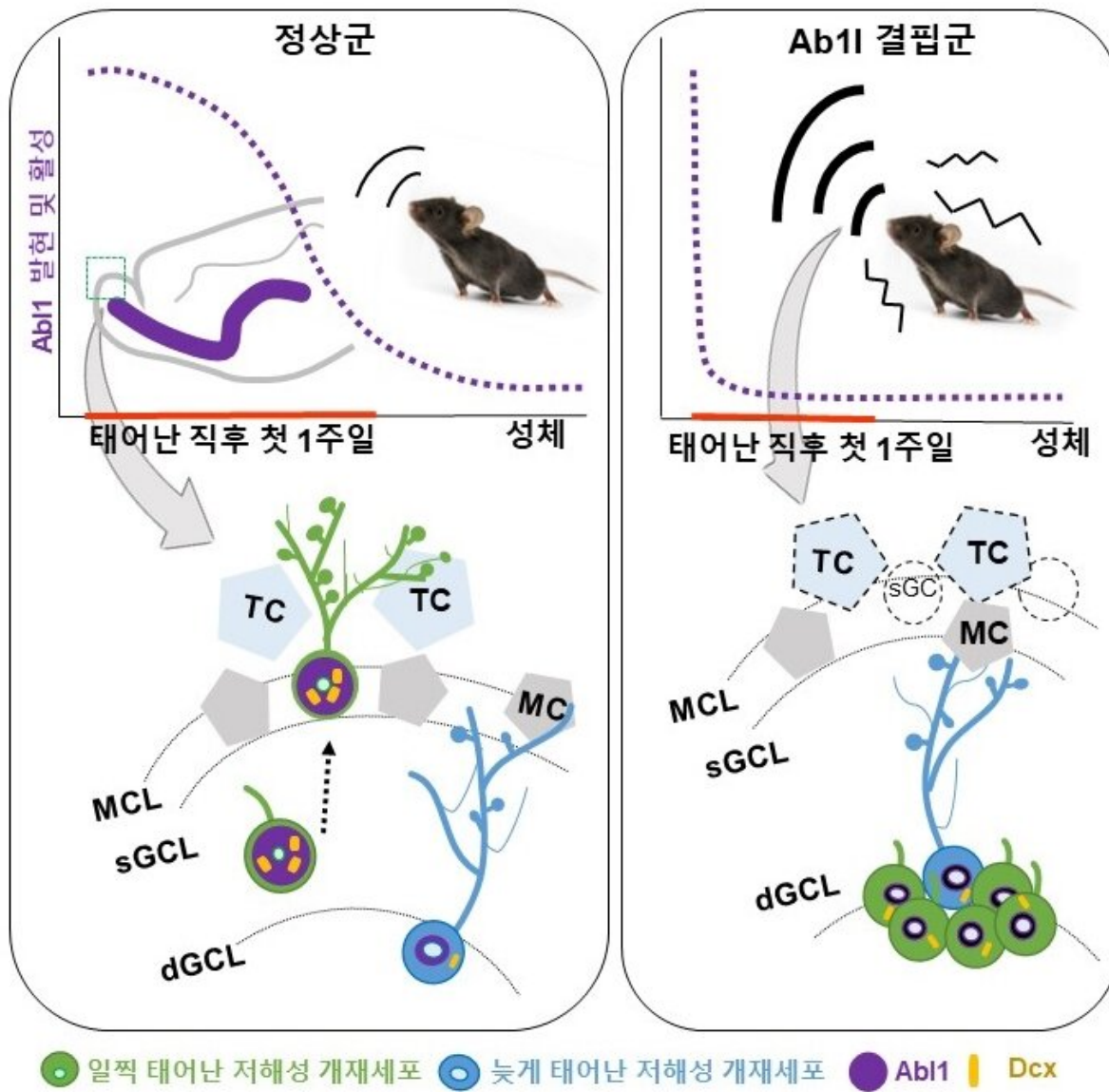


Increasing the possibility of early diagnosis for neuro-developmental disorders

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A mimetic diagram on the roles of Abl1 in the early development of inhibitory neurons in olfactory bulb. Credit: DGIST

DGIST researchers have identified the causes of hypersensitivity accompanied by neurodevelopmental disorders such as autism-spectrum disorder (ASD). This is expected to make huge contributions to the early diagnosis of sensory-defective symptoms accompanying neurodevelopmental disorders and cancer as well as the improvement of anti-cancer drug side effects.

DGIST announced that the Department of Brain and Cognitive Sciences found the important mechanism of 'Abl1' gene, which is involved in the early developmental stage of inhibitory neurons for forming normal sensory circuits.

Before formation of cognitive or verbal neural circuits in [brain development](#), sensory circuits are developed explosively for one year after birth. An ASD with cognitive and sensory defects is caused if the inhibitory neural circuit is not formed properly due to genetic or environmental factors during brain development. While studies on ASD treatment have focused on the abnormal development of inhibitory neurons related to [cognitive disorder](#), sufficient research has not been made on the specific causes and mechanisms of sensory defects that occur first.

The DGIST research team discovered for the first time that the Abl1 gene is expressed and activated explosively during the early development of inhibitory neurons in the mouse olfactory bulb. They also learned that if the expression or activation of Abl1 is inhibited using lenti-virus, inhibitory neurons cannot reach their cell layers accurately due to structural defects.

A candidate gene of ASD, Abl1 is also well known to cause cancer. If [chronic myelogenous leukemia](#) (CML) patients aged 2-9 with active brain development are treated with target anti-cancer drug Gleevec (Imatinib), an Abl1 deactivator, more than 60% of them show sensory related-side effects such as olfactory hallucinations. Based on this, the research team confirmed that the inhibition of Abl1 expression and activation greatly increased the olfactory sensitivity of mice as the side effect of Gleevec intake.

The research team also discovered, using proteomics, that Abl1 temporarily phosphorylated doublecortin (Dcx), a cytoskeletal protein that plays a crucial role in the structural development of the [brain](#). This discovery supports the hypothesis that Abl1 regulates the dynamic of microtubule with a new signal transmission system between Abl1 and Dcx.

Professor Cheil Moon in the Department of Brain and Cognitive Sciences at DGIST said "We found a very important clue to understand the mechanism of hypersensitivity appearing in neurodevelopmental [disorders](#) and cancer, which are yet to be known clearly. We hope to see follow-up research to overcome other sensory disorders based on our research."

More information: Jae Yeon Kim et al, Timely Inhibitory Circuit Formation Controlled by Abl1 Regulates Innate Olfactory Behaviors in Mouse, *Cell Reports* (2020). [DOI: 10.1016/j.celrep.2019.12.004](https://doi.org/10.1016/j.celrep.2019.12.004)

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