Development of Human Papillomavirus Vaccine against a Broader Spectrum of Oncogenic Types

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Human papillomavirus (HPV) is a small nonenveloped DNA virus found in proliferative lesions of the skin or mucosa. Of more than 100 genotypes fifteen oncogenic HPVs, such as types of 16,18,31,52, and 58, cause cervical cancer, and HPV16 accounts for about 50% of the cases. An icosahedral HPV capsid is composed of major capsid protein L1 and minor capsid protein L2. The N-terminal region of L2 is displayed on the surface of the capsid. Expression of L1 alone in surrogate systems can produce L1-capsids, also called virus-like particles (VLP), which are morphologically indistinguishable from HPV virions extracted from the lesions

Animal model studies show that the anti-L1-capsid antibody can protect animals from challenge with the papillomavirus type used for vaccination, which led to the development of HPV16 and 18 VLP vaccines by scientists at the US National Cancer Institute. Interim data of the on-going large scale clinical trials showed that the vaccines induced high titers of type-specific neutralizing antibodies with nearly complete protection from the occurrence of cervical dysplasia without serious side effects. To establish a standard protocol of the vaccination, more data need to be collected on the kinetics of the serum neutralizing antibody level and the minimal level preventing the recipients from HPV infection. The data would provide bases to determine an appropriate dose regimen and possible need for boosting.

Anti-L2 antibody also can protect animals from papillomavirus challenge and furthermore can cross-neutralize in vitro some HPV types not used for vaccination. We found several cross-neutralization epitopes in the HPV16 L2-surface region, whose amino acids sequences are well conserved among the oncogenic HPVs. Given a large number of the existing and yet unidentified HPV types, it would be desirable to have a vaccine effective against a broader spectrum of HPVs. Assuming that the antibodies binding to the surface region of L2 can effectively protect humans against infection with most of the oncogenic HPVs, we are developing a vaccine antigen capable of inducing antibodies recognizing the type-common L2-epitopes.