Circular RNAs for the Diagnosis and Treatment of Brain Disorders

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Background

Psychiatric disorders are diverse and heterogeneous brain disorders that together affect approximately 20% of the adult population, impose a robust socioeconomic burden, and are a leading cause of disability worldwide. With growing concerns surrounding mental health, not only is it important to detect and diagnose these psychiatric disorders during their early stages, but also to monitor therapeutic efficacy and uncover better therapeutic alternatives. Moreover, the identification of proper early biomarkers for such diseases can serve as a valuable tool in evaluating a patient's risk of acquiring a psychiatric disease before the disease presents symptoms. Current RNA biomarker approaches are based on detecting linear RNA expression in adult tissue or bodily fluids. However, linear mRNAs are notoriously prone to degradation and most have very low half-lives (a few hours), thus making their expression unstable and transient, especially in blood/serum samples, which contain high levels of enzymes that break down linear RNA. Circular RNAs are produced from the backsplicing and covalent joining of exons and/or introns and are by far the most resistant to degradation RNA molecules with half-lives of several days. Thus, circRNAs can serve as robust biomarkers in both tissue and bodily fluids. Based on our work, specific circRNAs altered in the brain of subjects with psychiatric disorders, can also be found to be altered in induced pluripotent stem cell (iPSC)-derived neuronal cultures produced by patient fibroblasts, which is a popular model to study early brain development that can also be used for monitoring risk for psychiatric disorders. As a result, the development of a very stable biomarker that can be used to diagnose psychiatric disorders through both bodily fluid samples and patient-derived cultures would revolutionize early diagnosis and overall treatment of psychiatric disorders.

Technology Breakthrough

A researcher at the University of New Mexico has identified a relationship between circular RNAs (circRNAs) and psychiatric disorders. The relationship and correlations found between circRNAs and psychiatric disorders can be used in order to further develop circRNAs as biomarkers to effectively and efficiently identify psychiatric disorders in patients during early stages of the disease, or before the onset of the disease, help examine therapeutic efficacy and compliance, and design novel drug targets. The unique properties of circRNAs not only allow for early diagnosis, but hold potential for the development of quick and direct diagnosis of psychiatric disease through the use of blood samples and patient-derived cultures. With this, a tool is given to directly diagnose SCZ, BD and other types of mental disease.

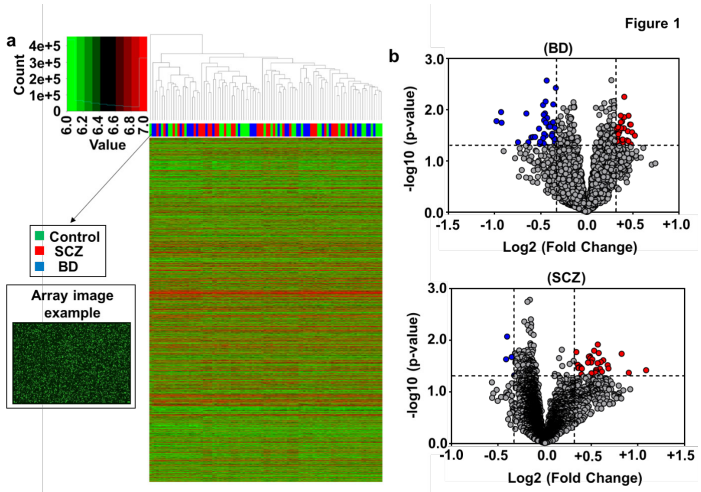

***Figure 1| Alterations in circRNA expression in Bipolar Disorder (BD) and Schizophrenia (SCZ) postmortem brains. a**, Hierarchical clustering analysis of circRNA array data in 100 orbitofrontal (OFC) postmortem RNA samples treated with RNase-R for linear RNA digestion. Example of circRNA array raw image is also shown. **b**, Volcano plots showing differential circRNA expression in BD (upper) and SCZ (lower) patients vs unaffected Controls (x-axis = relative to control log2 fold changes; y-axis: negative log10 of the p-values). Vertical lines correspond to >1.25-fold changes, and the horizontal line represents p < .05. Example of validated circRNAs are shown in the graph.*

Key Advantages

- *Fast and accurate diagnosis of mental disease with stable biomarkers.*
- *Allows for earlier detection of disease and determining an individual's risk for developing disease.*
- *Explores the role of circRNAs in brain function and disease.*
- *Able to identify presence or risk of mental disease through bodily fluid samples and patient-derived cultures.*

Intellectual Property

PCT Application: PCT/US19/29065

Contact

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