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Virus-Like Particle: The Next Generation Vaccine?

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With the persistence of prevalent and often fatal diseases not easily treated using conventional therapeutic vaccines, there is growing interest in an emerging vaccine platform to prevent infections, relevant particularly to aggressive virus-caused diseases. Many infectious diseases, such as the common cold, influenza, rabies, measles, and different forms of diarrhea, hepatitis, yellow fever, polio, smallpox, and Acquired Immune Deficiency Syndrome (AIDS) are all caused by viruses. Some viruses, known as oncoviruses, contribute to certain forms of cancer, such as liver cancer associated with the hepatitis B and hepatitis C viruses. The most common example of an oncovirus is cervical cancer caused by Human Papillomavirus (HPV). Recently the Virus-Like Particle (VLP) has been proven as an effective antigen in the development of vaccines for virus-caused diseases. A virus-like particle is an assembly of virus structural proteins that mimics the configuration of a real virus, except that it contains no genetic material. Thus if a patient is vaccinated with VLPs then an immune response is generated as if the immune system has been presented with a real virus [1]. However, as the VLPs do not contain any genetic material, they are unable to replicate and as such are harmless and safe. These characteristics create enormous potential for use of the VLP platform as an effective anti-viral vaccine. As of today there are a few VLP-based vaccines on the market such as Engerix and Recombivax HB for the hepatitis B virus, and Gardasil and Cervarix for Human Papillomavirus (HPV). There are more VLP-based vaccine candidates addressing influenza, parvovirus, norwalk, and various chimeric VLPs are either in clinical trials or in the preclinical phase [1].

The advantages of using VLPs as antigens in vaccines are many. They are excellent prophylactics because they are self-assembling bionanoparticles (20 to 60 nm in diameter) that expose multiple epitopes on their surface and faithfully mimic the native virions [2]. Unlike attenuated bacterial vaccines, the authentic and attenuated virions cannot be used as antigens in a prophylactic vaccine because they would contain oncogenic viral genomes that would be infectious [3], VLPs eliminate this risk. Virus-like particles not only resemble authentic virions morphologically, but they also mimic virions immunologically which means they are able to induce high titers of neutralizing antibodies to conformational epitopes when vaccinated [4,5]. On the surface of VLPs there is an array of antigenic epitopes that mimics the surface of native virions more reliably than specific isolated subunits or subcomponents of the virus [2]. According to virology, VLPs are a class of subunit vaccines that differentiate themselves from soluble recombinant antigens by stronger protective immunogenicity associated with the VLP structure. Like parental viruses, VLPs can be either non-enveloped or enveloped, and they can form following expression of one or several viral structural proteins in a recombinant heterologous system [6].

The VLP can be produced in either a prokaryotic or eukaryotic expression system using target-encoding recombinant vectors, or in some cases can be assembled in cell-free conditions. Virus-like particles can be assembled by expressing the protein in a different medium such as mammalian cells, insect cells, yeast, or even bacteria [7]. Recent research also showed that it is possible to obtain plant derived VLP in a cost-effective way [8]. To date, a wide variety of VLP-based candidate vaccines targeting various viral, bacterial, parasitic, and fungal pathogens, as well as non-infectious diseases, have been produced in different expression systems. The advantages in safety, immunogenicity, and manufacturing of the virus-like particle platform to prevent and treat infectious diseases promise to dramatically shift the effectiveness and accessibility of much-needed vaccines. However the production of VLPs is not simple. In order to produce a functional VLP that effectively mimics a real virus, good yields of multiple virus structural proteins are needed. These must then be correctly assembled into a particle that reproduces the confirmation of the outer shell (capsid) of an infectious virus [9].

A robust formulation to deliver this next-generation VLP vaccine is urgently needed to make a highly efficient, cost-effective vaccine. Previously it has been found that nano-micro particle based formulation for small molecule drugs such as dexamethasone, antisense was very successful [10,11]. The similar biodegradable polymer based nano-micro particle can address the major production challenges to develop a sustainable platform in a less complicated manner, generating higher yields on a larger scale, reducing production time, and increasing cost-effectiveness VLP formulation which will be next generation vaccine.

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