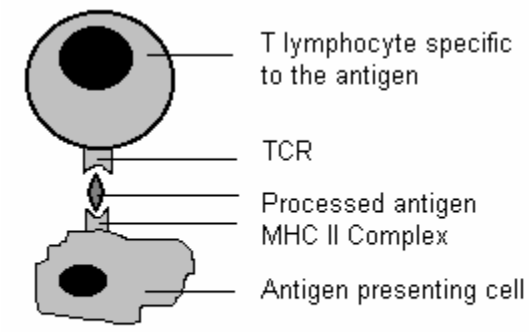
SUPERANTIGEN

When the immune system encounters a conventional T-dependent antigen, only a small fraction of the T cell population is able to recognize the antigen and become activated. However, some antigens can polyclonally activate a large fraction of the T cells, setting off massive immune response. These antigens are called superantigens. Superantigens stimulate up to 10% of T cells to respond whereas antigen would normally stimulate only 0.001-0.01% of T cells to respond.

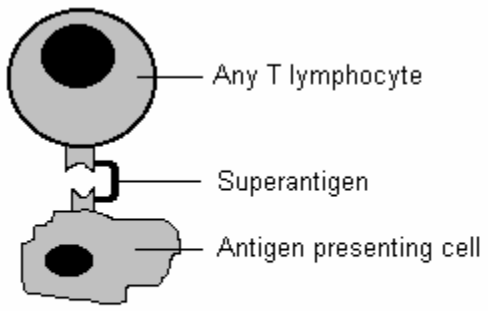
Examples of superantigens include:

- Staphylococcal enterotoxins
- Staphylococcal toxic shock toxin (TSST-1)
- Streptococcal pyrogenic exotoxins (exotoxin A and exotoxin B)
- Mouse mammary tumor virus (retrovirus), which causes breast cancer in mice, is also known to produce superantigen.

Mechanism of action:
Protein antigens are normally processed by macrophages and other antigen-presenting cells (APC) into peptide fragments, which are expressed on the surface of these cells in association with MHC class II molecules. Only those T-cells with receptors (TCR), which recognize the antigen together with the MHC molecule, are activated. Superantigens are not processed in this way but can bind to MHC class II molecules on many APC surfaces directly. Superantigens simultaneously bind to MHC class II molecules on the APCs and to the variable region of the TCR. This leads to the stimulation of many T-cells and an excessive production of interleukin-2 and other inflammatory cytokines. The over-production of interleukins/cytokines by T-cells can have the same effects as those observed in septic shock.



Normal activation of specific T lymphocyte by Antigen presenting cell



Non-specific activation of any T lymphocyte by superantigen

A typical antigen must be processed by an APC, after which it binds to both the α and β chain of the TCR. Superantigens don't require processing and do not bind to the α chain. Instead, they link the β chain of the TCR directly to the class II MHC molecule on the APC, an interaction that is sufficient to activate the T cell in the absence of any other co-stimulatory signals.

Significance of superantigens:
Superantigens are considered virulence factors, the stimulated T cells respond by secreting cytokines that suppress immune responses. Superantigen also induces apoptosis in the superantigen-binding CD4 T cells, so T cells that can respond to the pathogen are deleted.

Responsible for diseases like Staphylococcal food poisoning, Staphylococcal Toxic shock syndrome, Streptococcal toxic shock like syndrome etc. Staphylococcal enterotoxins bind to MHC II molecules and stimulate T cells to divide

and produce lymphokines such as IL-2 and TNF-alpha, which induce diarrhea. *Streptococcus pyogenes* exotoxin A (SPEA) and *S pyogenes* exotoxin B (SPEB) are the major toxins produced by group A beta-hemolytic streptococci.

Toxic shock syndrome: Toxic shock syndrome (TSS) is an inflammatory response syndrome produced by Toxic shock syndrome toxin-1 producing strains of *S.aureus*, characterized by fever, rash, nausea, vomiting, diarrhea, hypotension and multiorgan involvement. TSS has been typically associated with tampon use in healthy menstruating women. Highly absorbent tampons are believed to absorb Mg^{2+} resulting in decreased concentration in vagina, which in turn stimulates toxin production. The disease is now known to also occur in men, neonates, and nonmenstruating women in conditions including post-operative wound infection or post-influenza staphylococcal infection.