Antitumor and cytotoxic properties of a humanized antibody specific for the GM3 (Neu5Gc) Ganglioside

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Abstract

Gangliosides are sialic acid-containing glycosphingolipids that are found on the cell surface of many mammalian cells, and
participate in several important cellular processes. Some gangliosides have been reported to be tumor-associated antigens.
Of particular interest are the Neu5Gc-gangliosides, which are absent from human normal tissues, due to an exon deletion in
the gene encoding the enzyme cytidine monophospho-N-acetyl-neuraminic acid hydroxylase, responsible for the conversion
of Neu5Ac to Neu5Gc. However, gangliosides bearing the Neu5Gc variant have been detected in human malignancies, in
particular GM3(Neu5Gc) ganglioside has been found in numerous human tumors but not limited to melanoma, breast cancer,
hepatocellular carcinoma, renal, ovarian and prostate tumors, etc., and it is considered one of the few tumor specific antigen.
14F7 Mab is a mouse IgG1 that has high specificity for GM3 (Neu5Gc) and does not react with the Neu5Ac counterpart or
other related N-glycolyl gangliosides. This Mab has the interesting ability to kill tumor cells expressing the ganglioside in a
complement-independent manner and by a non-apoptotic cell death mechanism. The humanized version of 14F7 retained the
binding and cytotoxic properties of the mouse counterpart and has the additional ability to trigger ADCC. This antibody has
shown antitumor response in different mouse and human tumor models from different histological origins. In this work, we
will summarize the unique properties of 14F7 as a potential drug for the therapy and diagnostic of human cancer.