Published in final edited form as:

Curr Opin Virol. 2013 June ; 3(3): 307–308. doi:10.1016/j.coviro.2013.06.007.

VIRAL VACCINES: PAST SUCCESSES AND FUTURE CHALLENGES

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Vaccines have transformed the landscape of viral diseases during the past century and saved the lives of millions of children worldwide. The most striking of these successes is the complete elimination of small pox, one of the worst scourges of mankind. In addition, we are on the verge of eliminating poliomyelitis, and have brought under control viral diseases such as measles, mumps, rubella, chicken pox, yellow fever, rabies, and hepatitis B. More recently highly effective vaccines have been developed against human papilloma viruses and rotavirus. Despite these remarkable successes, considerable challenges remain and we still do not have vaccines against several viral infections of global importance – most notably HIV, HCV, RSV and dengue.

This issue of Current Opinion in Virology contains nine reviews on viral vaccines. We have grouped these nine articles into three sections. In the first section, we start with an article on polio describing the endgame of a successful vaccine and then have a review on influenza virus as an example of a licensed vaccine that needs improvement. The second section contains articles on HIV, RSV, hemorrhagic fever viruses and dengue – major global diseases for which no vaccines currently exist. In the last section, we end with three articles on basic vaccine science emphasizing the need for fundamental research in meeting the future challenges.

Both the inactivated (Salk) and the live (Sabin) polio vaccine are among the most effective vaccines ever developed and they have greatly reduced the number of poliovirus infections world-wide. However, going from reduced infections to complete elimination of a disease is a quantum leap and achieving this goal represents a formidable challenge. Estivariz, Orenstein and colleagues discuss the poliovirus endgame and the drive to eradicate polio – a topic currently of very high global health priority. Although influenza virus vaccines have been available for many years the virus continues to take a heavy toll due to its ability to undergo antigenic variation and evade the immune system. However, recent studies showing that it is possible to generate neutralizing antibodies that target highly conserved regions of the virus has raised the possibility of developing more effective vaccines against influenza virus. Yewdell discusses the challenges of developing a universal influenza vaccine and of dreaming the impossible dream.

One of the most exciting recent developments in human vaccines has been the advent of approaches based on structural understanding of the interplay of neutralizing antibodies and viruses. This is particularly relevant for the highly antigenically variable viruses such as HIV, HCV and influenza virus. Kulp and Schief describe the recent exciting developments in structural vaccine design and illustrate how this could be a highly promising avenue to vaccine development for some of the most difficult pathogens such as HIV. One of the most sought after pediatric vaccines is that to RSV. Despite more than 40 years of work such a vaccine is still not available and there have been severe setbacks. Dormitzer and colleagues discuss the many challenges in developing an RSV vaccine, some of the historical problems and the recent developments that encourage belief that a safe and effective RSV vaccine may indeed be possible. Viruses that cause hemorrhagic fever are some of the most feared human pathogens. Filoviruses such as Ebola have attracted much attention but Lassa virus and dengue virus cause far greater morbidity and mortality. In particular, dengue virus has been spreading globally and accounts for nearly 500 million infections yearly. Falzrano and Feldmann describe the experimental vaccines that are under development for various hemorrhagic fever viruses and discuss the progress and limitations of these vaccines. Wallace and colleagues describe recent progress in testing dengue vaccines in human clinical trials.

A hugely important question for viral vaccines is how B cell responses are initiated and how these cells first see antigen. Live viruses tend to be particularly good at inducing B cell responses. This is in part due to their ability to replicate but it is also due to the structural nature of virus particles that allows optimal multimeric antigen presentation to B cells. Vaccination often seeks to mimic this property as discussed by Bachmann and colleagues, who illustrate how and why virus particle-based vaccines are so successful in inducing B cell immunity. The other critical component for inducing high affinity and long-lived antibody responses is CD4 T help for B cell responses. Crotty and colleagues describe the nature of T:B cell interactions and discuss how a better understanding of these interactions can improve vaccination strategies. Finally, Youngblood and colleagues highlight the importance of epigenetic changes during memory CD8 and CD4 T cell differentiation and propose that epigenetic analysis of vaccine induced memory T cells will provide new insights into the quality of T cells induced by different vaccines.

Acknowledgments

We would like to thank all the authors for their outstanding contributions and hope that the readers will find the articles to be timely, interesting and informative. These are exciting times for vaccine research and development and the confluence of significant advances in fundamental and translational immunology along with the novel approaches in structure-based vaccine design have opened up extraordinary opportunities for meeting the challenges ahead.

Biographies

Dr. Ahmed holds the title of Georgia Research Alliance Scholar in Vaccine Research and is a Professor of Microbiology and Immunology in the Emory University School of Medicine. He received his Ph.D. in microbiology from Harvard University. Before coming to Emory in 1995, he was a Professor in the Department of Microbiology and Immunology at the University of California, Los Angeles School of Medicine.

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