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The New Era of Virus-Like Particles Based Vaccines

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Opinion

Virus-like particles or what is called VLPs for short are considered a useful tool in the development of vaccines. These VLPs-based vaccines have attracted the attention of many biotech and pharmaceutical companies as effective treatment for many types of non-infectious chronic diseases. VLPs simply resemble viruses; however they are non-infectious due to the lack of viral genome. The expression of envelop or capsid proteins result in the self-assembly of the particle, this assembly can easily be carried out in bacteria, yeast, plant cells or insect cell lines. The presence of repetitive viral surface protein epitopes is successful in eliciting strong B cell responses. VLPs have also high safety profile due to the lack of viral genome and lack of the ability to replicate. This area of research is not really new, the discovery of hepatitis B virus derived VLPs goes back to 1976.

An interesting class of VLPs is the "bacteriophage Qβ", an icosahedral virus with a diameter of about 30nm. This virus can replicate efficiently in *E.coli*. The capsid protein, which is ~ 14kDa, can be re-combinantly expressed in *E.coli* and spontaneously assembles in the cytoplasmic compartment of the bacteria. The VLPs are then ready for the purification process using the modern biotechnology techniques. The VLPs themselves are not the target of the vaccine but rather a template to display different antigens of interest. The idea is to improve the immunogenicity of conjugated antigens (the targets of the vaccine) to enhance B cell receptor cross-linking and uptake by dendritic cells resulting in efficient presentation to the adaptive immunocytes, an efficient active immunisation strategy.

Active immunization using VLPs has several advantages over the passive method where monoclonal antibodies are used. mAbs have already shown significant results in the research and clinical settings such as in the case of arthritis or other chronic diseases. However, mAbs suffer from several drawbacks, such as primary and secondary treatment failure, the undesirable cost production specially for long term treatment in chronic diseases and tolerability issues.

The following paragraphs summarize some interesting work carried out in this field by the pioneer in VLPs-Based Vaccines (Martin Bachmann); the professor of vaccinology at the University of Oxford and the professor of Immunology at the University of Bern. A VLP-based vaccine for hypertension has shown promising results in the preclinical studies and reached phase II clinical trial with good safety and efficacy profile. Simply Angiotensin-II peptide was efficiently conjugated to VLPs (Qβ) which was highly immunogenic in different animal models as well as humans. The results obtained in the phase II study indicated that (AngQβ) can reduce the blood pressure to the same levels obtained by ACE blockers. This vaccine is favourable over the conventional treatment as it induces long lasting effect with less number of doses. Also this may overcome the problem of inconsistency happened with daily tablets.

VLPs have also been tested as an effective vaccine in allergy representing a major problem worldwide. Qβ particles were filled up with DNA-oligonucleotides containing CpG-motifs which is known to stimulate toll receptor 9 of the innate immune system. The authors have focused on allergic rhinitis and asthma and they concluded that clinically effective treatment can be obtained even in the absence of allergens. Results encourage further investigation of virus-like particles and CpG-motifs in immunotherapy, either as a stand-alone product, or as adjuvants for allergen-specific immunotherapy.

VLPs have also shown promising results with cancer; a melanoma specific peptide was chemically linked to Qβ particles which also have been loaded with DNA oligonucleotides containing CpGs motifs. In this study they have used Melan-A/Mart-1 peptide as a potent inducer of specific cytotoxic T-cells responses. The vaccine was tested in phase I/II clinical trials with melanoma patients in stages II-IV. The vaccine was very well tolerated in these patients and a good percentage showed detectable specific T-cell response to the above mentioned antigen with significant levels of INFg as well. The research concluded that vaccination with CpGs loaded virus-like nanoparticles is associated with a human CD8 T-cell response with properties of a potential long-term immune protection from the disease.

In conclusion, VLPs-Based Vaccines constitute a promising field for treating different non-infectious chronic diseases with affordable expenses, high efficacy and large safety profiles.