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Developing Highly Specific Monoclonal Antibodies to Peptide in the Context of MHC II

Technology No. 20160218

IP Status: Pending US Patent; **Application #:** 15/952,965

Rapid Generation of p:MHC II Antibodies

A novel approach generates monoclonal antibodies (MAb) against peptide presented in major histocompatibility complex II (MHC II). The methodology centers on having a soluble peptide:MHC (p:MHC) Class II complex linked to biotin as the B cell antigenic target. The approach uses recombinant peptide:MHC monomers as immunogens and subsequently relies on multimers to enrich the responding antigen specific B cells prior to fusion and screening. It first immunizes a subject with a composition comprising an antigen, isolates a population of cells from the subject and enriches a subpopulation of those cells, and then forms a hybridoma using a cell from the subpopulation. This technology sets the standard for generating monoclonal antibodies against peptide MHC and could be used for any MAb protein target (not just p:MHC II).

Monoclonal Antibodies Specific for Peptide Bound To MHC II

Monoclonal antibodies specific for foreign antigens, auto-antigens, allogeneic-antigens, and tumor neo-antigens in the context of major histocompatibility complex II (MHC II) are highly desirable. However, there is no standard protocol for generating monoclonal antibodies that recognize peptide in the context of MHC II, and only a limited number of such reagents exist. The unique approach to producing and screening monoclonal antibodies specific for peptide bound to MHC II has several advantages:

1. **Immunization with stable peptide:MHC complexes:** allows the immune response to generate an antibody response specific for peptide in the context of MHC,
2. **Ability to discard clones:** a decoy screening process discards clones responding to unrelated peptides from the same MHC or clones reactive to MHC directly,

3. **Magnetic enrichment of antibody-producing B cells:** exploiting site-directed biotinylation of the target antigen allows for enrichment of B cells reactive to the target protein/peptide by generating a tetrameric form of the antigen, thus increasing the avidity of B cells for antigen and enabling the capture and enrichment of antigen specific B cells, and
4. **Significant time and cost savings:** fewer colonies are screened and a higher percentage of hybridomas screened produce MAb against p:MH CII.

BENEFITS AND FEATURES:

- Rapid generation of peptide:MHC II antibodies
- Methods could be used for any MAb protein target
- Site-directed biotinylation on a peptide allows for the enrichment of B cells reactive to the target protein/peptide
- Allows the immune response to generate an antibody response specific for peptide in the context of MHC
- Can directly discard clones
- Significant time and cost savings

>APPLICATIONS:

- Generation of peptide:MHC specific monoclonal antibodies for therapeutic and research tool use
- Used on any MAb protein target

Phase of Development - Pre-clinical validation. In vitro and in vivo proof of concept is completed.

Researchers

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Publications

Efficient generation of monoclonal antibodies against peptide in the context of MHC II using magnetic enrichment.
Nature Communications, 2016 Jun 13;7:11804. PMID: 27292946

https://license.umn.edu/product/developing-highly-specific-monoclonal-antibodies-to-peptide-in-the-context-of-mhc-ii