

# New dimensions in serology

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## Abstract

Immunization of heterologous species with cancer cells or extracts to analyze the resulting antisera for cancer-specific antibodies inaugurated the search for human tumor antigens that could be used in cancer diagnosis and therapy. Technologies for generating monoclonal antibodies revolutionized the discovery process for cell surface and intracellular antigens of human cancer cells, beginning a new era in the clinical application of antibodies. The capacity of the immune system to recognize human cancer antigens was further substantiated with the development of autologous typing—an approach in which tumor cells, lymphocytes, antibody, and control cells are all derived from the same patient, thus eliminating the contribution of alloreactivity in the observed results. This development has led to a growing list of antibody-recognized antigens that are immunogenic in the host of origin, including mutational, overexpressed, viral, and cancer-testis (CT) antigens. Antigens in the latter category, including NY-ESO-1 and MAGE-A3, have been extensively studied and shown to spontaneously elicit antibody responses in a proportion of patients that correlate with T-cell immunity.

With the sequencing of the human genome and rapid and effective protein expression systems, it is now possible to envisage screening the human proteome with the human antibody repertoire, a process we refer to as seromic analysis. To this end, human protein arrays including a subset of antigens identified in the Cancer Immunome: SEREX Database were constructed, in collaboration with ProCognia, using their novel method for attaching proteins to the glass surface. Sera previously shown by ELISA to have reactivity to selected antigens were analyzed for reactivity to the same antigens using the arrays to evaluate their sensitivity and specificity. This technology has provided us with the analytic tools necessary to identify antigens with immunogenicity in cancer patients, as well as to expand the analysis to more antigens in larger cohorts of cancer patients. Preliminary results from array-based serological analyses of NSCLC patients identified a variety of novel antigens that may have utility as targets for cancer vaccine development. These data could also contribute to the elucidation of biomarker signatures for NSCLC based on seroreactivity, and help to define immune responses that can be correlated with clinical benefit for the cancer patient.