Ganglioside Modulation of GM-CSF-induced Proliferation

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Gangliosides are glycosphingolipids with at least one residue of sialic acid. They localize mainly at plasma membrane, frequently in microdomains enriched in cholesterol and glycosphingolipids. Gangliosides have been extensively reported to be involved in proliferation trough the modulation of several growth factor receptors and signaling cascades. GM-CSF (granulocyte-macrophage colony-stimulating factor) is one of the major cytokines that regulate myelopoiesis. Its receptor is a heterodimer composed of a specific ligand-binding alpha subunit (GMRa) and a beta subunit (ßc) responsible for signal transduction. This work aimed to study the modulation of ganglioside in the GM-CSF-induced proliferation in a myeloid cell lineage FDC-P1. For that, we used complementary approaches of ganglioside exogenous addition and/or biosynthesis inhibition. We showed that exogenous gangliosides stimulate GM-CSF-induced proliferation in a synergistically mode. In addition, ganglioside depletion, by the use of D-PDMP, causes a decrease in the proliferation, which could be restored by addition of GD1a. The proliferative response to GM-CSF in GM3- or GD1a-treated cells was accompanied by enhanced activation of ERK1/2 and increased expression of C/EBPa (a transcription factor for GMRa gene). We also demonstrated the expression of GMRα isoforms (tmGMRα and solGMRα) in FDC-P1 cells and assessed the possibility that differential expression could be modulated by exogenous gangliosides.

Key words: cell proliferation, ganglioside, GM-CSF

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