# GANGLIOSIDE GM3 DOES NOT MODULATE Neu ONCOGENE ACTIVATION IN MG1361 BREAST ADENOCARCINOMA CELLS

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Experimental evidences indicate that gangliosides, sialic acid containing glycosphingolipids, are actively involved in cell functions including growth, differentiation and malignant transformation (1). Many studies were set out to indagate the mechanisms whereby gangliosides mediate these effects. Data suggest that both phosphorilation and dimerization of growth factor receptors can be modulated by gangliosides in different ways, depending on the ganglioside species, the receptor protein and the cell line considered. Ganglioside GM3 inhibits epidermal growth factor (EGF)-dependent receptor autophosphorilation and cell growth in KB and A431 cells (2). Analogous behaviour has been observed for GM3 and GM1 for platelet derived growth factor receptor (PDGF-R) in Swiss 3T3 cells and SH-SY5Y cells (3, 4).

The neu proto-oncogene encodes a glycoprotein of 185 kDa (p185), which shares extensive structural and fuctional homology with the EGF-R. Activation of p185 results in receptor aggregation and stimulation of tyrosine autophosphorilation, causing signal transduction into the cell. Transforming neu oncogene differs from the wild type gene by a point mutation inducing a selective aminoacid substitution at position 664 (val to glu) and undergoes constitutively dimerization and auto-phosphorilation (5). Previous studies in our laboratory (6) in order to characterize the ganglioside pattern of tumor mammary tissues, induced in transgenic mice by the activated form of the rat neu oncogene (MMTV-neu transgenic mice) (7), indicated that mouse mammary control tissues expressed quite exclusively ganglioside GM3 whereas all tumors presented a substantial decrease in this ganglioside content accompanied by the accumulation of GM3-derived species. Consequently, we hypothesized that ganglioside GM3 decrease could be important for the cascade of events responsible for oncogenic transformation. To investigate this possibility, the MG 1361 breast adenocarcinoma cell line (8), derived from the MMTV-neu transgenic mice, was employed as experimental model. MG 1361 ganglioside profile was evalued and characterized by HP-TLC and TLC-immunostaining. Expression, phosphorilation and dimerization levels of the neu oncogene product, before anf after treatment of the cell line with various concentration of GM3, were analyzed by Western blot. These cells result deficient in ganglioside GM3, whereas GM2, GM1, GD1a, GD2, GD1b, GT and GQ are clearly expressed, confirming ganglioside pattern observed in tumor mammary tissues. Moreover, results indicate that p185 is present in the phosphorilated dimeric form and that ganglioside GM3 is unable to produce any detectable modification in p185 expression, phosphorilation and dimerization degree, suggesting that this ganglioside does not have a role in modulating the transforming potential of the neu oncogene.

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