Mucosal immunisation and vaccines

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INTRODUCTION

The immunisation of mucosal surfaces in mammals is vitally important to the survival of any given species. A large number of pathogenic microorganisms are first encountered at the mucosal surface. It is this first contact that may lead to the invasion and colonisation by a pathogen and the subsequent onset of disease. The gastrointestinal mucosa has a very large surface area, approximately 250 m² in the adult human (1), which can be used by microorganisms for invasion. This interaction between the microorganisms and host mucosal cells allows the scientist and the clinician an excellent field of battle for immunological priming and therefore vaccination against the invading pathogens. This approach has great potential in barring the entry to a range of bacterial, viral or protozoan pathogens before colonisation and the onset of disease. The prevention of such infections is very important both on a social and an economic scale. Rapid and relentless transmission is all too common when an infection can establish a base within the community. Fortunately, these outbreaks are decreasing in frequency in the developed world, however, in periods of human crisis or natural disaster the spectre raises its head. This has been evident in recent years with cholera outbreaks. In 1994, 45,000 people died and an estimated 600,000 were infected as a result of Vibrio cholerae O1 outbreak in Rwandan refugee camps in just a three week period (2). Additionally, the need for a clean and rapid method of dispensation is also required, which is where the case for orally delivered vaccines also needs to...
be addressed. This approach is not limited to diseases of the developing world such as cholera and enteric fever, but also to infections prevalent in the developed world, such as that due to *Helicobacter pylori*. These diseases represent a great cost both in terms of health care and in mortality and one of the best methods for controlling or even eradicating a given infection within a population is to vaccinate. Vaccinating individuals is a first, effective step in the control of a pathogen and one of the simplest methods of obtaining this protection is to enable the patient to prevent the invading organism gaining access.

An efficacious mucosal vaccine protects the host by preventing a pathogenic microorganism from gaining entry into the host. Mucosal protection pre-exists in the gastrointestinal tract in the form of non-specific innate immunity to microorganisms (see Chapter 1). It is the development of specific immunological defence mediated by secretory immunoglobulins and cell mediated immunity (see Chapter 2), that is utilised in the development of an efficacious vaccine against microbial infections at the mucosal surface.

The induction of non-tolerising, protective immunity at mucosal surfaces has been a heavily researched area in recent times with a variety of methods being exploited to achieve effective and safe vaccination. Some of the different recent approaches and models of mucosal immunisation and vaccination will be reviewed and discussed in this chapter.

**MUTANT SALMONELLA VACCINES**

Although many strains of *Salmonella* are major pathogens and causative agents of food and water born disease, avirulent *Salmonella* spp. have also been utilised as vectors of heterologous antigens. These organisms were chosen initially because of their pathogenic behaviour such as the ability to interact with the gut associated lymphoid tissue (GALT), leading to the development of strong cell-mediated immunity as well as mucosal and systemic antibody responses. *Salmonella* vaccine vectors have therefore become appealing candidates for immunisation in mucosal locations other than the gut. This has been highlighted in a study using human papilloma virus (HPV) type 16 (3). In a murine model, animals were given a double nasal immunisation with *Salmonella typhimurium* strain CS022 expressing the (HPV) type 16 major capsid protein, L1. This L1 protein was shown to be consititively expressed in the vector and the development of immunity was demonstrated by serum antibodies that where able to neutralise (HPV) 16 pseudotyped virions in an infectivity challenge. At mucosal sites such as the mouth and the vagina, IgA and IgG antibodies against viral epitopes