

P020 Targeting the MHC class-II presentation pathway in allergy vaccine development

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The worldwide increasing incidence of allergic disease and the limited efficacy of current vaccination schedules require the development of new, efficient vaccination strategies. Based on the TAT protein translocation domain, we have engineered modular antigen translocating (MAT) molecules aimed to enhance antigen presentation through intracellular targeting of the MHC class-II presentation pathway. MAT vaccines consist of a cloning cassette fusing a [His]₆-purification-tag to the TAT peptide and to a truncated invariable chain, which is able to target antigens to the trans-Golgi compartment. To test the efficacy of intracellular targeting, we engineered an array of MAT-fusions and compared the effects of [His]₆-tagged allergens, TAT- and MAT-allergens for their ability to stimulate T-cell proliferation and cytokine production in human PBMC cultures derived from allergic individuals, and to elicit protective immune responses in mice. MAT-vaccines induce strong proliferation in PBMC's at low concentration and induce a Th1/Th2 shift in the cytokine profile reflecting those reported in successfully desensitized allergics. In mouse models of allergy, we show that MAT-vaccines are highly efficient in desensitizing mice and protect them from anaphylactic shock. This present approach is not only applicable for the treatment of allergies, but for preventive vaccines in general.