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*Peripheral Neural-Derived Exosomal microRNAs as
Biomarkers for Suicidality and Treatment Response*

Dr. Dwivedi received his Ph.D. from Central Drug Research Institute, India, a premier research institution focused on developing novel drugs. He did his post-doctoral training at the Illinois State Psychiatric Research Institute, Chicago. He then joined the University of Illinois at Chicago as Assistant Professor and reached the rank of tenured Professor. He joined the Department of Psychiatry and Behavioral Neuroscience, the University of Alabama at Birmingham, in August 2013 as the Elesabeth Ridgely Shook Endowed Chair in Psychiatry and tenured Professor and Director of Translational Research, UAB Mood Disorders Program. He is also the Division Director of Behavioral Neurobiology and Director of the UAB Depression and Suicide Center. Dr. Dwivedi is an internationally recognized molecular neuroscientist who has significantly contributed to the understanding of fundamental molecular mechanisms associated with stress biology and mood disorders, and suicide. He has received numerous awards and is a member of the US National Institute of Mental Health study section, Chair of PMDA NIMH study section, and member of the Scientific Council of American Foundation of Suicide Prevention and Genetics and Neurobiology Task Force associated with the International Association of Suicide Prevention. He has been consistently funded by the National Institute of Mental Health and the American Foundation for Suicide Prevention. He has published 160 peer-reviewed papers and numerous book chapters and has edited a book: *The Neurobiological Basis of Suicide*. He serves on the editorial Board of several scientific journals and has been invited worldwide for various talks and symposia.

Dr. Dwivedi's research primarily focuses on understanding the neurobiological mechanisms associated with major depression and suicidal behavior. To increase the understanding of these disorders and identify new therapeutic targets and treatment approaches, Dr. Dwivedi's lab examines the molecular and cellular nature of events in the brain that may lead to suicidal and depressive behavior. To achieve this, he is utilizing various approaches using human postmortem brain studies, peripheral blood cell studies from the patient population, rat brain studies involving manipulation of the stress axis, rodent models of depression and post-traumatic disorder, and gene knock-out mice. His primary area of research includes neurotransmitter receptors, cytokines, neurotrophins, cellular signaling, neural plasticity, and gene regulation in depression and suicide risk using gene expression, RNA sequencing, microRNAs, and epigenetic approaches.

Abstract: Suicide is the 10th leading cause of death in the US. Thus, there is a desperate need for identifying risk factors and for non-invasive, reliable biomarkers that can be used for early detection of suicidality and treatment response. MicroRNAs (miRNAs) have emerged as an important class of small non-coding RNAs that suppress the translation and stability of specific target genes. Since miRNAs show a highly regulated expression, they contribute to developing and maintaining specific transcriptomes and thus have the unique ability to influence physiological and disease phenotypes. Using preclinical and clinical studies, I will provide evidence of the role of miRNAs in stress resiliency and susceptibility to developing depression phenotype. I will also discuss the role of synaptosomal miRNAs in depression. Recently, we found that a subset of miRNAs is specifically altered in the brain of suicide subjects regardless of psychopathology. Neural miRNAs are responsive to environmental and pathological changes and can be actively secreted by cells such as exosomes from the brain into blood. Using a neural-specific surface marker, we successfully isolated neural-derived exosomes from blood plasma and found that these exosomes are enriched with miRNAs expressed in the brain. Using this novel approach, we have examined whether neural-derived exosomal miRNAs can be used as a diagnostic tool to identify suicidality and treatment response. I will discuss our preliminary data on neural-derived exosomal miRNAs in depressed suicidal patients and their response to acute ketamine treatment.