Abstract title: HOW TO IMPROVE THE IMMUNOGENICITY OF T-CELL EPITOPE PEPTIDES

Presenting author: Kata Horváti
Author and co-authors: Kata Horváti[1], Bernadett Pályi[2], Judit Henczkó[2], Gyula Balka[3], Eleonóra Szabó[4], Viktor Farkas[5], Beáta Biri-Kovács[1,6], Bálint Szeder[7], Kinga Fodor[8], Szilvia Bősze[1]
Affiliation details: 1 MTA-ELTE Research Group of Peptide Chemistry, Eötvös Loránd University, Hungarian Academy of Sciences, Budapest
2 National Biosafety Laboratory, National Public Health Center, Budapest
3 Department of Pathology, University of Veterinary Medicine, Budapest
4 Laboratory of Bacteriology, Korányi National Institute for Tuberculosis and Respiratory Medicine, Budapest
5 MTA-ELTE Protein Modelling Research Group, Eötvös Loránd University, Hungarian Academy of Sciences, Budapest
6 Institute of Chemistry, Eötvös Loránd University, Budapest
7 Research Centre for Natural Sciences, Hungarian Academy of Sciences, Budapest
8 Department of Laboratory Animal and Animal Protection, University of Veterinary Medicine, Budapest

Abstract text:

T-cell epitopes from different proteins expressed by *Mycobacterium tuberculosis* (*Rv1886c*, *Rv0341*, *Rv3873*) were selected based on previously reported antigenic properties. Relatively short linear T-cell epitope peptides generally have unordered structure, limited immunogenicity, and low *in vivo* stability. Therefore, they rely on proper formulation and on the addition of adjuvants.

Here we report a convenient synthetic route to induce a more potent immune response by the formation of a trivalent conjugate in spatial arrangement. As a core sequence, a Tuftsin derivative was used, which has been reported as a macrophage targeting peptide. Chemical and structural characterization of the vaccine conjugates was followed by the study of cellular uptake and localization. Immune response was assayed by the measurement of splenocyte proliferation and cytokine production, while vaccine efficacy was studied in a murine model of tuberculosis.

The conjugate showed higher tendency to fold and increased internalization rate into professional antigen presenting cells compared to free epitopes. Cellular uptake was further improved by the incorporation of a palmitoyl group to the conjugate and the resulted derivative possessed an internalization rate 10-times higher than the free epitope peptides. Vaccination of CB6F1 mice with free peptides resulted in low T-cell response. In contrast, significantly higher T-cell proliferation with prominent expression of IFN-γ, IL-2, and IL-10 cytokines was measured for the palmitoylated conjugate. Furthermore, the resulted conjugate showed relevant vaccine efficacy against *Mycobacterium tuberculosis* infection.

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