Introductory Remarks

'Superantigens' is the designation of a group of molecules that have in common an extremely potent activating effect on T lymphocytes of several species. This designation originates from the finding that the mechanism of T lymphocyte stimulation closely mimics the recognition of specific antigen: superantigens cross-link variable parts of the T-cell antigen receptor with MHC class II molecules on accessory or target cells. Toxic shock syndrome toxin 1 is the prototype superantigen. The superantigens known so far are produced by bacteria (Staphylococcus aureus and Streptococcus pyogenes, both gram-positive cocci), a mycoplasma (Mycoplasma arthritidis) and by murine retroviruses (mouse mammary tumor viruses). Thus, surprisingly distinct pathogens have evolved the same basic mechanism of T-cell stimulation in evolution. The interaction site on the T-cell receptor is the variable part of the β-chain (Vβ). Stimulation of T cells with a superantigen in vitro leads to a dramatic increase of T-cell subsets carrying certain Vβs. In vivo, the application of a superantigen leads to a transient expansion and subsequent death and anergy of T cells with the appropriate Vβs. That such selective enrichment or deletion occurs in certain immunopathological conditions, e.g. AIDS or rheumatoid arthritis, has been taken as evidence for the involvement of superantigens. This opens exciting aspects for the role of these molecules in human immunopathology. One has to keep in mind, however, that also antigenic peptides can selectively stimulate T cells carrying certain Vβs or Vδs. Due to the popularity of superantigens and probably due to their attractive name, a number of other candidate molecules have been proposed to belong to this group. For these, however, the definite proof of their superantigenicity is still missing.
Most contributions to this book describe the effects of superantigens on T lymphocytes. Although the basic mechanisms of T-cell stimulation by these molecules is similar, each superantigen has its own unique features. The enormous potency of these molecules is reflected by the biological consequences found when superantigens are introduced into the body. Most prominent and discussed in several contributions are the shock-like symptoms induced by the staphylococcal enterotoxins and the toxic shock syndrome toxin 1. It is now recognized that these symptoms are caused by an effect of the toxins on T cells, leading to a massive release of lymphokines and monokines.

Another important feature of all superantigens is the induction of immunosuppression in vivo by superantigens. Although the underlying molecular mechanisms are not completely clear, it is accepted that death of T cells occurs after an initial stimulation in vivo. In the long run this may open possibilities for the selective depletion of T cells for therapeutic purposes. Progress in research on superantigens has been extremely rapid in the last few years and is accelerating. It is possible that as this book goes to print it will miss important developments. We can expect further exciting findings in the near future.