Title: MicroRNA expression profiles from peripheral blood may serve as biomarkers for depression risk in children and adolescents

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Background: Discovering objective molecular markers of psychiatric risk, particularly complemented with longitudinal clinical records, will aid early prevention and intervention. Emerging role of microRNAs in neurodevelopment and mental illness warrants a non-invasive investigation focused on early life. In this study we conducted a high-throughput analysis of microRNA profiles in peripheral fluids derived from blood in adolescents with or without clinical levels of depression.

Methods: A total of 62 dried blood spots samples the Teen Inflammation Glutamate Emotion Research (TIGER; N=62) cohort were sequenced using small RNA protocol. Trimmed reads were processed following exceRpt small RNA-Seq pipeline and differential expression analyzed using DESeq2 package. Categorical groups were assigned based on the clinical diagnosis and Reynolds Adolescent Depression Scale (RADS).

Results: Differentially expressed (DE) microRNAs (padj<0.05) were upregulated in individuals diagnosed with MDD compared to controls. Further analysis revealed DE microRNAs between adolescents with scores above or below the RADS cutoff threshold, and high versus low suicidal ideation score threshold.

Conclusions: To our knowledge, this is the first investigation of blood microRNA expression signatures of depression in youth. Identified microRNA profiles will serve as the basis of gene target prediction and creation of expression-based gene networks within brain regions relevant in depression, which will improve our understanding of the functional mechanisms underlying psychiatric vulnerability in adolescence.