# Exploring the versatility of human β-glucosidases and related glycosylated metabolites with novel chemical tools

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Propositions

Accompanying the thesis

Exploring the Versatility of Human β-Glucosidases and Related Glycosylated Metabolites with Novel Chemical Tools

1. The heterogeneous phenotypical outcome of different GBA1 mutations has been an unsolved mystery for a long time and will probably remain so for a longer time.
Beutler, E. Grabowski, G. A. Gaucher Disease, in McGraw-Hill (Ed). Metab. Mol. bases Inherit. Dis. 2001, 3635–3668.

2. Although the observed link between Parkinson's Disease and GBA1 mutations are interesting and have promoted a lot of novel research into GD they make the performed research too focused on one aspect of the underlying problems.
Stoker, T. B.; Torsney, K. M.; Barker, R. A. Pathological Mechanisms and Clinical Aspects of GBA1 Mutation-Associated Parkinson's Disease. Park. Dis. Pathog. Clin. Asp. 2018, 45–64.

3. The accumulation of plant-derived glycosylated phytosterols in Gaucher disease patients could suggest a non-genetic cause for the accumulation of exogenous lipids, potentially explaining the low but significant manifestation of Parkinson's disease in GBA1 variant carriers.
Shayman, J. A. β-glucocerebrosidase deficiency, and Parkinson's disease, Journal of Lipid Research, 2024, 65-12, This thesis Chapter 2.

4. Although the introduction of charged handles has been shown to be a good solution for the detection of low-abundant metabolites, the increase in synthetic burden of these molecules should be taken into account.
Ghirardello, M.; Zhang, Y. Y.; Voglmeir, J.; Galan, M. C. Recent Applications of Ionic Liquid-Based Tags in Glycoscience. Carbohydr. Res. 2022, 520.

5. No matter how hard you try, you will always make mistakes.
This thesis.

6. Finding a way to "Resolve" Acyl(um) migration is not only a difficult topic in The Hague.
This thesis Chapter 4.

7. Using GBA2 specific inhibitors as a basis for the generation of GBA2 specific substrates gives a good starting point in theory but is not necessarily effective in practice.
This thesis Chapter 5.

8. "Simple" looking molecules can be deceivingly difficult to synthesize.
This thesis Chapter 4.

9. Chemistry would be more enjoyable if it could be done outside.

10. Maintaining a positive attitude is not only good for oneself but also beneficial to the people around you.

11. Attempting to solve a scientific problem can often evoke the feeling of the Greek legend of Sisyphus.

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