7. Summary

Interleukin-4 (IL-4) is the major factor in the development of allergic diseases like hay fever or asthma. The most important cytoplasmic event following stimulation with IL-4 is the activation of the transcription factor Stat6 (signal transducer and activator of transcription 6). Stat6 binds via a single SH2 domain first to tyrosine-phosphorylated motifs in the IL-4Rα-chain, and then to another Stat6 molecule, which results in the formation of active dimers. Since Stat6 is exclusively used by the IL-4 receptor, it is a promising approach to specifically disrupt IL-4 signal-transduction by inhibiting Stat6 activation.

A vector system was established for the delivery of hydrophilic agents into living cells. To this purpose, a 16 amino acid membrane-permeable peptide derived from the *Drosophila* transcription factor Antennapedia was used. The Antennapedia peptide has been shown to internalize into living cell in a receptor- and energy-independent manner.

In this thesis it is shown that a peptide derived from the Stat6-binding region of IL-4Rα (Stat6BP) is an effective inhibitor when it is delivered into cells by coupling with the Antennapedia peptide. Stat6BP completely inhibited IL-4 dependent phosphorylation of Stat6 in different human and murine cell lines, while IL-3 and IL-4 dependent phosphorylation of Stat5 was not affected. The inhibitory effect of Stat6BP was transient, but could be prolonged by treating the cells with the phospatase inhibitor sodium pervanadate. Transcription from a reporter gene construct with a Stat6-dependent promoter was inhibited by Stat6BP as well, indicating that the peptide is a suitable inhibitor for cellular responses downstream from Stat6 phosphorylation.

Another aim of this study was to investigate the role of the src-kinases $p56^{lck}$ and $p59^{fyn}$ in IL-4 signaltransduction. The results indicate, that the activation of both kinases is celline dependent. In some T-cellines $p56^{lck}$ was activated dominantly, in others $p59^{fyn}$.