ME-CFS-CC26-003 - Rare Variant and Epigenomic Analysis in ME/CFS

Zusammenfassung

The aim of this project is to investigate whether a subset of individuals currently diagnosed with ME/CFS carry previously unrecognized rare genetic disorders that contribute to clinically overlapping phenotypes. To address this question, we will establish a physician-led Austrian cohort in collaboration with ME/CFS specialist practitioners. Participants will undergo deep phenotypic characterization, and a subset will be selected for Oxford Nanopore Technologies (ONT) whole-genome sequencing. Genetic findings will be evaluated by a newly established multidisciplinary ME/CFS Rare Disease Board comprising experts in ME/CFS, neurogenetics, and rare diseases. Through this approach, we aim to estimate the contribution of rare genetic disorders to ME/CFS diagnoses, identify enriched disease mechanisms, and evaluate whether phenotype-aware variant prioritization approaches can identify novel rare disease genes and genetic mechanisms relevant to ME/CFS.

In parallel, the project will leverage the unique capabilities of ONT sequencing to generate both genomic and DNA methylation data from the same biological samples. The project will therefore analyse DNA methylation profiles in the SequenceME discovery cohort and subsequently evaluate the reproducibility of identified signals in the Austrian replication cohort. The Austrian ONT cohort will serve as an independent replication resource for epigenetic findings identified in the larger SequenceME study. This is particularly important because, unlike genetic variation, DNA methylation signatures are highly tissue-specific and sensitive to technical variation, making independent validation cohorts difficult to establish. In this project will investigate DNA methylation markers associated with disease status, disease severity, and disease duration, and explore whether methylation-based models can capture temporal aspects of disease progression.

Wissenschaftliche Disziplinen:
Human genetics (60%) | Epidemiology (30%) | Bioinformatics (10%)

Schlagworte:
ME/CFS Rare Variant and Epigenomic Analysis Phenotyping

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Weiterführende Links zu den beteiligten Personen und zum Projekt finden Sie unter
https://wwtf.at/funding/programmes/ei/ME-CFS-CC26-003/