Summary

Molecular cloning and characterization of serpins as potential immunomodulators

Filarial parasites are constantly exposed to an array of immune effector mechanisms of their hosts. Their survival therefore depends on the evasion or modulation of harmful immune responses. One strategy to cope with the host's immune responses is the release of immunomodulators that block effector mechanisms. Serpins (serine protease inhibitors) are secretory molecules that have been described to have functions in immune evasion (Zang et al. 1999, 2000, Maizels et al. 2001).

To determine parasite-specific properties of serpins, the immunomodulatory capacity of a serpin of the rodent filarial nematode *Acanthocheilonema viteae* was analysed in comparison to a homologous protein of the free-living nematode *Caenorhabditis elegans*. The aim of the project was to investigate whether serpins of *A. viteae* are specifically used by the parasite to evade immune responses of the host or whether serpins of the free-living nematode *C. elegans* have similar immunomodulatory activities.

Homologous serpins from *A. viteae* and *C. elegans* were cloned, expressed as proteins in *E. coli*, and their inhibitory and immunomodulatory properties were characterised.

The serine proteases from *C. elegans* (rCe-Serpin) showed trypsin and cathepsin G specificity. In addition, it inhibited the proliferation of polyclonally as well as antigen-stimulated spleen cells of mice, and enhanced the production of IL-10. The inhibition of the mitogenic cathepsin G and the induction of the IL-10 production are important factors in cellular hyporesponsiveness.

On the other hand, the serine protease from *A. viteae* (rAv-Serpin) showed no inhibitory property on the same proteases or T cell proliferation.

Since the serpin of the free-living *C. elegans* posseses immunomodulatory properties, serpins have probably not been specifically modified by parasitic nematodes for influencing the host's immune response. It may therefore be surmised that serpins are a preadaption to a parasitic life style of nematodes.

To further verify whether serpins of parasites have specific properties, a serpin of the parasitic protozoon *E. tenella* (rEt-Serpin) was also cloned and expressed. It inhibited the serine proteases trypsin, chymotrypsin, porcine pancreatic elastase and cathepsin G. The rEt-Serpin inhibited the proliferation of polyclonal stimulated spleen cells of mice and showed a tendency to enhance the IL-10 production. However, proliferation of antigen specific stimulated spleen cells was not inhibited by rEt-Serpin.