Valproic acid (VPA) and its derivatives are widely used to treat psychiatric conditions including bipolar disorder and schizophrenia. VPA increases circulating proline levels, which can modulate glutamatergic synapses. Psychiatric patients with certain genetic polymorphisms, however, experience worsening negative symptoms with increased proline, and conversely, those with other DNA variants have decreased negative symptoms with higher proline. This technology describes methods for predicting a patient’s response to VPA treatment based on circulating proline levels and genotype for catechol-o-methyltransferase, a gene that influences patients’ response to increased proline. This test can help physicians target VPA to patients who will benefit from treatment. Compared to conventional VPA treatment, this technology ensures that patients receive personalized treatment and minimizes negative symptoms and safety risks.

Predicts patients’ responses to VPA treatment based on polymorphisms in catechol-o-methyltransferase

Psychiatric patients display varied responses to VPA treatment in part due to interactions between circulating proline levels and polymorphisms in catechol-o-methyltransferase (COMT), an enzyme that breaks down neurotransmitters when a neuron fires. The COMT valine/methionine determines whether the enzyme has high, low, or intermediate activity. Schizophrenic patients with high COMT activity have improved negative symptoms when they have higher proline levels, whereas patients with intermediate or low activity have worse negative symptoms with high proline levels. This technology describes methods to determine proline levels and COMT genotype, which can inform physicians as to whether VPA, or an alternative proline modulator, should be prescribed. This technology further provides methods to monitor proline levels over time and modify treatment as needed, allowing for highly specific, adaptable treatment for negative symptoms.

Assays for determining proline levels and COMT genotyping have been performed in humans. The interaction between proline and COMT on negative symptoms has been demonstrated in humans using correlative statistical analysis.
Lead Inventor:

Catherine Clelland, Ph.D.

Applications:

• Test to predict patients’ response to VPA treatment
• Assay to determine and monitor circulating proline levels in humans
• Assay to determine genotype for an enzyme involved in neurotransmitter breakdown
• Method to predict whether psychiatric patients can benefit from proline modulator treatment

Advantages:

• Targets VPA treatment to patients who will benefit most
• Results can be used to identify alternative treatment strategies
• Minimizes unnecessary safety risks associated with VPA treatment
• Diagnostic kits and instructions make this easy-to-use for physicians
• Methods for monitoring treatment can be used to modify treatment as needed

Patent Information:

Patent Pending

Tech Ventures Reference: IR CU15242, IR CU13022, IR CU12071

Related Publications:


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