Vaccines and adjuvants – Special Issue

A symposium on vaccines was held at the SGM Spring Conference in Harrogate on 11–14 April 2011. The symposium, which attracted over 140 attendees, consisted of 32 invited presentations and eight offered papers. Speakers, selected from the worlds of academia and industry, travelled from around the globe, including the USA, Australia, Africa and Europe, as well as the UK and Ireland, to showcase the leading research on vaccines for major public health diseases.

The main aim of the symposium was to discuss the current difficulties encountered in vaccine development and to comprehensively cover the latest advances in vaccines against major bacterial, viral, fungal and parasitic infections. The huge impact of such pathogens on affected populations was presented by some speakers who had been searching for effective vaccines for many years and this provided some real-life insights into the problems that researchers are addressing. In addition to discussions on optimal choice of vaccine antigens, there was also an emphasis on vaccine-mediated stimulation of immune responses, both systemically and for the protection of mucosal surfaces, which constitute major portals for entry of pathogens into the body. Several novel adjuvants and vaccine-delivery technologies were highlighted and current findings on the currently poorly understood mechanisms of action of traditional adjuvants were described. In addition, there were also very interesting presentations on immunization strategies to block the transmission, as opposed to infection, of pathogens and how immune evasion strategies of some pathogens can be a problem, or may even be harnessed, in vaccine development.

Contributors to the meeting were invited to submit review articles for this vaccine-themed special issue of the Journal of Medical Microbiology. Articles were subjected to an independent peer-review process and these seven reviews were accepted as a representation of the major themes discussed at the symposium. The special issue starts off with a review by ourselves (Oyston & Robinson, 2012), outlining the current major challenges in vaccine development. This includes the hurdles arising from how vaccine research is usually conducted and also the financial difficulties associated with vaccine production and use. We also review some initiatives that have been attempted in order to deliver new vaccines to the populations most in need.

Vaccines remain elusive for certain organisms or groups of pathogens, despite there being a great need for them and a lot of intensive research. We included three papers exemplifying this, which review the main challenges and discuss the strategies being employed. The first of these, by Edwards (2012), is a review of the advances being made in the development of fungal cell-wall vaccines. This article, which mainly focuses on Candida albicans, but also describes vaccine development for several other important fungal infections, describes the increasing clinical need for such vaccines and highlights the fact that none have yet been approved for use. Innovative vaccine strategies are described, including the successful preclinical use of a live attenuated Candida strain and a heat-killed Saccharomyces vaccine formulation that protects mice against a variety of fungal infections. The leading rALa3p-N Candida vaccine is also reviewed, describing its successful performance in recent Phase I clinical trials and its protective mechanisms in mice.

Bijker & Sauerwein (2012) provide a very interesting perspective on strategies for successful immunization against malaria. This important goal has not yet been achieved despite work by a huge number of research teams worldwide and many millions of dollars of funding over at least 60 years. It has been known for some time that recurrent natural infections in endemic areas elicit immunity. The authors focus on the idea that innovative use of antimalaria drugs could provide the key to safely generating protective immunization. It may be possible to avoid many of the problems with vaccine development, such as poor immunogenicity of parasite antigens and finding the optimal delivery system, by using controlled human malaria infections under chemoprophylaxis to induce effective protective immunity. Recent data from human volunteer studies and the pros and cons of such a strategy are discussed from the point of view of visitors to, or inhabitants of, endemic areas.

The paper by Williamson & Oyston (2012), reviews the natural history of Yersinia pestis infections and the advances being made towards achieving a protective human plague vaccine. This dangerous pathogen has been a scourge of humanity for centuries. A crude killed vaccine has been used historically but has been known to provide suboptimal protection. The increased awareness of biodefence needs in recent years has reinvigorated research in this area, applying modern techniques in vaccinology to an ancient problem. It is interesting how, despite the advantages of conducting research in the ‘post-genomic era’, the immunogenic, protective antigens pursued were discovered by empirical methods in the first half of the last century. Thus, although there has been much hype about exploiting genomic information for ‘reverse vaccinology’, the traditional methods should not be forgotten or ignored. This article also highlights the considerable challenges that now exist for licensing vaccines in development, such as the requirements for robust assays for correlates of protection and relevant animal models of human disease.

The second part of the symposium focused on vaccine technologies and we selected three review articles along this theme. Many bacterial vaccines currently in use in humans are composed of protein coupled to a glycan, such as capsular polysaccharide. The production of these conjugates is problematic and requires an expensive multi-step process. Terra et al. (2012) review the discovery of the Campylobacter jejuni N-linked glycosylation system and how it may be harnessed in the ready production of...
novel and inexpensive glycoconjugate vaccine antigens using a recombinant *E. coli*-based expression system.

Two further papers review the use and mechanisms of action of adjuvants, both old and new. The first of these, by Kool *et al.* (2012), is concerned with alum which has been the main adjuvant in clinical use over many decades. Despite its widespread use, information on its mode of action is only just coming to the fore. Having a detailed knowledge of how it stimulates the immune system is vital for determining when it may be best utilized and how it may be improved in future formulations. In contrast, Baz Morelli *et al.* (2012) describe a recently developed adjuvant, ISCOMATRIX®. This formulation has undergone extensive preclinical and clinical testing in a variety of studies. Unlike alum, there has been much work undertaken to understand the mechanism of action in order to facilitate licensing. This adjuvant appears to stimulate CD8+ T-cell responses as well as CD4+ cells and antibodies. It has been used with a wide variety of vaccine antigen systems, including those for control of infectious diseases and cancer. This article reviews the nature of the adjuvant, how it is currently thought to stimulate the immune system and the results of various studies in animal models and humans, with an update on very recent findings.

In summary, there are many efforts under way to develop new vaccines or to develop adjuvants to make current and novel vaccines more effective. The research featured in this themed volume draws out many of the challenges facing vaccine research and development efforts generally, using specific examples.

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