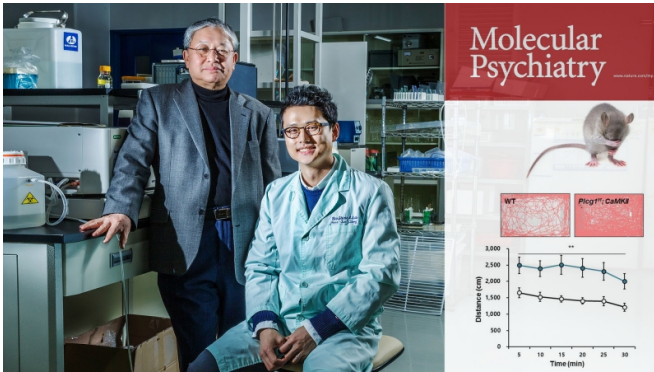


Bipolar disorder candidate gene, validated in mouse experiment

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Professor Pann-Ghill Suh (left) and Y R Yang (right) of Life Sciences at UNIST. Credit: UNIST

A team of researchers, affiliated with UNIST has made a significant breakthrough in the search for the potential root causes of bipolar disorder.

The research team, led by Professor Pann-Ghill Suh of Life Sciences at UNIST conducted a study that suggests the cellular protein Phospholipase C?1 (PLC?1) could be a new promising candidate gene for bipolar disorder, also known as manic-depressive illness.

The research published by the journal *Molecular Psychiatry* outlines the findings on January 31, 2017. The findings provide evidence that PLC?1 is critical for synaptic function and plasticity and that the loss of PLC?1 from the forebrain results in manic-like behavior. This breakthrough is expected to be widely used in research for the treatment of the manic symptoms associated with bipolar disorder.

The PLC?1 has once been proposed as a [candidate gene](#) for bipolar disorder in previous studies. However, it has been unclear that how the PLC?1 plays a role in neuron-to-neuron signaling and how it is related to mental illnesses, like

bipolar disorder.

In the study, Professor Suh and his team created forebrain-specific PLC?1-deficient mice and observed what happened in the brain synapse of this mouse. Synapse is the part of the neuron where the signal is transmitted from the end.

To test whether dysfunction of PLC?1 in the brain contributes to development of neuropsychiatric disorders, the research team generated mouse models, lacking PLC?1 in the forebrain and studied the synaptic and neuronal changes in mouse models.

The research team reported that mice with forebrain-selective deletion of PLC?1 also exhibit manic-like behavior, as well as deficits in inhibitory transmission and BDNF-dependent synaptic plasticity.

This resulted in the imbalance between excitatory and inhibitory synaptic transmission in forebrain circuits, leading to behavioral abnormalities and manic episodes of bipolar disorder. These symptoms were alleviated after the drug treatment for bipolar disorder was given.

"In the brain, excitatory synapses and inhibitory synapses work together to remain balanced for proper neurotransmission," says Professor Suh. "Our study demonstrated that the imbalance between these two is a major cause of various neuropsychiatric disorders and the GABAergic dysfunction observed in the hippocampi of bipolar disorder patients."

According to the research team, the inhibitory synapses that lacks PLC?1 protein do not work properly in excitatory neurons. This is due to the improper signaling of BDNF, which is critical for the synapse formation. This leads to an imbalance of [excitatory synapses](#) and [inhibitory synapses](#), and causes mental illnesses, like bipolar disorder.

"After 10 years of research, we have finally revealed PLC β 1 protein plays a major role in the onset of [bipolar disorder](#)," says Professor Suh. "Our findings, therefore, provide evidence that PLC β 1 is critical for synaptic function and plasticity and that the loss of PLC β 1 from the forebrain results in manic-like behavior."

More information: Y R Yang et al, Forebrain-specific ablation of phospholipase C β 1 causes manic-like behavior, *Molecular Psychiatry* (2017).
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