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Improving influenza vaccines

Suryaprakash Sambhara,

Influenza Division, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, 1600 Clifton Road, Atlanta, GA 30333, USA

Rino Rappuoli

Novartis Vaccines and Diagnostics Srl, Via Fiorentina 1, 53100 Siena, Italy

It is clear that the immune system is still immature and developing in infants and young children, while its function begins to decline in older adults. Furthermore, immune function is also modulated during pregnancy to facilitate the survival of the developing fetus, a semiallograft. This natural immunosuppression leaves these populations vulnerable to seasonal and pandemic influenza infections and other infectious diseases. In addition, owing to the altered immune status, these populations are also poor responders to vaccinations. Understanding the effect of these physiological conditions on immune responses to infections and vaccinations will enable us to improve vaccines to confer better protection in these target populations.

The recent influenza pandemic of 2009 has highlighted the importance of protecting children and pregnant women against novel viruses. Older adults continue to be the target population for annual influenza vaccination. Understanding the immune response to infection, vaccination or antiviral therapy at the molecular level requires integration of cell biology, immunology, genomics and systems biology approaches so that effective and immunogenic vaccines tailormade for these target populations can be developed. Direct transmission of avian influenza to humans and the recent pandemic that resulted from a swine-origin triple-reassortant virus with gene segments from avian, human and swine influenza viruses highlights the need for multipronged approaches to prevent and control the spread of novel influenza viruses. Enhanced surveillance efforts in monitoring influenza viruses in animals, effective prevention and control measures to contain influenza animals and developing new classes of antiviral agents for humans and nonpharmaceutical intervention efforts need to be considered in parallel with the development of effective public health vaccination strategies.

Antibody against the influenza virus hemagglutinin protein, the primary target of current vaccines, is crucial to prevent infection. However, the roles of T cells, NK cells and

Author for correspondence: Influenza Division, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, 1600 Clifton Road, Atlanta, GA 30333, USA, ssambhara@cdc.gov.

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cross-reactive, non-neutralizing antibodies by complement-mediated or antibody-dependent cell-mediated cytotoxicity mechanisms in conferring cross-protection need to be explored and appropriate *in vitro* assessment assays need to be developed. There is accumulating evidence that antibody responses directed against the stem region of hemagglutinin protein may confer cross-protection, perhaps through antibody-dependent cell-mediated cytotoxicity or complement. Certainly, these observations will lead to the development of vaccine technologies that will boost responses to enhance cross-reactive antibodies, T cells and NK cells. Adjuvanted vaccines have shown much promise in protecting certain target populations by enhancing the magnitude as well as the breadth of antibody responses. Influenza vaccines may need to be developed/formulated differently to cater to the needs of naturally immunosuppressed populations.

Huge investments were made in exploring egg-independent vaccine production technologies for influenza that utilize vaccines derived from mammalian, plant or insect cells, which consist of recombinant proteins, conventional inactivated and split vaccines or virus-like particles. Other novel vaccine technologies include viral or bacterial vectors expressing influenza viral proteins and ligands of Toll-like receptors coupled to influenza viral antigens. Together with new vaccine technologies, novel transdermal and mucosal delivery systems are being explored with promising results both in preclinical and Phase I and II clinical trials. These novel technologies and alternate delivery systems also require the development of appropriate methods for standardization of antigens, well-defined protective correlates and standardization of immunological assessment protocols, as the methods developed for traditional egg-based technologies may not be appropriate for new-generation vaccines.

As guest editors of this special issue of *Expert Review of Vaccines*, we are pleased to bring an excellent collection of articles from distinguished researchers addressing various aspects of influenza to provide an in-depth coverage with potential solutions. Public health is everyone’s responsibility and the role of nongovernmental organizations and public and private partnerships cannot be underestimated.

Several articles in the issue cover vaccination of special populations, including vaccine safety in children and the elderly [1], a special report on vaccination during pregnancy [2] and an insightful review on the T-cell response in children [3]. T-cell responses are also the focus of another review article that argues in favor of greater research focus on this cell type [4].

An interesting article takes a systems biology approach to understanding the immune response of older adults to seasonal influenza vaccines [5]. Another piece presents virus-like particles as a potential route to a universal influenza vaccine [6]. Rounding off the review section of the issue is a fascinating consideration of pandemic intervention plans [7].

Three opinion pieces in the form of Perspective articles contribute more personal viewpoints on some of the hot topics in influenza vaccinology. An article from PATH highlights their efforts in supporting the technologies to prevent and control influenza in the developing world [8]. A stimulating article discusses ethnographic studies of human influenza

quarantine trials [9], and a short piece provides an excellent overview of the prospect of a universal influenza vaccine [10].

In the issue, we also present a selection of Editorial articles that offer brief insights into the aspect of influenza vaccine research [11–13]. Two Key Paper Evaluation articles bring the issue up-to-the-minute with critical reviews of recently published primary work from the field [14,15].

We are confident that these articles will benefit novices as well as vaccinologists, clinicians, and experts in immunology, public health and policy.

Biographies

Suryaprakash Sambhara

Author for correspondence: Influenza Division, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, 1600 Clifton Road, Atlanta, GA 30333, USA

Rino Rappuoli

Novartis Vaccines and Diagnostics Srl, Via Fiorentina 1, 53100 Siena, Italy

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