rated on high performance thin layer chromatography (HPTLC) plates was studied. The human MAb was found to bind strongly to NeuAcGM3, IV^3NeuAcnLc$_4$ and sulfate containing glycolipids and weakly to NeuGcGM3, suggesting that the binding epitope of IM-11 is the terminal sugar residue NeuAcα2-3Galβ1-4Glc but also NeuAcα2-3Galβ1-4GlcNAc present in IV^3NeuAcnLc$_4$. The HPTLC immunostaining of glycolipid extracts from different human tumors (lung, colon, liver and melanoma) with IM-11 revealed a specific recognition of NeuAcGM3 and sulfated glycolipids.

In addition, immunohistological staining of different melanoma and breast cancer biopsy sections has shown a positive reactivity of IM-11 with tumor cells with an intensity which varied among different tumors and when treatment of the tissue sections with neuraminidase from *Vibrio cholerae* was performed, a substantial reduction of the staining was observed in the melanoma sections analyzed, while immunostaining of the breast cancer cells was unaffected.

The variable region of the heavy chain gene was cloned and sequenced indicating that it belong to the heavy chain subgroup III, showing a high homology with previously reported germline sequences.

MULTISPECIFIC ANTI-IDIOTYPE MONOCLONAL ANTIBODIES AS IMMUNOREGULATORS

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Introduction

In the last decades the paradigm of the Immune Network has evolved, stating that the Immune System behaves as a whole, and part of its regulation is based on the idiotypic interaction between the different lymphocytes clones (1). This view opens a new approach for the treatment of some of the so named "immune diseases" such as some autoimmune syndromes, or cancer. The manipulation of the idiotypical interaction has shown to be of real value, as suggested by the success reported for the treatment of various autoimmune diseases with a human IgG pool (2), containing an important fraction of antibodies capables of recognizing other antibodies or some autoantigens (idiotipically connected natural autoantibodies).

We have obtained highly connected anti-idiotypic MAbs by immunizing mice with anti-ganglioside IgM MAbs. Here we describe the preliminary characterization of one of such antibodies.

Results and Discussion

The anti-idiotypic MAbB7 belongs to the IgG2a subclass, and was generated in a singeneic model by immunizing Balb/c mice with an anti-GM2 specific IgM antibody. The MAbB7 was classified as an "alfa" anti-idiotype, it did not block the binding of the Ab1 antibody with the ganglioside GM2(NeuAc), however, when coupled to KLH and injected in Balb/c mice induced an antigen-independent serological antibody response (Ab1') against GM2(NeuAc) but also to other gangliosides, suggesting the activation of ganglioside multi-specific natural autoantibodies.

The MAbB7 showed other striking properties, such as heterogeneous binding to different murine IgG monoclonal antibodies, to high idiotypically connected neonatal murine IgM MAbs, and to different F(ab)'2 fragments from human mieloma proteins. By fluorometric cytometry analysis (FACS), we also showed that MAbB7 bound to normal human lymphocytes and to different human B tumor cell lines. All these results suggested us that the MAbB7 is a multispecific anti-idiotypic antibody, that binds to the variable regions of murine and human immunoglobulins. We also demonstrated that the anti-idiotypic MAbB7 produced some *in vitro* effects reported for the human immunoglobulin pool, like depletion of bone marrow cells in short term cultures, and inhibition of the mitogenic responses to PHA, Con A and PMW by peripheral blood cells from healthy donors (3).

All these immunochemical and *in vitro* data suggest us to assess the possible use of the multi-specific anti-idiotypic MAbB7 as an immunoglobulin pool surrogate. It will be of major importance to determine the effect that this antibody could have in the evolution of autoimmune syndromes in some experimental models.

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