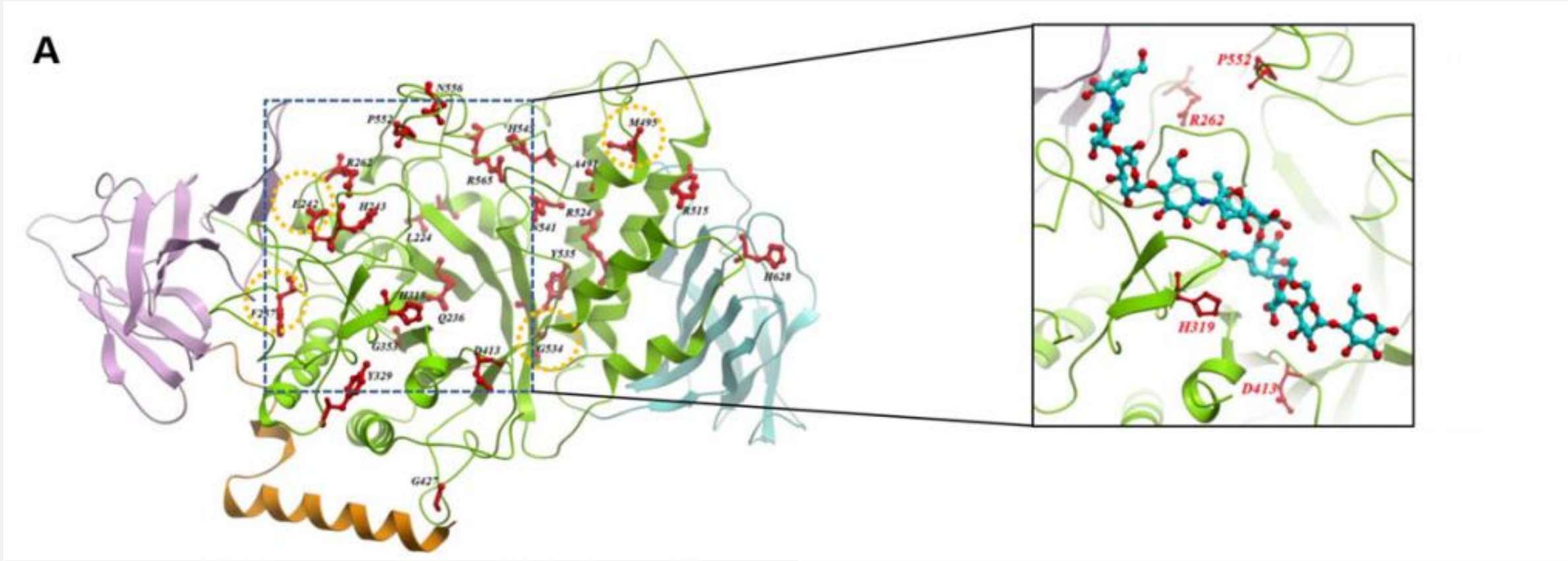



54 reported mutations




28 Missense mutations location

# GBE mutations



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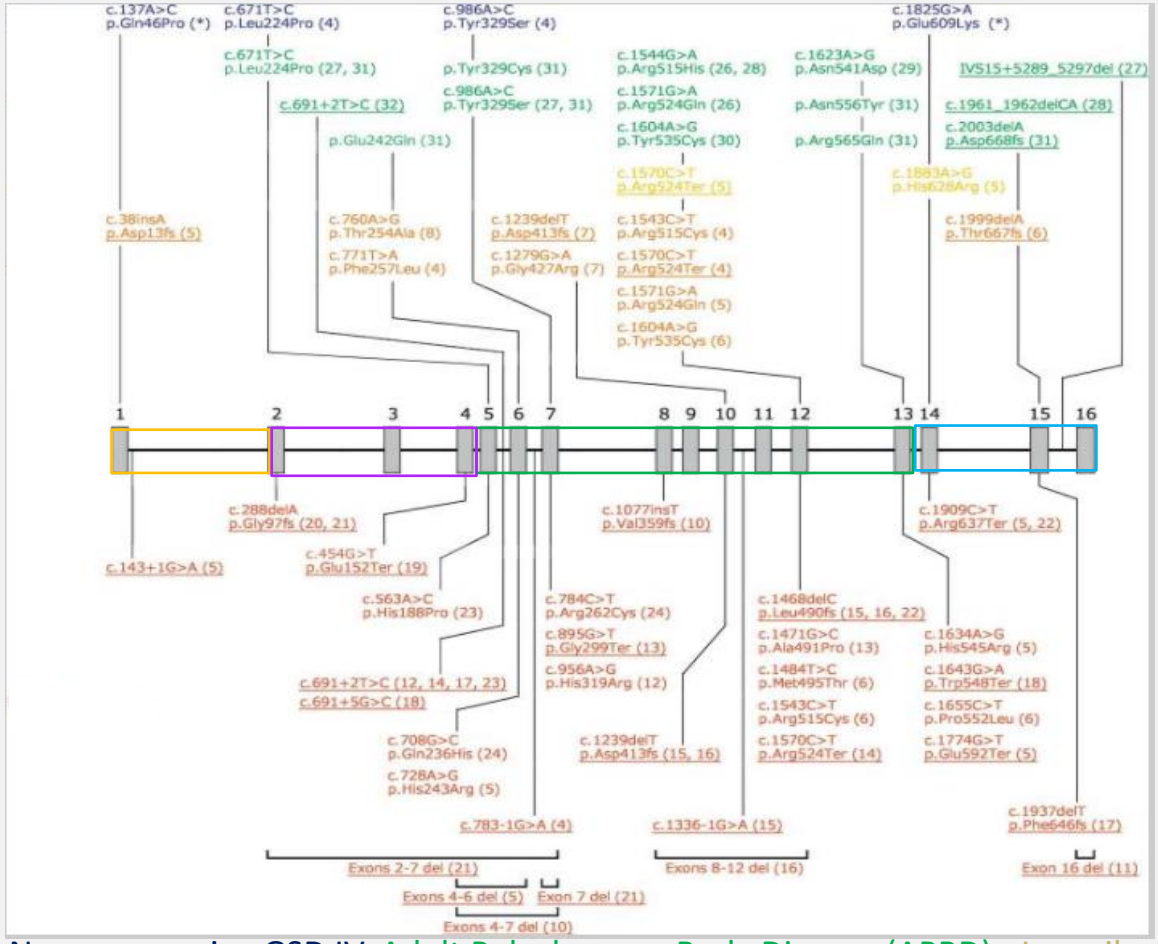
# GBE mutations




