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Developing molecular genetic biomarkers in neuropsychiatric disorders

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Discovering genetic susceptibility and protective factors for complex diseases such as the neuropsychiatric disorders is of fundamental importance for advancing new diagnostic and therapeutic approaches. These goals are challenging in a field where diagnoses rely largely on clinical presentation, which may be heterogeneous and the underlying genetic susceptibility and/or protective factors may respond to environmental effects.

While genome-wide association studies (GWAS) have powerfully identified components

of the genetic basis for complex multiple genetic traits, there likely remain additional genetic risk factors that underlie the liability to these conditions. Furthermore, identification and characterization of the causal risk variant(s) in each of the susceptibility loci constitute a formidable task, particularly in the absence of any prior knowledge about their biological function or mechanism of action. Biologically relevant, quantitative phenotypes (endophenotypes) provide an alternative to traditional binary disease phenotypes in the discovery of susceptibility genes for neuropsychiatric conditions. I provide an overview of these issues highlighting potential genetic effects on gene expression, neuropathology, and cognitive endophenotypes in the normally aging brain, with an example demonstrating the potential for functional approaches to discover the role of genetic variants associated with disease susceptibility and/or protective pathways. In addition, I discuss how this approach may help understand mechanisms of pharmacologic response to therapy.

Biography

Robert Lipsky is Director of translational research at Inova's Department of Neurosciences and holds multiple university appointments as a full Professor, and is Chief of Inova's translational neuroscience research laboratory at the Krasnow Institute for Advanced Study at George Mason University. Dr. Lipsky pursues translational research to understand the etiology of complex disorders involving the brain through an understanding of genetics and its intersection with the patient's environment, insights that will lead to new treatment approaches as well as better targeting of existing therapies. He has co-authored more than 100 peer-reviewed scientific publications and holds two U.S. patents.

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