Isolation and characterization of protrudin, a master regulator of neurite formation

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【Outline of survey】

Various cell types extend processes, which, in the case of neurons, can reach more than 1 m in length. The molecular mechanisms that underlie neurite extension are thought to include both cytoskeletal remodeling and membrane transport, the latter of which supplies lipids and proteins to the growing ends of projections but is largely uncharacterized. We have now identified a novel multidomain protein that contributes to this process. We named this protein "protrudin" because its forced expression induced the formation of long protrusions in all cell types examined. These protrusions were much larger than small processes such as filopodia that are generated as a result of the activation of cytoskeletal remodeling. Inhibition of protrudin function, either by RNA interference or by expression of a dominant negative mutant, revealed that the protein is necessary for neurite formation. Protrudin seems to facilitate the increase in cell surface area at the tip of cellular projections and thereby to promote process outgrowth. Our results suggest that protrudin-mediated membrane traffic underlies process extension not only in neurons, but also in glial cells, dendritic cells, and other cell types. We believe that our findings provide important new insight into the molecular mechanism of membrane transport during process extension.

【Expected results】

The molecular mechanisms that underlie neurite extension include both remodeling of the cytoskeleton and membrane transport. Membrane transport supplies lipids and proteins to the growing ends of neurites, but the precise mechanism underlying the selective transport of membrane components to the sites of membrane extension remains largely unknown. Our results now indicate that protrudin is a key molecule in the initiation of membrane transport to the growth cones of neurons. Understanding of the molecular mechanism underlying neurite formation will facilitate the application of this molecule to the nerve transplantation.

【References by the principal researcher】

Shirane, M., Nakayama, K.I.: Inherent calcineurin inhibitor FKBP38 targets Bcl-2 to mitochondria and inhibits apoptosis. Nature Cell Biol., 5: 28-37 (2003).

【Term of project】 FY 2005 - 2009 | **【Budget allocation】** 85,900,000 yen

【Homepage address】 http://www.bioreg.kyushu-u.ac.jp/saibou/index.html