Anti-Idiotypic Peptide Sequences

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Summary:
The invention provides a method for identifying peptides for use in increasing a cytotoxic T lymphocytes (CTL) response to an antigen. The method comprises the steps of comparing the amino acid sequence of the VH and/or VL portions of an anti-idiotypic monoclonal antibody to the amino acid sequence of an antigen to identify regions of homology between the Ab2 and the antigen, and to further identify an HLA binding motif in a homologous region. The identified homologous region which comprises an HLA binding motif defines a peptide sequence that is useful for stimulating a CTL response. Also provided are peptides identified by the method, and a method of using the peptides to stimulate a CTL response in an individual.

Detail:
The invention provides a method for identifying peptides for use in immunotherapeutic approaches. The peptides are identified as short regions (8-20 amino acid) of an anti-idiotypic antibody having homology with a region of the corresponding antigen and further comprising one or more HLA binding motif(s). These peptides have the ability to stimulate a cytotoxic T lymphocyte (CTL) response. The peptide regions of the ant-id antibodies may be modified to further enhance the immunogenic response.In one embodiment, the method comprises obtaining the amino acid sequences of the VH and/or VL portions of the anti-idiotypic antibody (Ab2), obtaining the sequence of the antigen, comparing the sequences to identify candidate homologous regions within the Ab2 (i.e., regions that show homology to regions of the corresponding antigen), and further identifying those candidate homologous regions of Ab2 which also comprise HLA binding motifs. These peptides are then tested for their ability to stimulate a CTL response. Preferred peptides are those which stimulate a greater CTL response than the corresponding antigen or a peptide derived from the antigen. In another embodiment, the invention also provides peptides identified by the method. In this regard, the peptide sequences are homologous to a portion of Ab2 and a portion of the antigen, and further comprise an HLA binding motif.In another embodiment, the method further comprises modifying the peptide sequences identified as homologous regions of Ab2 to further enhance their ability to stimulate a CTL response. This invention also provides a method for using the peptides identified by the method in generating an increased immunogenic response in an individual against the tumor antigen. The method comprises administering to the individual an amount of peptide which has homology to a portion of the antigen and to a portion of an Ab2 which mimics an epitope on the antigen, and wherein the peptide comprises an HLA binding motif, effective to stimulate a CTL mediated immune response against the antigen.