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Methods to measure vaccine immunity

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Abstract

“Today, owing to strict health and safety issues of vaccine manufacturing, vaccines must meet higher standards of safety and biochemical characterization than they did in the past.”

The biggest triumph in vaccination is the eradication of smallpox. Ironically, no methods to measure vaccine immunity were set in place. Protection and immunity was achieved without detailed analysis nor knowledge of cellular or humoral immunity induction. Today, owing to strict health and safety issues of vaccine manufacturing, vaccines must meet higher standards of safety and biochemical characterization than they did in the past. This has led to the production of highly purified vaccines, and the identification and isolation of the antigens responsible for protection. A vaccine cannot move forward without the demonstration of effective immunity induced by the regime. Moreover, contrary to the vaccination strategy that eradicated smallpox and other acute viral infections, several modern vaccines aim at the eradication of established chronic diseases such as chronic viral infections or cancer. As the pathogens or cancer antigens are generally intracellular, modern vaccines can rely less effectively on the neutralizing properties of antibody responses that cannot cross the cell membrane, and depend predominantly on T-cell-based recognition of affected cells for their elimination. Thus, new technologies have to be developed to measure vaccine immunity.

Are we going round and round in circles? Are we making it harder for ourselves? Is vaccine development getting too hard? Why do we have to demonstrate immunity, if we can show protection? No regulatory agency will take a vaccine forward that is not highly purified and can demonstrate immunity induction.

Several methods of measuring humoral and cellular immunity have been required to be developed to meet this criteria. Some methods include ELISA, cytotoxic T-lymphocyte (CTL) assay, CTL precursor frequency assay, T-cell proliferation assays, carboxyfluorescein diacetate succinimidyl ester assays, intracellular and extracellular cytokine production by

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cells in culture using either ELISA or multiplex and flow cytometry, polyfunctional T-cell assays, ELISpot and MHC class I/II tetramers. Thus, there is an enormous amount of information and reagents available for guiding vaccine and immunotherapeutics development.

This special issue on 'Methods to measure vaccine immunity' focuses on a number of recent and promising approaches used to measure immunity induced following vaccination. Topics included in this special focus issue are as follows:

- Gene-expression profiling in vaccine therapy and immunotherapy for cancer [1]. The use of microarrays is described in order to understand the mechanism by which tumors are rejected;
- Antibody-profiling technologies for studying humoral responses to infectious agents [2]. Protein microarrays are used to evaluate antibody responses to thousands of antigens at one time. The luciferase immunoprecipitation system overcomes some drawbacks of the conventional protein microarray assay. These new technologies offer a new tool for understanding humoral immunity induction to proteins;
- Vaccine-induced antibody responses in patients with carcinoma [3]. A nice overview of current methods utilized for measuring antibody responses and for assessing their antitumor efficacy in the context of clinical trials;
- Methods to measure T-cell responses [4]. A mini review on recent methods used to measure T-cell immunity, such as the use of CTL, CTL precursor frequency assays, carboxyfluorescein diacetate succinimidyl ester, flow cytometric approaches, spectrophotometric approaches and use of ovalbumin-specific CD8⁺ T cells from OTI and OTII T-cell receptor transgenic mice;
- New flow cytometric assays for monitoring cell-mediated cytotoxicity [5]. A comparison of IFN- γ ELISpot, granzyme B ELISpot and conventional ⁵¹Cr-release assays is given. A detailed analysis of the use of flow cytometric methods to measure T-cell immunity induction is demonstrated;
- Evaluation of cellular immune responses in cancer vaccine recipients [6]. Measurement of cellular immunity is addressed using NY-ESO-1 as an example and techniques such as delayed-type hypersensitivity, measurement of T cells from peripheral blood, use of overlapping peptides to measure CD4 and CD8 T cells, and the role of Treg cells in vaccine immunity induction are described;
- Development and application of phosphoflow as a tool for immunomonitoring [7]. This article describes the new flow cytometry technology, phosphoflow for measuring multiple intracellular signaling molecules in the immune system at a single-cell level for lymphocyte immune monitoring;
- Surface plasmon resonance for vaccine design and efficacy studies [8]. An outline of how surface plasmon resonance biosensors are emerging to understand how serum is used to monitor antibody immunity;
- The challenges of assessing infant vaccine responses in resource-poor settings [9]. A very nice and comprehensive article on methods to measure vaccine immune responses where only poor settings are available.

There is a vast amount of information already available to promote a greater understanding into the role of specific immune induction to a vaccination regime. The use of newer immune monitoring tools as described in this special focus issue will serve to improve

immune monitoring and determine the effectiveness of vaccine strategies for the treatment or immunotherapeutic approaches to diseases.

Biographies

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