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Editorial

In this Issue: Shifting the Focus to Modern Vaccinology

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In the present issue, we honor the memory of Dr. George Emil Palade (1912–2008), one of the founders of the modern cellular biology, whose discoveries paved the way to rapid progress in various fields including immunology. We then continue our journey in vaccinology and anti-microbial immunity, with focus on several viruses of high interest: Hepatitis B and C, HIV and influenza.

In an Editorial dedicated to current and future strategies to tackle hepatitis viruses, Dr. Inchauspe and her collaborators offer a systematic, industry perspective on what are current challenges and opportunities in this area. First, the authors define the medical need for therapeutic vaccination against Hepatitis B and C viruses—since chronic infection is still difficult or impossible to treat—and propose a stepwise strategy towards designing new and more potent approaches, based on characterizing immune correlates of viral control in man. The latter aspect is extremely important since it leads to definition of appropriate target antigens and the type and magnitude of immune response that needs to be generated to control the disease. They caution against relying too much on preclinical models, yet emphasize the need for more potent platform vaccines and in particular, understanding how to position therapeutic vaccination versus standard of care encompassing anti-viral agents.

Then we shift focus to the HIV vaccine development, an area marked by quite numerous challenges and setbacks in the recent past. Drs. Demberg and Robert-Guroff bring solid arguments in support of expanding efforts to understand the principles of mucosal immunity, since

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there seem to be several drawbacks associated with parenteral vaccines. In addition, it would be important to understand to a higher extent the mechanisms of mucosal transmission of HIV and whether induction of protective IgA is the desired endpoint to achieve protection against infection, in light of the slow onset of CTL and other arms of immune response. However, irrespectively of route, viral antigenic diversity remains a huge challenge. Drs. Sealy, Hurwitz et al., developed a multivalent approach encompassing DNA, virus and protein antigens aimed to tackle this diversity. This approach consists of heterologous prime-boost vaccination against dozens of envelope antigens, to elicit a broad based cross-clade response. The testing of this investigational vaccine reached clinical phase; preliminary analysis of preclinical and the limited clinical data available to date, show the generation of neutralizing antibodies against heterologous strains. In the end, there is still much more to be done in this challenging area of developing anti-HIV vaccines; nevertheless, it is clear that an effective vaccination approach should trigger the right type of immunity—both potent, local and eventually systemic as well as broadly reactive against the strains in circulation. It may be that this goal is achievable only by complementing a variety of platform technologies in development.

We then change focus to influenza viruses; Drs. Martinez and collaborators outline key aspects in influenza immunology—through generating and characterizing specific, virus-neutralizing antibodies—with impact on developing therapies and new vaccines. They focus on the need to characterize in depth the antibody response against hemagglutinin and introduce a variety of approaches to generate a large diversity of antibodies neutralizing H5N1 strains, of major global interest. One of the major messages of this review/analysis consists in the need to deeply understand the nature and specificity of human monoclonal antibodies generated naturally or artificially, that cross-react and neutralize a diversity of drift and shift variants. In addition, besides implications regarding the design of new vaccines, one should not overlook the potential of such monoclonal antibodies in the therapy of influenza virus infection.

We finalize this issue with a general article by Drs. Habbal and Al-Jabri discussing an issue less investigated, namely the circadian rhythm of immunity and the complex relationship between the neuroendocrine and immune systems. The latter becomes a veritable 'sensory organ' connected with the environment and regulated through soluble mediators associated with the circadian rhythm: melatonin, cortisol, neurotransmitters and cytokines. Finally, the authors discuss

interesting implications relative to understanding mechanisms of diseases associated with such mediators.

In the upcoming issues, we will continue to entertain vaccinology topics but diversify our content to include several others such as the immunology of transplant rejection and preventive or therapeutic means; and the emerging yet important subject of miRNA mediated regulation of immunity in normal and pathological state.