



Generation, characterization and Isolation of primary human antibody *in vitro*

The Challenge: Monoclonal antibodies derived from mice are most commonly used in *in vivo* therapeutic and diagnostic procedures and for *in vitro* diagnostic testing. However, murine monoclonal antibodies are not identical to human antibodies and they themselves can elicit an immune response by the human host. Currently, the only method for the generation of humanized monoclonal antibodies is through the immunization of a human volunteer or collection of antibodies from an infected human host (B cell donor). Locating a suitable B-cell donor is problematic if the target disease is rare or life-threatening. Thus, there is an acute need for an *in vitro* system that allows for the generation of human antibody responses on demand.

UMBI Solution: UMBI scientists have developed a system and method for generating primary human antibody responses *in vitro*. In this method, peripheral blood is obtained from healthy human volunteers and three populations of hematopoietic cells are isolated: naïve human T and B cells, and monocytes. There are two phases of cell culture required to develop an antibody response *in vitro*. In the first phase, monocytes are differentiated into monocyte-derived antigen presenting dendritic cells (MDCs). In the second phase, MDCs are cultured *in vitro* with naïve T and B cells with the target antigen, which allows generation of primary antibody response. Antibody responses can be easily quantified by ELISA, ELISPOT, or direct antigen binding to the responding B cells (using fluorescently labeled antigens). Thus, this system can be used to measure responses in all of the cell populations relevant for generation of primary human antibody responses and to generate human monoclonal antibodies.

Commercial Applications:

- Generation of fully humanized monoclonal antibodies on demand.
- Development and evaluation of potential vaccines for human use.
- Generation and quantification of primary antibody responses in humans.
- Platform technology for passive immunotherapy – *in vitro* system that allows the generation of human antibody responses to any foreign antigen - appropriate for mass treatment with human monoclonal antibodies in response to bio-threat such as ricin and botulinum toxin.

Advantages:

- *In vitro* system for generation of fully humanized monoclonal antibodies against a wide range of agents without direct immunization of patient.

- *In vitro* system based on cell isolation from readily accessible tissues such as human peripheral blood.

Stage of Development: This method has been shown to work on several antigen-adjuvant pairs and with multiple donors. It is immediately adaptable to a high-throughput screening platform.

Patent Status: Pending PCT application WO 2007/134220 A2

Licensing Potential: UMBI is seeking non-exclusive and exclusive licensees to all or part of this technology platform. The UMBI inventors would welcome the opportunity to work with any licensee to further refine or extend the capabilities of this invention.

Lead Inventor & UMBI References: Lewis, 06-006; 07-002

Relevant Publications:

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3. Vinuesa, C. G., S. G. Tangye, B. Moser, and C. R. Mackay. 2005. Follicular B helper T cells in antibody responses and autoimmunity. *Nat Rev Immunol* 5:853-865.
4. Babatz, J., C. Rollig, U. Oelschlagel, S. Zhao, G. Ehninger, M. Schmitz, and M. Bornhauser. 2003. Large-scale immunomagnetic selection of CD14+ monocytes to generate dendritic cells for cancer immunotherapy: a phase I study. *J Hematother Stem Cell Res* 12:515-523.

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