

Pharma Biotech 2018: Epitranscriptomic blood biomarkers to manage psychiatric disorders

Dinah Weissmann
ALCEDIAG, France

E-mail: hanneke.later-nijland@axonlawyers.com

Abstract

Major depressive and bipolar disorders are leading causes of disability worldwide yet, many people remain undiagnosed or misdiagnosed or ineffectively treated. Diagnosis relies on the clinical assessment of symptoms and currently, there is no molecular diagnostic test available. Identifying and validating blood biomarkers could provide a more accurate and objective means of diagnosis. Genetic and epigenetic events are involved in psychiatric aetiology, among them RNA editing modifications have been associated with inflammation and neuropsychiatric disorders. Adenosine to inosine RNA editing constitutes a physiological cellular process that translates environmental cues by regulating protein function at the synaptic level in health and disease. RNA editing is post-transcriptional process that leads to functional diversity of proteins. These marks form the molecular interface between the genome and the environment. Of particular interest is the RNA editing modification that occurs on the phosphodiesterase 8A gene located on chromosome 15q25.3, a genomic region that has recurrently been associated with early onset of major depressive disorder. ALCEDIAG's test, EDITDIAG, identifies in blood specific signatures through the RNA editing modifications of patients in different pathological conditions such as a cohort of hepatitis C infected patients, treated with interferon alpha and ribavirin were followed during 16 weeks. This treatment is well known to trigger depression in 50% of patients. RNA editing modifications were measured each two weeks as well as clinical evaluations of depression (MINI). An algorithm was identified which allows to discriminate patients with depression from others with a high specificity and sensitivity; a cohort of depressed patients (n=163) was compared to controls (n=69). A specific RNA editing signature was identified in depressed patients. The test shows that RNA editing related blood biomarkers allow to stratify patients, characterizes psychiatric conditions and follows up the disease/treatment modifications along time. This test paves the way for a better management of psychiatric patients. Recent Publications 1. Weissmann D, Underwood M, Salvatat N, Cavarec L and Vincent L (2016) Region specific alterations of A-to-I RNA editin of serotonin 2c receptor in cortex of suicides with major depression. *Translational Psychiatry* 6(8):e878. 2. Van Der Laan S, Salvatat N, Weissmann D and Molina F (2017) Emerging RNA editing biomarkers will foster drug development. *Drug Discovery Today* 22(7):1056-1063. 3. Cavarec L, Vincent L, Le Borgne C, Plusquellec C and Ollivier N (2013) In Vitro screening for drug-induced depression and/or suicidal adverse effects: a new toxicogenomic assay based on CE-SSCP analysis of HTR2C mRNA editing in SHSY5Y cells. *Neurotox Res.* 23(1):49-62. 4. Cambon K, Dos-Santos Coura R, Groc L, Carbon A and Weissmann D (2010) Aggressive behavior during social interaction in mice is controlled by the modulation of tyrosine hydroxylase expression in the prefrontal cortex. *Neuroscience* 171(3):840-51.

Biography

Dinah Weissmann is an Executive Vice President at ALCEDIAG's, biotech company dedicated to the development of innovative diagnostics based on epigenetic biomarkers mainly RNA editing. She is also Co-director of a public private laboratory, Sys2Diag that was created in 2015 and dedicated to the understanding of molecular basis of complex diseases. Her research fields are mainly in neuroscience which leads to the discovery of a specific plasticity in adult brain coined phenotype plasticity that gave rise to a novel class of antidepressant drugs. Later on, she focused on epigenetic mechanism understanding and developed new tests for diagnosis and management of psychiatric patients as well as prediction of psychiatric adverse effects. She has 15 years of research experience as Director of Research at the CNRS (French academic research institute) and has worked at various leader positions in pharma and biotech companies.

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