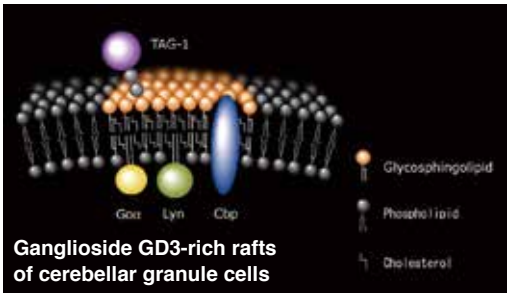
Unit Leader **Kohji Kasahara** Biomembrane Unit

Physiological Functions of Lipid Rafts / Glycosphingolipid Microdomains in Transmembrane Signaling

Lipid rafts are dynamic assemblies of glycosphingolipids, sphingomyelin, cholesterol, and proteins that can be stabilized into microdomains involved in the regulation of a number of cellular processes.
We have been investigating the association of glycosphingolipids with specific proteins in the nervous system and blood platelets.
We demonstrated that anti-ganglioside GD3 antibody co-precipitates GPI-anchored neural cell adhesion molecule TAG-1, src-family kinase Lyn, its substrate Cbp, trimeric G protein Goα of cerebellar granule cells.

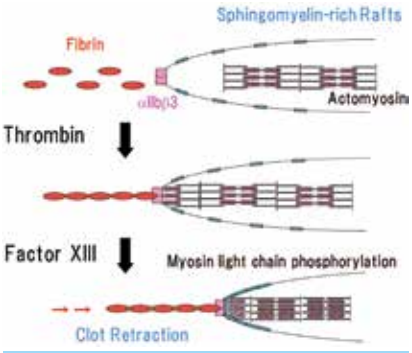


Ganglioside GD3-rich rafts of cerebellar granule cells

TAG-1 plays roles in axonal guidance, and cellular migration. GPI anchors have no direct contact with the cytoplasm. We demonstrated that TAG-1 transduces signal via Lyn/Cbp in ganglioside GD3-rich rafts of cerebellar granule cells. Chemokine SDF-1α triggers the chemoattraction of cerebellar granule cells during cerebellar development.
We demonstrated that SDF-1α stimulates GTPγS binding to Goα, and causes Goα translocation to lipid rafts, leading to growth cone collapse of cerebellar granule cells.

"We found that glycosphingolipids function as platforms in transmembrane signaling for the attachment of various signaling molecules of neurons and platelets."

Fibrin associates with lipid rafts on the platelets and raft integrity is required for clot retraction. We propose that clot retraction is mediated by factor XIII-dependent fibrin-integrin αIIbβ3-myosin axis in sphingomyelin-rich membrane rafts.



Sphingomyelin-rich rafts of platelets

Members: Ikuo Kawashima, Kiyoshi Ogura, Tomohiro Iguchi, Keisuke Komatsuya

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