A novel human Respiratory Syncytial Virus vaccine based on the extracellular domain of the Small Hydrophobic protein

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There is no vaccine available against RSV. We propose an entirely novel approach for the development of an RSV vaccine that is based on the extracellular domain of the viral Small Hydrophobic protein (SHe). The 23 amino acid residue long SHe display little homology between RSV-A and –B but its sequence is conserved within either RSV subgroup. We have produced and characterized genetic as well as chemical fusions of SHe with a diverse set of antigen-presenting carriers. These carriers included recombinant virus-like particles and pentameric leucine zippers. The choice of the latter carrier was inspired by the natural oligomeric configuration of SH, which is a pentamer. Immunization of BALB/c mice with these SHe-based fusion proteins resulted in significant SHe-specific serum IgG titers. SHe-immunized mice displayed strongly reduced lung virus titers following challenge with the RSV-A2 strain, compared to control vaccinated animals. We also demonstrate that vaccination with SHe peptide coupled to a virus-like particle significantly reduces pulmonary immune cell infiltration compared to control vaccinated mice. Serum IgG induced by vaccination with SHe-fusion constructs or a SHe-specific monoclonal antibody did not neutralize RSV in vitro. However, RSV-infected cells abundantly express SH on the cell membrane as was revealed by immunostaining with SHe-specific IgG. Furthermore, passive transfer of these antibodies resulted in significant reduction of pulmonary RSV-A replication, indicating that antibodies contribute strongly to protection.

We conclude that a vaccine based on SHe is promising new candidate for the development of a prophylactic RSV vaccine.