Integration of Functional Genomics and Data Mining Methodologies in the Study of Bipolar Disorder and Schizophrenia

av

Marianthi Logotheti

Akademisk avhandling

Avhandling för medicine doktorsexamen i Medicinsk vetenskap, inriktning biomedicin, som kommer att förvaras offentligt fredagen den 09 december 2016 kl. 09.00
Sal HSC3, Campus Universitetssjukhuset Örebro

Opponent: Professor Nikos Stefanis
Dept. Psychiatry, Eginition Hospital, Medical School, University of Athens, Greece

Örebro universitet
Institutionen för hälsovetenskap och medicin
701 82 ÖREBRO
Abstract


Bipolar disorder and schizophrenia are two severe psychiatric disorders characterized by a complex genetic basis, coupled to the influence of environmental factors. In this thesis, functional genomic analysis tools were used for the study of the underlying pathophysiology of these disorders, focusing on gene expression and function on a global scale with the application of high-throughput methods. Datasets from public databases regarding transcriptomic data of postmortem brain and skin fibroblast cells of patients with either schizophrenia or bipolar disorder were analyzed in order to identify differentially expressed genes. In addition, fibroblast cells of bipolar disorder patients obtained from the Biobank of the Neuropsychiatric Research Laboratory of Örebro University were cultured, RNA was extracted and used for microarray analysis. In order to gain deeper insight into the biological mechanisms related to the studied psychiatric disorders, the differentially expressed gene lists were subjected to pathway and target prioritization analysis, using proprietary tools developed by the group of Metabolic Engineering and Bioinformatics, of the National Hellenic Research Foundation, thus indicating various cellular processes as significantly altered. Many of the molecular processes derived from the analysis of the postmortem brain data of schizophrenia and bipolar disorder were also identified in the skin fibroblast cells. Additionally, through the use of machine learning methods, gene expression data from patients with schizophrenia were exploited for the identification of a subset of genes with discriminative ability between schizophrenia and healthy control subjects. Interestingly, a set of genes with high separating efficiency was derived from fibroblast gene expression profiling. This thesis suggests the suitability of skin fibroblasts as a reliable model for the diagnostic evaluation of psychiatric disorders and schizophrenia in particular, through the construction of promising machine-learning based classification models, exploiting gene expression data from peripheral tissues.

Keywords: Bipolar Disorder, Schizophrenia, Fibroblasts, DNA Microarrays, Machine Learning, Functional Analysis, Gene Expression, Transcriptomics

Marianthi Logotheti, School of Medical Sciences, Örebro University, SE-701 82 Örebro, Sweden, malogotheti@oru.se