Characterization of Binding Epitopes of CA125 Monoclonal Antibodies

The most used cancer serum biomarker is the CA125 immunoassay for ovarian cancer that detects the mucin glycoprotein MUC16. Several monoclonal antibodies (mAbs) including OC125 and M11 are used in CA125 assays. However, despite considerable efforts, our knowledge of the molecular characteristics of the recognized epitopes and the role played by glycosylation has remained elusive. Here a comprehensive set of recombinant MUG 16 tandem repeats (TRs) expressed in glycoengineered mammalian cells and E. coli, together with overlapping peptides, was used to probe antigen-binding epitopes. We present a complete analysis of N- and O-glycosylation sites of a MUC16 TR expressed in CHO cells and demonstrate that neither N- nor O-glycosylation appear to substantially influence binding of OC125 and M11 mAbs. A series of successive N- and C-terminal truncations of a MUC16 TR construct expressed in E. coli narrowed down the epitopes for OC125 and M11 to a segment containing parts of two consecutive SEA domains with a linker. Thus, a complete SEA domain is not required. These findings suggest that binding epitopes of mAbs OC125 and M11 are dependent on conformation but not on glycosylation. The availability of recombinant TR constructs with and without aberrant glycosylation now opens the way for vaccine studies.

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