TOPICAL Seminar

Date: 22 January
Time: 10.00-11.00
Venue: 1874-132

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Professor

Diversity in depression-induced molecular adaptations

The neuropsychiatric disorders major depressive disorder (MDD) and bipolar disorder (BD) are leading causes of disability globally. These disorders have partially overlapping symptoms, complicating diagnosis, and often lead to inaccurate treatment. Identifying what sets them apart at the molecular level can improve diagnosis and therapies to manage their impact on quality of life.

Here, we performed a quantitative proteomics analysis on the Netherlands Brain Bank Psy-cohort (patients with MDD, and BD (n=24-30 per disease), and controls), comprising grey matter of the superior temporal (GTS) and frontal gyrus (GFS), from donors with extensive clinical data compiled in the Netherlands Neurogenetics Database. The brain areas chosen were previously implicated in these disorders. Our aims were to 1) establish a molecular profile of disease status to find global disease-specific markers, and 2) use these profiles to cluster patients and examine how much these disease types overlap based on their molecular signature.

Patient-clustering based on >6000 high confidence identified and quantified proteins (peptide detection rate 75%; ≥2 peptides per protein) from these two brain areas showed a clear separation based on tissue type, and age. Analysis per tissue type with sex and age as co-factor showed the most differentially regulated proteins between patients and controls for GFS tissue (2% of proteome; FDR q-value 0.05). Surprisingly, MDD showed clear post-synaptic protein dysregulation compared to BD (SYNGO analysis). Multiple sex-specific DEP were identified, pointing to sex as an important factor to consider. Moreover, disease state has a large effect on the adapted proteome. Lastly, we find GWAS correlation of our differentially expressed proteins.

Together, these high-content proteomics techniques can offer new insights into dysregulated proteins and pathways in the brain and potentially lead to discovering new targets for more effective treatment.

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