Internship project

Plasma proteomics and proteogenomic in the diagnosis of VWD patients

Von Willebrand Disease (VWD) is a disease which is characterized by low reduced levels or a missing or dysfunction in Von Willebrand factor. There are three subtypes: Type 1 and 3 classified by quantitative defect and type 2 is a group of four subvariants (2A, 2B, 2M, 2N) by qualitative defect of VWF. The diagnosis of VWD is complex and not always straight forward due the heterogeneity of genetic variants in the gene encoding for VWF (chromosome 12p13) Approximately 35% of patients with type 1 von Willebrand disease (VWD) do not have a known pathogenic variant in the von Willebrand factor (VWF) gene [1]. Mass spectrometry-based plasma proteomics allows identification of thousands peptides of simultaneously by matching experimental to theoretical spectra calculated from protein sequence databases usually based on the most prevalent form of all proteins encoded by one gene as canonical sequence. Recently we integrated genomics and MS-based plasma proteomics to identify genetic pathogenic variants in a cohort of Von Willebrand (VWD) patients. In total, we generated two databases one with the known genetic variants from the 29 VWD patients (40 peptides). Second, a database based on all possible variants in VWF containing single amino-acid changes resulting in 53447 peptides. In principle, the generated data could uniquely identify VWF mutations using the combination of variant peptides.

The aim of this project is to analyze the existing proteogenomic data by (i) improving the data analysis workflow (ii) extending its functionality and (iii) potentially validate the outcomes using external (patient) cohort data.

Requirements:
Duration of at least 6 months
Master student with an interest in bioinformatics and who are looking for a dynamic and interesting internship are encouraged to contact Iris kreft or Maartje van den Biggelaar