- Heterogenous mutations
- Various phenotypes
- Non hotspot deficiencies

Non progressive GSD IV, Adult Polyglucosan Body Disease (APBD), Juvenile, Classic Hepatic Form, Neonatal neuromuscular forms

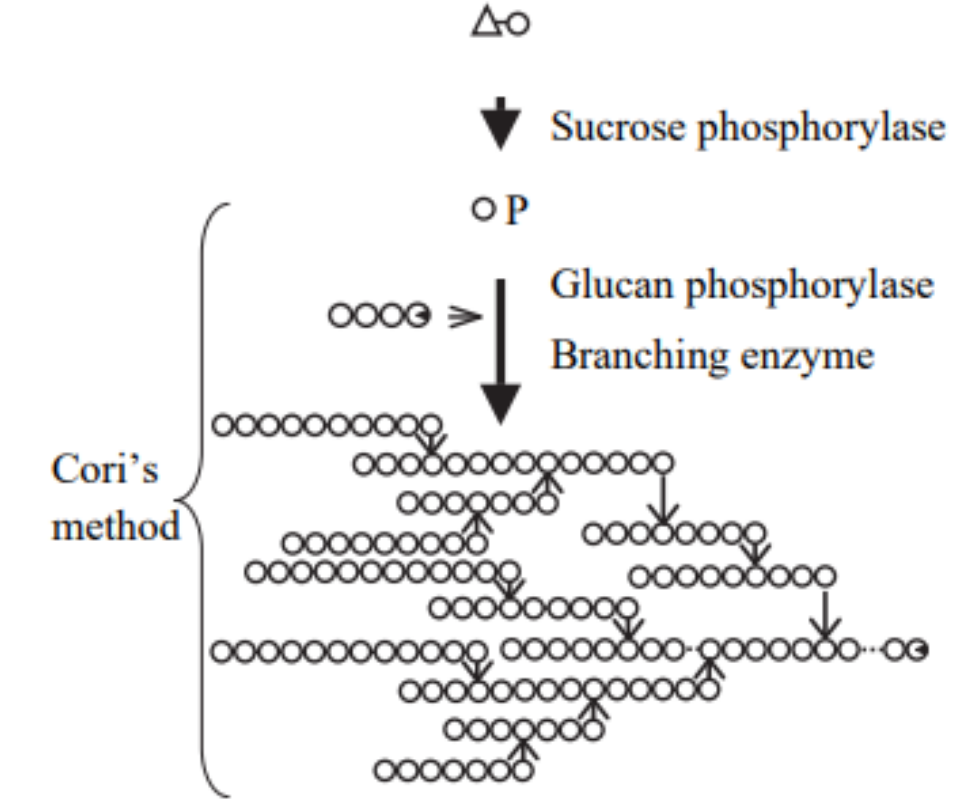


Iijima, H, Kurosawa, K., & Adachi, M. (2018). Analysis of GBE1 mutations via protein expression studies in glycogen storage disease type IV: A report on a non-progressive form with a literature review. Molecular genetics and metabolism reports, 17, 31–37. https://doi.org/10.1016/j.ymgmr.2018.09.00

*Thank you!*

# In vitro synthesis

## I. De novo synthesis




## II. Degradative synthesis from starch