The number of AMPA receptors on the cell surface is abnormally increased in the brain of Cln3-knock-out mice

Nerve cells in the brain communicate with each other by electrical and chemical signals. The amino acid, glutamate is the main stimulatory chemical signal in the brain. When a nerve terminal releases glutamate, it binds and activates different types of glutamate receptors located on the cell surface of neighboring nerve cells. When glutamate receptors are activated sodium and calcium ions enter the cells, generating an electrical signal, which propagates along the cell membrane. AMPA-type glutamate receptors are essential for transmitting glutamate stimulation, and their function is primarily regulated by the number of AMPA receptors on the cell surface.

Mutations in the *CLN3* gene cause a fatal neurodegenerative disorder, juvenile CLN3 disease, also known as juvenile Batten disease. The *Cln3*-knock-out (*Cln3*$^{-/-}$) mouse model of the disease displays several characteristic features of the human disease including a deficit in motor coordination. Exploring the cause of the motor coordination deficit in *Cln3*$^{-/-}$ mice we have previously found that attenuation of AMPA-type glutamate receptor activity with a specific AMPA receptor inhibitor in 1-month-old *Cln3*$^{-/-}$ mice significantly improved their motor coordination. To reveal the mechanism of the abnormally increased AMPA receptor function in *Cln3*$^{-/-}$ mice, we examined the number of AMPA receptors on the cell surface using surface cross-linking in brain slices from 1-month-old wild type and *Cln3*$^{-/-}$ mice. We found that the number of AMPA receptors on the cell surface is abnormally increased in the brain of *Cln3*$^{-/-}$ mice. Our results suggest that the CLN3 protein is involved in the regulation of how many AMPA receptors are on the cell surface.

Publication

Abnormally increased surface expression of AMPA receptors in the cerebellum, cortex and striatum of Cln3-/- mice.
Kovács AD, Hof C, Pearce DA
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