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Meeting Abstract

Human monoclonal antibodies and analytic vaccinology

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Abstract

Following appropriate priming by infection or vaccination memory B cells and serum antibody levels are sustained for a lifetime conferring immediate protection upon secondary encounter with the pathogen. I will first discuss the differential requirements for activation of human naïve and memory B cells and propose a homeostatic model for the maintenance of the memory B cell pool and of serum antibody levels. I will then describe two methods that can be used to interrogate the human memory B-cell repertoire. The first is based on limiting dilution analysis of polyclonally stimulated mononuclear cells. Using this method we measured the frequency and fine specificity of memory B cells in serial samples under steady state conditions and after vaccination. In particular we found that only a small fraction of virus-specific memory B cells produce neutralizing antibodies, while the majority recognizes internal or denatured antigens. The second method is based on the efficient immortalization and cloning of memory B cells. Using this method we have been able to isolate from the human memory repertoire several potent and broadly neutralizing monoclonal antibodies against viruses such as SARS, Dengue, H5N1, HCMV and HIV-1. I will discuss how such antibodies can be used not only to provide immediate protection, but also as probes for epitope discovery and vaccine design.