A synthetic virus-like particle streptococcal vaccine candidate using B-cell epitopes from the proline-rich region of pneumococcal surface protein A

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Alternatives to the well-established capsular polysaccharide-based vaccines against Streptococcus pneumoniae that circumvent limitations arising from limited serotype coverage and the emergence of resistance due to capsule switching (serotype replacement) are being widely pursued. Much attention is now focused on the development of recombinant subunit vaccines based on highly conserved pneumococcal surface proteins and virulence factors. A further step might involve focusing the host humoral immune response onto protective protein epitopes using as immunogens structurally optimized epitope mimetics. One approach to deliver such epitope mimetics to the immune system is through the use of synthetic virus-like particles (SVLPs). SVLPs are made from synthetic coiled-coil lipopeptides that are designed to spontaneously self-assemble into 20-30 nm diameter nanoparticles in aqueous buffer. Multivalent display of epitope mimetics on the surface of SVLPs generates highly immunogenic nanoparticles that elicit strong epitope-specific humoral immune responses without the need for external adjuvants. Here, we set out to demonstrate that this approach can yield vaccine candidates able to elicit a protective immune response, using epitopes derived from the proline-rich region of pneumococcal surface protein A (PspA). These streptococcal SVLP-based vaccine candidates are shown to elicit strong humoral immune responses in mice. Following active immunization and challenge with lethal doses of streptococcus, SVLP-based immunogens are able to elicit significant protection in mice. Furthermore, a mimetic-specific monoclonal antibody is shown to mediate partial protection upon passive immunization. The results show that SVLPs combined with synthetic epitope mimetics may have potential for the development of an effective vaccine against Streptococcus pneumoniae.
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