MicroRNA Correlates of Childhood Maltreatment and Suicidality

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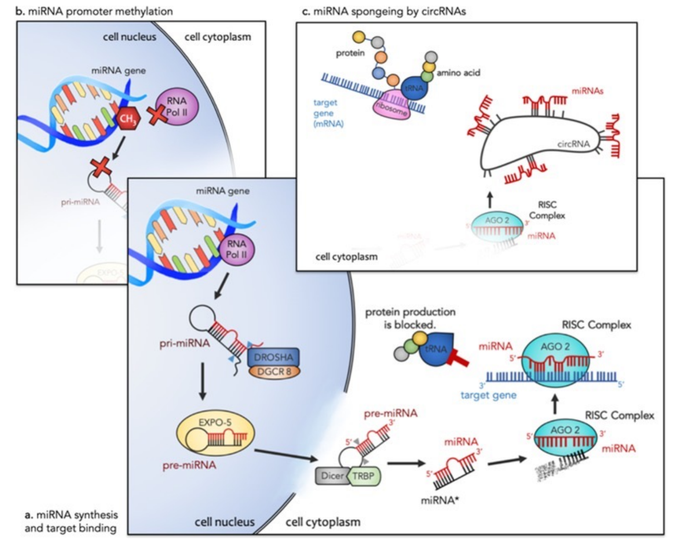
Background

- **Early life trauma, especially physical, sexual, or emotional abuse, are strong risk factors for both depression and suicide.** However, the precise mechanisms that link abuse with depression and suicide risk are not well understood.
- One hypothesis is that these **environmental events induce chemical modifications of DNA**, and that these changes link early life abuse with later development of depression and suicide attempts.
- Our preliminary data indicate that **chemical modification of the DNA sequences for micro RNAs (miRNAs) link early trauma with depression and suicide.**
- Micro RNAs are short regulatory RNAs that are an important mechanism for environmental regulation of RNA and protein expression.
- These are **significantly altered in people with early life trauma**, and specific micro RNA changes are associated with depression and suicide risk.
- The overarching hypothesis of this study is that **childhood maltreatment can induce long-term chemical modifications of DNA for micro RNAs**. The net effect of these changes may lead to **long-term cellular (mal)adaptations** which may lead to **depression and suicide vulnerability** in people with a history of childhood maltreatment.

Methods

- Our research group has developed a novel method of extracting miRNAs that are specific to neurons, which are contained in small vesicles called exosomes in peripheral blood samples. We have shown that the patterns of miRNA expression are very similar in neuron-specific exosomes and human post-mortem brain samples.
- This study will recruit participants in three groups – depression with recent serious suicidal ideation or attempt, depressed without recent ideation or attempt, and normal volunteer controls. All studies will be done in a blinded fashion with coded samples
- We will also conduct a widely used experimental stressor called the Trier Social Stress Test (TSST). The TSST is a standardized mildly stressful experience that reliably induces an increase in blood cortisol. We have also shown that the TSST induces changes in miRNA expression that are different in people with a history of childhood maltreatment who are depressed and suicidal. Ten ml. blood samples will be obtained at baseline and immediately post-TSST and 15, 30, 60, and 90 minutes after the test.

The blood samples will be immediately processed and stored at -80□C. Exosomes will be extracted from the blood plasma samples and miRNA analyzed using an RNA sequencing method.



Allen, L., Dwivedi, Y. MicroRNA mediators of early life stress vulnerability to depression and suicidal behavior. *Mol Psychiatry* **25,** 308–320 (2020). https://doi.org/10.1038/s41380-019-0597-8

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