Physikalisch-Technische Bundesanstalt
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Nationales Metrologieinstitut

Artificial intelligence and metabolite markers in the diagnosis and prognosis of Parkinson's disease

Type: Postdoc

Principal Investigators

- Prof. Dr. Gavin O'Connor (PTB, AG 3.24)
- Prof. Dr. Karsten Hiller (Technische Universität Braunschweig)
- Prof. Dr. Tim Kacprowski (Peter L. Reichertz Institute for Medical Informatics of TU Braunschweig and Hannover Medical School)

Background

Progressive neurodegenerative diseases, such as Parkinson's disease (PD) often present heterogenous symptoms making clinical diagnosis and patient prognosis difficult. The clinical diagnosis of PD relies mainly on the physical symptoms of the disease combined with medical history and a patient's response to dopamine treatment. However, the clinical manifestations are very heterogeneous and often lag far behind pathological changes, which can lead to a late diagnosis of the disease, which is known to impact on disease progression. The exact causes of PD are still providing a fertile area for clinical research and are thought to involve both genetic and environmental contributions, which somewhat explains the diversity of symptoms and differences in the rate of disease progression. This diversity leaves patients uncertain about their long-term quality of life and hampers objective assessment of clinical trials.

Metabolomics aims to detect global differences between samples based on the numerous metabolites, followed by datamining and bioinformatics. The metabolites detected are not only endogenous but also consist of co-metabolites from gut biota as well as exogenous sources, such as ingested pharmaceuticals and environmental chemicals. Current methods are capable of distinguishing between minor changes in endogenous or exogenous stimulus, enabling a link between genetic, environmental, and physical status, to specific pathological states. The last decade has seen advances in the biological sample treatment and instrumentation that now enable the identification and quantification of metabolites on a global scale. This combined with the increased robustness of analytical platforms and robotic based automation enables the high throughput analysis of a broad range of metabolites from a range of sample types.

Currently PTB provides reference measurements for a discrete set of metabolites based on the accurate quantification of a single metabolite (single targeted quantification method) the proposed approach uses multi-parameter analysis and the standardisation of these approaches is still required. This is the focus of a new Junior research group at TU Braunschweig and the impact and use of standardisation approaches in data collection will be incorporated in this project

Project Aim, Objectives and Program

The main task will be the use of AI approaches for the identification of metabolite signals that result in the early diagnosis, stratification, prognosis, and progression of PD patient cohorts. Subtasks will include: the identification of single and multiple metabolite markers that could

enable the early diagnosis of PD and stratification of differen phenotypes; the investigation of the synergistic effects of the use of multiple metabolite markers in predicting disease progression; an assessment of the impact of improved quantitative uncertainty estimation on AI protocols and their ability to stratify patient cohorts.

Working with Prof. Brit Mollenhauer, who initiated and heads the DeNoPa (*de novo* Parkinson) cohort we will evaluate the use of AI in the identification of PD biomarkers. An established patient cohort and metabolomic data set is already available for use in this study. Within this cohort plasma and CSF from 159 PD patients and 110 matched controls have been collected longitudinally in 2 year follow-ups over a period of 10 years. Metabolomics data of matched CSF and plasma samples have already been recorded for baseline 2-, 4 and partially 6 year follow up visits and is available for the proposed project. In addition, samples for the 8 and 10 year follow up visits will be available for this project and metabolomics measurements will be contributed by the Hiller group. This combined with the activities of the new PTB/TU Braunschweig planned Junior research group on metabonomic measurement standards will enable results from the preliminary AI assessments to influence a targeted based metabolomics measurement approach, exhibiting a lower measurement uncertainty, which will enable an assessment of the impact on data refinement on the power of AI procedures.

Available data

- Non-targeted MS based metabolomics data of matched plasma and CSF samples for baseline, 2-, 4- and 6-year follow-up samples measured in analytical triplicates. In total ~400 measurements for CSF and ~500 for plasma samples.
- Samples for 8- and 10 year follow-up are available and will be measured upon project start.

Collaboration

- TU Braunschweig BRICS, Prof. Dr. Karsten Hiller,
- Paracelsus-Elena Hospital Kassel, Prof. Dr. Brit Mollenhauer

Candidate Requirements

- PhD in bioinformatics or computing programming,
- Experience in processing of omics data and biochemical measurement procedures would be an advantage.

References

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