COMBINED PROPHYLACTIC AND THERAPEUTIC VACCINES OF HPV

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BACKGROUND

Cervical cancer is women’s second most frequent cancer worldwide. Clinical and molecular studies have shown that certain types of HPV, referred to as high-risk types, are the etiological agents of this disease. Two anti-HPV vaccines for the prophylaxis of cervical cancer have been licensed recently by Merck (GardasilTM) and GlaxoSmithKline (CervarixTM). Both vaccines rely on the major capsid protein L1 in the form of virus-like particles (VLPs) as antigen; they protect against the HPV types from which the L1-VLPs were derived, yet are largely ineffective against all but the most closely related HPV types. The two most prominent high-risk HPV types, 16 and 18, are the major targets of both vaccines, although there is evidence for partial cross-protection against HPV types 31 and 45. The limited cross-protective capacity of L1-based vaccines, which is the main reason for the continuing effort toward the development of improved vaccination strategies, likely reflects the HPV type specificity of L1 neutralizing epitopes.

Antibodies against the minor capsid protein L2 also neutralize HPV infection and are often capable to cross-neutralize various non-cognate virions, although with varying efficiencies. The N-terminal region of L2 interacts with an as yet unidentified secondary receptor on the surface of target cells and this interaction can be blocked by anti-L2 antibodies. Perhaps the most prominent N-terminal epitope is the one located between aa 17-36.

A recently developed alternative strategy for increasing peptide immunogenicity relies on the use of thioredoxin (Trx) as a scaffold protein with the ability to constrain the structure of single-copy as well as multimeric (tandemly repeated) peptide epitopes inserted within its surface-exposed active site loop. This strategy has also been used to present HPV L2 peptides for immunization. In a subsequent improvement of the thioredoxin scaffold, it was found that by using Trx variants from Archaeabacteria, induction of anti-host thioredoxin antibodies can be significantly reduced.

SOLUTION

- The vaccine can be used in prophylactic and therapeutic approaches against infections with human papillomaviruses.
ADVANTAGES

Prophylactic and therapeutic treatment of infections with HPV types before or after infection.

SCOPE OF APPLICATION

- Pharmaceutical composition
- Vaccine