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HOT TOPICS

Blood-based biomarkers for suicide in depression: moving a step closer to prediction

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Every year ~800,000 individuals worldwide and 48,000 in the United States (US) alone lose their lives to suicide (Centers for Disease Control and Prevention). In the US, suicide rates have dramatically increased by 35% since 2016 [1] despite efforts to curve the suicide epidemic. These statistics underscore that suicide is a major public health issue requiring increased attention and the urgent need for the development of rapid, novel, and reliable strategies for the identification of individuals at high risk for suicide early enough to intervene in a timely manner.

Major depressive disorder (MDD) is the most common psychiatric diagnosis among suicide victims [2] but only a subset of depressed patients ever actually commit suicide [3]. Approximately 45% of suicide victims visit a clinician in the month preceding their suicide and a third see a healthcare professional within the week of death [4]. There is a lack of easily available, reliable, and fast tools to determine suicide risk throughout these visits and a blood-based suicide biomarker screen could be of great use to identify at risk patients.

Previous biomarker investigations have been conducted in subjects who died by suicide with various psychiatric diagnoses and investigated either blood or brain. Using both brain tissue and blood from a postmortem cohort consisting of MDD patients who died by suicide (MDD-S), MDD patients who died of other causes (MDD-NS), and non-psychiatric controls (C) we explored gene expression differences unique to suicide victims [5]. We used a custom NanoString assay, a technology not affected by RNA degradation, which is a concern with non-preserved blood and postmortem brain tissue. We identified 14 highly significant genes to be differentially expressed (DEG) in the blood of depressed suicides, with four of these also showing significant changes in the brain of MDD-S when compared to MDD-NS. The top six DEGs in suicide blood are: PER3, MTPAP, SLC25A26, CD19, SOX9, and GAR1. Of course, our identified biomarker will require validation in prospective clinical cohorts, and its ability to classify clinical gene expression profiles for assessing suicide risk needs to be evaluated using predictive algorithms in larger samples. The use of non-preserved blood is of critical importance because many labs, clinics, and/or coroners offices may not have access to blood tubes specific for RNA preservation or may already have previously collected blood tubes that can be used for a posteriori prediction studies.

Our findings clearly show that within the context of MDD, suicide victims have a gene expression signature distinct from non-suicides, which includes genes involved in stress response, polyamine metabolism, immune response, and telomere maintenance. While encouraging, future studies using cell-specific gene expression profiling, in brain and blood, may uncover additional suicide-specific molecular phenotypes since our findings suggest alterations in suicides that are specific to immune cell populations. Brain-blood comparisons of molecular signatures are particularly useful for the development of clinical biomarkers for neuropsychiatric disorders. These results bring us one step closer to the development of a molecular test to identify patients at highest risk for suicide.

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AUTHOR CONTRIBUTIONS

AS and FM conceived and wrote the manuscript.

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COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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