TALLINN UNIVERSITY
School of Natural Sciences and Health

Topic for Complex Systems in Natural Sciences doctoral studies 2021/2022 admission, Tallinn University

Glycemic profile and Parkinson's disease

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The PhD project focuses on finding new biomarkers for early detection of Parkinson's disease.

Parkinson's disease (PD) is a neurodegenerative disease with a complex etiology and variable pathology. Glucose control is impaired in patients with moderate to advanced PD without diabetes, but it is unknown whether it also occurs in patients with de novo PD and in the prodromal phase of the disease. The intriguing part of the relationship between sugars and PD is based on protein glycation. Under hyperglycemic conditions, intracerebral glucose levels also increase, which in turn increases glycation, resulting in a number of different reaction products known as glycation end products (as AGEs). AGEs accumulate especially in longevity proteins such as alpha-synuclein. Oligomerization is more likely to occur with glycated aSyn. Oligomers are currently thought to be the most toxic of these. In a case of hyperglycemia, the level of reactive dicarbonyls (GO, glyoxal; MGO, methylglyoxal) increases and may enhance aSyn oligomerization while inhibiting fibrillation and leading to the accumulation of toxic glycodated aSyn oligomers. In our study, we use blood, urine, and saliva and intestinal biopsies as biological material, in which we have isolated alpha-synuclein.

The main tasks of the project are as follows.

- The study included patients with a de novo PD diagnosis (patients who have not got dopaminergic treatment), PT patients treated for up to 5 years, a control group of same-aged people, and patients with constipation who may be in a prodromal phase of PD but have not yet developed clinical PD. We have planned to study a total of 200 individuals, 50 subjects in each group.
- Using biological tissue by patients who suffered from PD, we will look and compare any changes what we see to the severity of symptoms suffered by the patient and the changes that have occurred in the brain.
- To create a glycemic profile of PT patients as a new biomarker as a tool for early diagnosis of PD and for assessment of patient subtype.
- If our hypothesis is correct, we should see a correlation between the advancement of neuropathological features in the brain ("Braak staging") and the extent of glucose metabolism perturbation.
- Through this study, and further work, we will be able to characterize metabolic changes in PD, opening an entirely new avenue for therapeutics and research.
- This study has the potential to yield new and exciting diagnostic approaches to PD and hopefully take us a step closer to curing this debilitating disease.
- At the end of this study, we aim to have identified any changes to glucose metabolism in PD that may be occurring, which can be used for further research to look at these mechanisms in more detail and our collected data aimed at defining the glycemic profile of PD patients as a tool to help in diagnosis and patient subtyping.

- Extraction and purification of target compounds from biological materials (blood, urine, saliva, intestinal biopsy).
- Sample purification by SPE methods.
- Optimization of sample pretreatment and analytical methods for the analysis of simple and complex carbohydrates.
- Analysis of glycoconjugates and determination of glycosylation patterns of macromolecules.
- Development of rapid screening (fingerprinting) methods for the assessment of glycosylation patterns in biological samples.

The main analytical/instrumental methods used in the project are: multidetector HPLC, HPLC-PAD (pulsed ampherometric detection), HPLC-MS, GC-MS/FID, NMR, solid phase extraction, general sample pretreatment, purification and derivatization methods.

Keywords: Parkinson's disease, carbohydrates, metabolites, glycoconjugates, glycoproteins, glycosylation

More information about Complex Systems in Natural Sciences PhD programme:
https://www.tlu.ee/en/lti/complex-systems-natural-sciences-phd