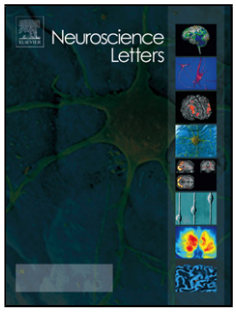

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Inhibitory effect of several sphingolipid metabolites on calcineurin

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Highlights

- Psychosine, glucosylsphingosine, and sphingosine inhibited calcineurin activity.
- They showed the effect through binding to calmodulin.
- Psychosine and glucosylsphingosine showed inhibitory effect on calcineurin B subunit.

Abstract

Neurons have well-developed membrane microdomains called “rafts” that are recovered as a detergent-resistant membrane microdomain fraction (DRM). NAP-22 is one of the major protein components of neuronal DRM. In a previous study, we showed that DRM-derived NAP-22 binds ganglioside and the inhibitory effect of ganglioside to calcineurin (CaN), a neuron-enriched calmodulin-regulated phosphoprotein phosphatase. Considering the important roles of CaN in neurons, identification of other cellular regulators of CaN could be a good clue to understand the molecular background of neuronal function. In this study, we screened the effect of several membrane lipid-derived molecules on the CaN activity and found sphingosine and some sphingosine-derived metabolites such as sphingosylphosphorylcholine, galactosylsphingosine (psychosine), and glucosylsphingosine, have inhibitory effect on CaN through the interaction with calmodulin.

Key words: calcineurin, calmodulin, sphingosylphosphorylcholine, psychosine,