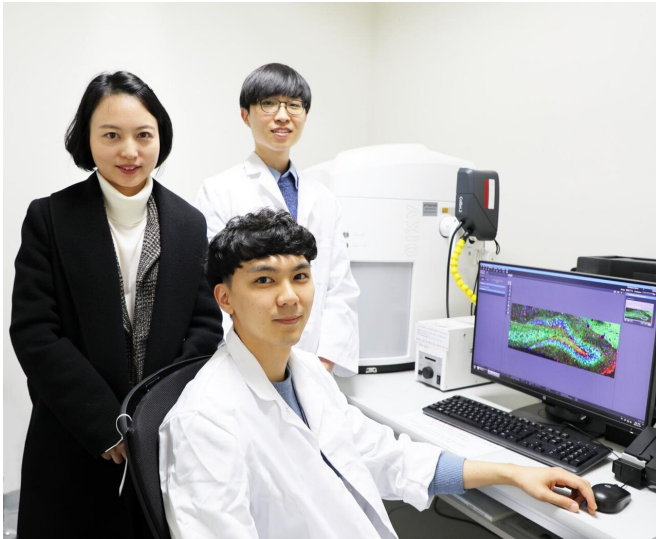


# Discovery of GABAergic synaptic regulations inside the brain for a new epilepsy treatment

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etc., due to various causes, account for 10-15% of the total population. However, how epilepsy begins in which parts of the brain, how it spreads to other parts of the brain, and how its symptoms are controlled, are largely unknown.

Professor Um's research team had been steadily discovering and researching key molecules that mediate the development of GABAergic synapses associated with brain diseases and discovered IQSEC3, a GABAergic synapse-specific protein, for the first time in 2016. In this research, her research team uncovered a new molecular mechanism that mediates GABAergic synaptic development by regulating neural circuit activity in the hippocampal dentate gyrus, in which IQSEC3 mediates higher brain functions such as memory and learning.

Professor Ji Won Um (left) as well as combined master's and doctoral dual degree program students Seungjoon Kim (front), and Hyeonho Kim (back) in the Department of Brain and Cognitive Sciences at DGIST Credit: dgist

DGIST announced on February 12 that the joint research team of Professor Jaewon Ko and Professor Ji Won Um in the Department of Brain and Cognitive Sciences found a new candidate target to treat epilepsy by regulating GABAergic synaptic functions. This research achievement is expected to set a milestone to develop new treatments such as epilepsy, an intractable brain disease.

Epilepsy is one of the intractable [brain](#) diseases with a high prevalence of 1% in South Korea's population, as more than 30% of the central nervous system does not respond well to conventional medications. In particular, the number of patients with epilepsy convulsions that occur with [high blood pressure](#), diabetes, hemorrhage,

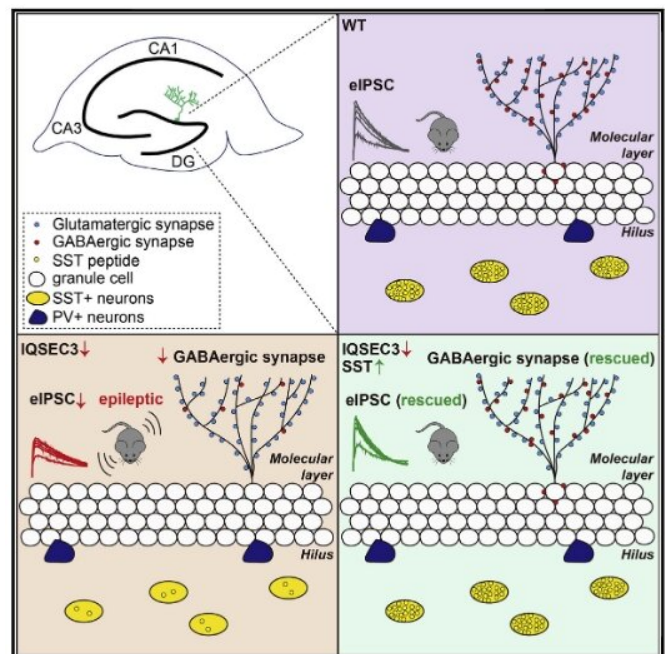


Photo 2. Mimetic diagram of key mechanisms of epilepsy expression according to the declined functions of

GABAergic synaptic protein IQSEC3. Credit: DGIST

To determine this, the research team produced a knockdown virus which eliminates IQSEC3 and injected it into the hippocampal dentate gyrus of mice, which showed a decrease in GABAergic synapse numbers and neurotransmission with severe seizures. This revealed that the IQSEC3 protein was a key factor in mediating GABAergic synaptic structure and function.

The researchers found that the amount of somatostatin peptide, originally known to be secreted from hypothalamus in the hippocampal dentate gyrus, was dramatically decreased. They confirmed that injecting somatostatin peptides into the specific type of GABAergic interneurons also completely restored GABAergic synaptic deficits and increased frequency of seizures caused by IQSEC3 deficiency.

Professor Um said, "We found a key clue that somatostatin, which is a key for regulation of synaptic transmission between nerve cells, directly mediates the development of GABAergic synapses. This can be used as a novel treatment strategy for [epilepsy](#) and various refractory brain diseases caused by a breakdown of the excitatory-GABAergic balance at synapses and neural circuits."

**More information:** Seungjoon Kim et al, Loss of IQSEC3 Disrupts GABAergic Synapse Maintenance and Decreases Somatostatin Expression in the Hippocampus, *Cell Reports* (2020). [DOI: 10.1016/j.celrep.2020.01.053](https://doi.org/10.1016/j.celrep.2020.01.053)

Provided by DGIST (Daegu Gyeongbuk Institute of Science and Technology)

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