Tamara Raschka et al., J Mol Genet Med 2016, 10:3 (Suppl)
http://dx.doi.org/10.4172/1747-0862.C1.012

Analytical strategy to unravel novel candidates from Alzheimer's disease gene regulatory networks using public transcriptomic studies

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Alzheimer's disease (AD) is the most common type of dementia, progressively destroying cognitive capabilities. Despite recent progress, there are no available curable drugs; questioning our current knowledge of AD pathology. Gene regulatory networks (GRNs), generated from meta-analysis of existing studies, could help us revisit our mechanistic understanding. However, they do not elaborate on the context specificity and additionally, miss out on lesser studied genes given the tendency to focus on differential expressed genes and prior knowledge. In this poster, we present a novel strategy to determine common mechanistic patterns across all publicly available AD gene expression datasets. An optimized method of BC3Net and WGCNA were used to get robust and coherent gene regulatory patterns. This approach leverages the power of literature and iterative functional enrichment approach (derived from the data) to define context specificity. The results show significant enrichment for pathways across disparate datasets that are involved in key signaling mechanisms, like neurotrophin and calcium signaling. Interestingly, there are no common genes involved in these pathways across datasets. Among these, genetic variant and linkage disequilibrium analysis prioritized novel candidate genes, which are less studied in AD, but prominent in AD comorbidity. Some of these genes encode for cytokines, which are part of the immune response, responsible for the cell growth and differentiation and inflammation. For the first time we show that functional enrichment to generate GRNs in neurodegeneration reveal unknown yet novel biomarkers. This may lead the way to mitigate the black-box pathogenesis of AD.

Biography

Tamara Raschka has received her Bachelor's degree from University of Applied Science Koblenz in 2015 and she is currently pursuing Masters in Applied Mathematics, Koblenz. She has joined Fraunhofer SCAI, Department of Bioinformatics as a student in March 2015. Her research work mainly focuses on building robust approaches for analyzing public gene expression studies to explore novel and previously unknown biomarkers in a defined disease context. Currently, she is involved in publicly funded IMI project AETIONOMY where the goal is to build a mechanism based taxonomy aiding in classification of disease sub groups for patient stratification.

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