A machine learning approach to identify Alzheimers disease therapeutic targets

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USA

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A machine learning approach to identify Alzheimers disease therapeutic targets

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Research Abstract

DESCRIPTION (provided by applicant): The ultimate goal of this project is to enable the use of molecular profiles (e.g., expression data, genetic data, and proteomic data) of Alzheimer’s disease (AD) patients to facilitate to identify therapeutic targets. There is a growing availabilit of

expression profiles of brain tissues from AD patients and normal subjects, which holds great promise for improving our molecular-level understanding of AD and developing new drugs. The most important step necessary to realize this goal is to identify molecular features, such as expression levels of certain genes, in these data that are predictive of AD phenotypes indicative of the disease progression, such as neuropathological and clinical phenotypes. Despite the pressing need, due to the high-dimensionality of the expression data, it is an open challenge to identify molecular features that are truly associated with a phenotype. This is a critical barrier that impedes progress in identifying therapeutic targets from high-throughput molecular profiles. To resolve this challenge, this project proposes to identify network-based features representing important molecular events in disease progression from gene expression data, and use the identified features to predict AD-related phenotypes. This approach can effectively reduce the dimensionality of the expression data by focusing on a small subset of genes that are likely relevant to AD. In particular, we focus on the following network-features: perturbed genes that have different connectivity patterns with other genes between different AD stages (Aim 1); hubs that are densely connected with other genes in the inferred network in AD (Aim 2); and common hubs (co-hubs) between AD and cardiovascular disease (Aim 2). In each aim, we will develop powerful machine learning (ML) algorithms that can jointly model interactions of genes that are present in multiple heterogeneous datasets. We will apply the identified network-based features to predict neuropathological and clinical phenotypes in the data from a densely phenotyped cohort in the Adult Changes in Thought (ACT) study. The features selected to be predictive of these phenotypes will provide us with better insights into the molecular mechanisms driving AD progression, which can lead to effective therapeutic targets. Successful completion of the proposed research will lead to the discovery of the molecular features that are informative of the disease processes and can thus guide drug development. The proposed research will lay the groundwork of an interdisciplinary team of computer scientists, a statistician, basic biologists, a internist and a neuropathologist to develop a systematic computational framework for identifying AD therapeutic targets from heterogeneous molecular and clinical profiles.

Further information available at:

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