Regulation of Gb3-Mediated Signal Transduction by Rhamnose-Binding Lectin

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Rhamnose-binding lectins (RBLs) are widely found in fish eggs. An RBL isolated from catfish (*Silurus asotus*) (SAL) has potent affinity to Gal □-linked carbohydrate chains of not only glycoproteins but also glycosphingolipids such as Gb3. SAL bound to surfaces of Gb3-expressing Burkitt's lymphoma cells, such as Raji cells, and strongly agglutinated the cells. After a short period treatment of Raji cells with SAL, the cell size was 10 smaller than that of untreated cells. Treatment of Gb3-expressing cells with SAL caused increase in binding of annexin V and incorporation of propidium iodide. These results suggest that SAL-induced phosphatidylserine exposure via P-glycoprotein (P-gp) will precede cell shrinkage based on K^+ release via G protein-activated inwardly rectifying K^+ channel (GIRK)-1. We have revealed that no cell shrinkage was observed in the Gb3-deficient Raji cells by SAL, indicating that Gb3 as well as P-gp and GIRK-1 localized in glycosphingolipid-enriched microdomain (GEM) was involved in SAL-induced cell shrinkage. However, neither caspase-8 and -3 activation nor DNA fragmentation was observed after treatment of SAL. Since SAL did not induce cell death to Gb3-expressing cells, SAL may function as an inducer of early apoptotic signal. Furthermore, SAL caused cell cycle arrest at G1 phase in Raji cells, and inhibited the cell proliferation and the expression of mitochondria-associated GM-CSF signaling (Magmas) gene that is up-regulated by the stimulation of GM-CSF. These results suggest that SAL leads the cells to early apoptotic status via binding to Gb3 existing in GEM, and that this binding is prerequisite condition to induce cell cycle G1 arrest and anti-proliferative effect via down-regulation of Magmas gene.