# Innovation in Vaccinology

Selene Baschieri
Editor

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## From Design, Through to Delivery and Testing

Springer

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# Preface

Prevention of infectious diseases by vaccination is one of the most significant achievements of modern medicine. During the twentieth century, the average human life span in the developed world was about 70 years and it is expected to increase, with a significant portion of this increase directly attributed to vaccination.

Since the first empiric vaccination trials, knowledge and technology have enormously evolved and even if many of the vaccines licensed for human use are still based on whole pathogens or on partially purified microbe components, new vaccination strategies are emerging on the market. Indeed, in spite of the great success, conventional vaccination strategies sometimes may result ineffective and, above all, may raise safety concerns.

The aim of this book is to provide an overview of some of the technology platforms that have been realized or currently under development to try to address unsolved and new issues in the field of vaccine development. I have identified three major crucial areas in this process: antigen selection, antigen delivery and antigen testing.

The first part dedicated to *Vaccine Design* illustrates how bioinformatics can be exploited to: (i) identify the most promising antigens of a given microorganism; (ii) predict the kind of immune response that an antigen is able to elicit. These *in silico* approaches are very demanding and require the big effort of extrapolating accurate computation formulas to delineate systems intrinsically "biological", therefore fuzzy.

The second part dedicated to *Vaccine Delivery* is a "wet" biology section and depicts the progress of tools and approaches used for the delivery of antigens endowed with specific immune properties. A big research effort to rationalize and identify in complex systems those factors crucial in the activation of a certain type of immune response is presented. I deliberately made the choice not to emphasize specific pathogens because I wanted to give the message that these delivery tools could be "universally" applied.

The last, but absolutely not the least, part is dedicated to *Pre-clinical Vaccine Testing*, a crucial step of vaccine research. The aim of this part is to illustrate the cutting edge instruments developed to evaluate the efficiency of innovative vaccines and therefore the parameters that may be predictive of vaccine efficacy.

The common denominator of all thematic areas described herein is the multidisciplinary approach/teamwork. Most of the enabling technologies have been established by putting in the "melting pot" expertise in fields that, at first glance, may appear very far apart. Indeed, since the basic goal of vaccination is to mimic as much as possible those variegated response mechanisms that result in pathogen clearance (innate and adaptive, antibody- and cell-mediated), the success is proportional to the multi-disciplinary scientific knowledge. This delicate "cross-fertilizing" process is the direct path to innovation and requires a large intellectual and financial investment.

Big pharmaceutical industries and small-medium enterprises are among the main contributors to vaccine innovation, and this is evident by simply going through the affiliation of the contributors to this book. The problem is that private companies convey this innovation only into those products that have the highest probability of economic success (i.e. reasonable commercial return to pass expenses onto consumers and governments). This because vaccine research requires considerable economic resources to face very stringent approval and manufacturing rules and clinical trials, overall making up two-thirds of the costs. This implies that companies focus their efforts primarily on the prevention or cure of diseases affecting mainly people living in industrialized countries.

Today, despite many infectious diseases caused by viruses and bacteria can be prevented by vaccination, infections are still a major cause of morbidity and mortality. The need to develop new or improved vaccines is urged also by the insurgence of different antibiotic-resistant bacteria and the risk of re-emergence of eradicated pathogens.

Due to dire financial straits there is a general tendency to grant funds mainly to some applied sciences. Nonetheless, the time is ripe to raise awareness of key health issues in the era of globalization and my personal belief is that the main, wide-ranging, goal of vaccinology should be directed towards the world-wide expansion of the health conditions reached in industrialized countries.

The contribution of vaccinologists to the achievement of this outstanding goal should very well be devising safer vaccines for a more efficient and "universally" active protection (as in the case of human immunodeficiency, dengue, or influenza viruses) and, above all, easily affordable also for developing countries. I am also convinced that a pivotal role in this interplay should be interpreted by public institutions that should work in favour of the development of socially-oriented science. Unfortunately, opportunities offered for public funding in the earliest stage of innovation are insufficient and often pioneering studies developed in academy end up languishing in the laboratory. Resources are insufficient to proceed through to the next, more expensive stages of product development, including patenting and patent valorization and management. Scientists of the public sector are "strongly invited" by decision-makers to collaborate with the private sector in the competition for funding, and companies are often allowed to participate in call receiving public funding to develop their products. The effects of such a policy in the field of vaccinology is that only 10% of the world's investment in R&D is employed to find solutions for diseases that affect 90% of the world's population.

In spite of these figures, I am still hopeful that things can change. The path may be "long and winding" but it is worth following. I am convinced that most scientists in this field share my dream and I am really grateful to all the contributors to this book. I hope that this collection of chapters will make the readers feel the passion that all the contributors put in their work and make them aware that vaccinology is rapidly taking a new direction, ceasing to be an empirical science.

Selene Baschieri

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# Abbreviations

| | |
|---|---|
| Ab | antibody |
| AIDS | acquired immunodeficiency syndrome |
| Ag | antigen |
| APC | antigen presenting cell |
| BCR | B cell receptor |
| BPV | Bovine papilloma virus |
| cDC | conventional DC |
| CTL | cytotoxic T lymphocyte |
| DC | dendritic cell |
| dsRNA | double stranded RNA |
| EBV | Epstein-Barr virus |
| ELISA | enzyme-linked immunosorbent assay |
| ELISPOT | enzyme-linked immunosorbent spot |
| FMDV | Foot and mouth disease virus |
| HAV | Hepatitis A virus |
| HBV | Hepatitis B virus |
| HBsAg | Hepatitis B surface antigen |
| HCV | Hepatitis C virus |
| HCMV | Human Cytomegalovirus |
| HIV-1 | Human immunodeficiency virus 1 |
| HPV | Human papilloma virus |
| HSV | Herpes simplex virus |
| IC | immune-complex |
| IFN | interferon |
| IL | interleukin |
| i.m. | intramuscular |
| i.p. | intraperitoneal |
| LCMV | Lymphocytic choriomeningitis virus |
| LPS | lipopolysaccharide |
| Mφ | macrophage |
| MHC | Major Histocompatibility Complex |

| | |
|---|---|
| MV | Measles virus |
| NDV | Newcastle disease virus |
| NK | natural killer cell |
| NV | Norwalk virus |
| ODN | oligodeoxynucleotides |
| PAMP | pathogen associated molecular pattern |
| pDC | plasmacytoid DC |
| PRR | pattern recognition receptor |
| RSV | Respiratory syncitial virus |
| SARS | severe acute respiratory syndrome |
| s.c. | subcutaneous |
| scFv | single chain antibody fragments |
| sIgA | secretory IgA |
| ssRNA | single stranded RNA |
| TB | tubercolosis |
| Th | T helper |
| Th0 | T helper 0 |
| Th1 | T helper 1 |
| Th2 | T helper 2 |
| Th17 | T helper 17 |
| TCR | T cell receptor |
| TLR | toll-like receptor |
| TNF | tumor necrosis factor |
| Tregs | regulatory T cells |
| VLP | virus-like particle |
| WVN | West Nile virus |