Invited Lecture

Regulation of Tumor Metastasis by Ganglioside GD1a in Mouse Osteosarcoma FBJ Cells

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Gangliosides, sialylated sphingoglycolipids, are associated with cell growth, cell adhesion, cell differentiation, tumorigenesis, and tumor metastasis, and changes in ganglioside expression in tumor cells are strongly related to the metastatic potential. In our previous studies, poorly metastatic murine FBJ-S1 cells derived from FBJ virus induced osteosarcoma were found to express disialylated ganglioside GD1a, whereas highly metastatic FBJ-LL cells only slightly express this ganglioside (Hyuga et al., 1997). The transfection of FBJ-LL cells with GM2/GD2 synthase (B4galnt1) cDNA resulted in increased GD1a expression (Hyuga et al., 1999). Transfectants expressing a similar amount of GD1a as FBJ-S1 cells behaved like FBJ-S1 cells and did not metastasize, whereas mock-transfectants were found to metastasize to the lung, liver, and adrenal gland, indicating that GD1a suppresses the metastatic ability of the tumor cells. GD1a has also been found to up-regulate caveolin-1 (Cav1) and stromal interaction molecule 1 (Stim1) (Wang et al., 2006) and to suppress the interaction between FBJ cells and vitronectin (Hyuga et al., 1999) and the expression of MMP-9 (Hu et al., 2007) and TNF-alpha (Wang et al., 2008). Thus, GD1a plays a role in suppressing the metastatic ability of tumor cells through the regulation of these molecules.

We have recently shown that NOS2 expression is higher in highly metastatic FBJ-LL cells compared to the expression in poorly metastatic FBJ-S1 cells. We also provided evidence that NOS2 silencing inhibits the proliferation, migration, and anchorage-independent growth of FBJ-LL cells and that NOS2 expression is inversely regulated by GD1a at the transcriptional level in FBJ cells, and extracellular signal-regulated kinase 1/2 (ERK1/2) inhibitor U0126 blocks GD1a suppression of

NOS2. We proposed that the GD1a signal leading to NOS2 suppression is mediated by the MEK/ERK pathway. To the best of our knowledge, this gives the first evidence that the GD1a signal is mediated by ERK1 phosphorylation (Cao et al, 2010).

References:

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