Summary

The development of new therapies to treat immune diseases is one of the aims of current immunological research. In a variety of these diseases the differentiation of T helper cells into different effector cell subpopulations is decisive for the pathogenesis.

In the study presented here, DNA immunisation was used to modulate the T-cell differentiation in order to prevent the development of subpopulations involved in the disease. The immunisation was carried out by using a vector encoding for an antigen, which is directly introduced into the MHC class II pathway. This leads to an antigen presentation restricted to directly transfected APCs.

We could show that antigen specific Th cells were efficiently activated *in vivo* and that the strength of activation was comparable to that of a secreted form of antigen. No B cell activation was observed because of the intracellular localisation of the antigen. Importantly we observed an increased Th1 polarisation characterised by a high number of IFNγ producing cells and an inhibition of IL-4 production. We could exclude CpG motifs in the vector DNA to be responsible for an increased activation of APCs leading to the Th1 shift. Furthermore the missing B cell activation was not responsible for the altered Th cell differentiation. Also another type of antigen restriction to transfected APCs using a membrane bound form of Ovalbumin did not lead to this Th1 shift. Thereby we could exclude a direct effect on the APCs by the transfection. Moreover we observed an elevated induction of memory cells by restricting the antigen presentation to transfected APCs. An increased antigen presentation by MHC class II molecules is likely to be the reason for the elevated generation of memory cells and the pronounced Th1 response.

Pursuing the aim to promote Th2 cell development co-immunisations were performed using IL-4 and an siRNA against IL-12, respectively. However, neither of these Th2-inducing factors were able to reverse the Th1 polarisation. The aforementioned strong Th1 response was obviously dominating over the co-immunisations.

Targeting the antigen to the MHC class II pathway is a very effective method for the induction of a strong immune response, with a concomitant increase of Th1 differentiation but without antibody production. Accordingly this immunisation strategy could be especially suitable for the treatment of Th2 dominated diseases or allergies.