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# Expression-based Diagnosis of Autism Spectrum Disorder and Potential Prognosis of other Complex Diseases

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## BACKGROUND

Autism spectrum disorder (ASD) is a neurodevelopmental disorder with prenatal and early postnatal biological onset. Genetic factors contribute to the predisposition and development of ASD with estimated heritability rates of 50-83%. Large-scale genetic studies have implicated several hundred risk (rASD) genes that appear to be associated with many different pathways, cell processes, and neurodevelopmental stages. This highly heterogeneous genetic landscape has raised challenges in elucidating the biological mechanisms involved in the disorder. While rigorous proof remains lacking, current evidence suggests that rASD genes fall into networks and biological processes that modulate one or more critical stages of prenatal and early postnatal brain development, including neuronal proliferation, migration, neurite growth, synapse formation and function. However, these insights are mostly gained from focused studies on single rASD genes or based on transcriptome data of non-ASD brains, leaving an incomplete picture of rASD-induced molecular changes at the individual level and relationships with early-age clinical heterogeneity.

## TECHNOLOGY DESCRIPTION

Researchers at UC San Diego have developed a novel method to identify ASD biomarkers. Traditionally, biomarkers are identified based on the expression patterns of differentially expressed genes and such methods rely on univariate aspects of genes (i.e., their fold change compared to normal controls). The current invention relies on a method that goes beyond that and considers the bivariate changes between genes. This methodology provides more robust signals that can be used as the disease signature. Specifically, our framework identifies dysregulated gene networks in the disease condition. Such network combines information on observed gene expression patterns with current state of knowledge on gene regulatory mechanisms, signaling pathways, and protein interactions. Next, it measures the activity level of the dysregulated network in different individuals based on the co-expression pattern of interacting genes in the network. The observed network activity levels correlate well with the clinically measured severity level of the complex diseases such as autism and develops an ASD signature.

This was achieved by analyzing the peripheral blood of living ASD individuals at very young ages and examining the transcriptomic data from leukocytes, stems cell models, and the developing brain to study the underlying architecture of transcriptional dysregulation in ASD, its connection to rASD genes, and its association with prenatal development and clinical outcomes of ASD toddlers. Specifically, we discovered a conserved dysregulated gene network by analyzing leukocyte transcriptomic data from 1-4 years old ASD and typically developing (TD) toddlers. The dysregulated network is enriched for pathways known to be perturbed in ASD neurons, impacts highly expressed processes in prenatal brain development, and is dysregulated in iPS cell-derived neurons from ASD cases. This is the first signature that correlates with the clinical severity of autistic individuals. Such signature has the promise for early diagnosis, prognosis and classification of autistic individuals at early ages.

## APPLICATIONS

The current invention is a signature for autism spectrum disorder. The developed framework works on the transcriptome data. For autism diagnosis, prognosis, and classification, our framework needs access to blood transcriptome data from autistic and normal control individuals.

## ADVANTAGES

The invention can be used for the biomarker development for diagnosis and prognosis of any complex disease and disorder.

## STATE OF DEVELOPMENT

We have experimental data from 240 male toddlers that support the functionality of the developed signature.

## INTELLECTUAL PROPERTY INFO

This technology is patent pending and available for licensing and/or research sponsorship.

## PATENT STATUS

| Country | Type | Number | Dated | Case |
|---|---|---|---|---|
| Patent Cooperation Treaty | Published Application | WO 2020/014620 | 01/16/2020 | 2018-256 |

OTHER INFORMATION

KEYWORDS

ASD, autism, autism spectrum disorder, biomarker, molecular signature, diagnosis, prognosis, transcriptional analysis, prenatal development

CATEGORIZED AS

▸ Medical
  ▸ Diagnostics
  ▸ Disease: Genetic Diseases and Dysmorphic Syndromes
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