Comparative study of the immunogenicity of two synthetic nanovaccines based on self-assembling peptides

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Subunit vaccines are safer than live-attenuated or inactivated vaccines. However, their limited immunogenicity and susceptibility to metabolic degradation require strong adjuvants and/or conjugation to delivery systems to induce a robust, antigen-specific immune response. Interestingly, synthetic peptides can be useful and polyvalent building blocks for the development of self-adjuvanted nanoparticles. Recent studies have shown that amphiphilic peptides can increase antigen density, promote cellular uptake by APCs and activate T and B lymphocytes. Additionally, short peptide monomers forming cross-β-sheet fibrils such as I_{10} have shown potential in inducing a strong immune response against the grafted epitope. However, a direct comparison of the intrinsic immunogenicity of peptide amphiphilic cylindrical micelles and cross-β peptide fibrils has never been performed. In this work, the amphiphilic peptide C_{16}-$V_3A_3K_3$(PA) and the I_{10} β-peptide were each linked to two epitope models, $OVA_{253-266}$ and $OVA_{323-339}$, able to polarize the resulting adaptive immune response differently. Biophysical analysis showed that both nanoplatforms formed β-sheet-rich nanofilament structures with the epitopes exposed on their surfaces. Intramuscular administration in mice led to a strong, antigen-specific humoral response without additional adjuvants. This study illuminates the potential of these synthetic self-assembling nanoplatforms as universal antigen carriers, enabling the rapid development of vaccines to combat infectious diseases.