Microreviews in Cell and Molecular Biology 2012

Vaccines and Advances: Carbohydrate Synthesis

Amber Price
Microbiology Junior
Department of Microbiology and Molecular Genetics, Oklahoma State University, Stillwater, OK 74078, USA

Key Words:
Vaccines, carbohydrate synthesis, bacterial resistance

Vaccines have been extremely important in the avoidance of certain diseases, but even then pathogens have continued to evolve and become resistant to vaccines, various types of antibiotics, and other drugs. This is in part due to the environment of the disease and also co-evolution and adaption, but there are issues with the types of vaccines and how they are delivered to the immune system. Some invoke a stronger immune system, and others remain weak and possibly risky. A recent advance in vaccination technology includes synthesizing carbohydrates and conjugating them to bacterial carrier proteins. This new technology aids in avoiding bacterial resistance.

Introduction

Scientists have come a long way in the development of vaccines, from just getting exposure all the way now to injections and even oral delivery. There are four main types of vaccines: inactivated, live attenuated, subunit, and virus-like particles (VLP) [1]. These types of vaccines can still carry problems, but scientists are continually trying to come up with new avenues to venture into when it comes to preventing diseases and worldwide epidemics. One of the new avenues has to do with carbohydrate synthesis. Today, carbohydrates are used as antibiotics, anticoagulants, and to treat diabetes [2]. Carbohydrates when purified and attached to bacterial carrier proteins have proved to help in vaccination efficiency.

Many vaccines that pathogens have become resistant to are protein based. These vaccines contain purified protein antigens from pathogenic organisms and stimulate the production of antibodies against the specific proteins that the organism produces. The problem with this type of vaccine is that proteins are under direct genetic control and can therefore become resistant to a vaccine over time due to gene mutations. Scientists involved in carbohydrate chemistry have isolated certain protective groups in oligosaccharides that are much less susceptible to mutational changes and are more complex than proteins.

Types of Vaccines

The first type of vaccine, inactivated, is the use of chemically killed pathogens by radiation or something of that nature, and then injected into the body to stimulate a buildup of antibodies. This can be dangerous if the pathogens are not completely dead or inactivated because it would mean directly inserting the disease into the subject. Another issue is that inactivated vaccines do not produce a strong immune response. There are still a number of inactivated vaccines used in medicine today which include vaccines against hepatitis A and influenza. Because the organisms are killed, immunity will continue to decrease and that is why boosters are needed, but this comes with the risk of the pathogen becoming more tolerant to the antigen.

Live attenuated vaccines produce lifelong protective antibodies, and memory cells. This type of vaccine inserts living organisms that are not virulent. Live organisms are grown in tissue cultures that search for less virulent strains of the pathogen or even mutations in the virulent part of their DNA. What ends up growing are the same pathogens, but they are not virulent. The only issue with this is that there is a possibility that the virus could

revert back to being virulent by secondary mutations. This type of vaccine is also not good for people who have immunocompromised systems. Subunit vaccines are quite possibly the ones that really opened up vaccine technology more than any vaccine thus far. Bacterial toxins are actually what cause disease, and these toxins are purified then inactivated creating a much safer approach to making vaccines. Conjugated vaccines and DNA vaccines also fit under the umbrella of subunit vaccines. Conjugated vaccines strive to build responses to poorly immunogenic subunits like tetanus and diphtheria vaccines. Their pathogenicity was protected by weak polysaccharides, so scientists converted the antigens to a thymus dependent form which stimulate T cells and improve immunological memory [1]. DNA vaccines contain a bacterial DNA plasmid that includes protein sequences from the pathogen and target T cell response. Both conjugated and DNA vaccines are cost effective and safer to produce.

The vaccines mentioned so far are good, but they still do not provide a strong immune response and buildup of antibodies and T cells, and that is why so often vaccines like the live attenuated or inactivated ones are given along with adjuvants. Adjuvants do not have any effect on antigens, but help increase the productivity of the immune system by advancing dendritic cell maturation and cytokine secretion. VLP use has been newer technology in vaccine science; the particles are coproducts in the viral replication process. VLP lack the genetic matter that normal viral particles have. Chemically linking desired antigens to the VLP surface, the antigen of choice is given the immunogenic properties of the VLP [1]. These types of vaccines have proven to protect against diseases like hepatitis B and HPV. There is continued research in this particular field of viruses that is getting closer to breakthroughs in medicine.

Recent Progress

There are two main focuses on protecting groups in carbohydrates, and both allow access to bulk quantities of building blocks [2]. Access to the building blocks of carbohydrates allows scientists the ability to alter them into being more useful for various immunological techniques. One particular protecting group in carbohydrate chemistry is called the *de novo* strategy. This strategy uses linear preprotected fragments that are connected through stereoselective C-C bond forming reactions to provide the desired, differentially protected, glycosylating agents [2]. The other strategy called the one-pot protection puts all of the useful building blocks into one pot. Both strategies are used to try and isolate carbohydrate antigen surfaces for purification. There are many structures of the pathogens oligosaccharides that are too similar to host glycans, and therefore require additional help attached covalently or the use of adjuvants. These areas of help do not aid in immunity directly, but help the immune system identify more readily the differences between the pathogen and host antigens.

Discussion

Carbohydrate antigens are less susceptible to future resistance, and therefore seem like the perfect solution to all the issues with vaccines today. Unfortunately, there are some downsides to carbohydrate-based vaccines. One downside is that carbohydrate antigens do not stimulate the human immune system as readily as proteins [5], and will not work properly unless they are conjugated with the proper adjuvant. The antigen surface densities are also very small, and are more difficult to isolate in large quantities [5]. There is still continued research in the areas of carbohydrate-based vaccines; how to isolate larger quantities for testing and for vaccine usage. Carbohydrate synthesis for vaccinations is very important and could lead to many other discoveries and cures for deadly diseases. It could also mean the death of certain diseases due to lack of resistance.

References

1 Mortellaro, Alessandra, Ricciardi-Castagnoli, Paola (2011) From vaccine practice to vaccine science: the contribution of human immunology to the prevention of infectious disease in *Immunology and Cell Biology* 89, 332-339

2 Hecht, Marie-Lyn, et al. (2009) Recent advances in carbohydrate-based vaccines in *Current Opinion in Chemical Biology* 13, 354-359

3 Pavot, Vincent, et al (2012) New insights in mucosal vaccine development in *Vaccine* 30 142-154

4 Williams, Paul David (2009) Darwinian interventions: taming pathogens through evolutionary ecology in *Trends in Parasitology* 26.2, 83-92

5 Wolfson, Wendy (2006) Ancora Cooks with Carbs Synthesizing Carbohydrate Vaccines in *Chemistry and Biology* 13.7, 689-691

