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Modulating the Antigen Density on the Surface of Peptide Nanofibrils by Molecular Co-Assembly

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Abstract: Peptides with the ability to self-assemble into defined nanoparticles have gained increase interest for the design of antigen delivery platform for subunit vaccines. By modulating the primary sequences and the self-assembly conditions, the shape, size and surface chemistry of the final supramolecular structures can be precisely modulated, opening to a diversity of immunological functionalities. We recently reported that nanofilaments with a cross-β quaternary structure and assembled from a short 10-mer amyloidogenic peptide derived from the islet amyloid polypeptide (I10), constitute promising self-adjuvanted assemblies suitable for anchoring antigenic determinants and increasing their immunogenicity. In the present study, we took advantage of non-covalent molecular self-assembly to integrate different densities of antigens on the fibril in a controlled manner by adjusting the stoichiometry of the different monomer building blocks. The M2e epitope derived from the matrix 2 protein of the influenza virus was conjugated to the I10 self-assembling sequence by a flexible short linker on solid support. Chimeric M2e-I10 peptides were assembled in presence of different molar ratio of naked I10 under continuous rotary agitation. Structural conversion of soluble peptides into cross-β filaments was followed by thioflavin T fluorescence, circular dichroism spectroscopy and atomic force microscopy. By ELISA, we observed that the density of the M2e epitope accessible on the fibril surface could be finely modulated by controlling the stoichiometry of the building blocks. Finally, the capacity of the assemblies to activate the Toll-like receptor 2 (TLR2) was evaluated using HEK-Blue-hTLR6/TLR2 cells that have a NFκB-inducible reporter gene SEAP (secreted embryonic alkaline phosphatase). Overall, this study indicates that the density of a given epitope on a nanofibril can be precisely controlled through molecular co-assembly, ultimately fine regulating the amplitude of the antigen-specific immune response.