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Identification of Staphylococcal enterotoxin B sequences important for binding to a glycosphingolipid receptor imparting renal cell death and T lymphocyte proliferation

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Staphylococcal enterotoxin-B (SEB) is an enterotoxin produced by S. aureus. This superantigenis known to be harbored in the kidney in experimental animals and subsequently enters the intestine to cause diarrhea, and toxic shock. In this study we have used SEB and a series of synthetic SEB peptides to evaluate their binding to the putative receptors on cultured human proximal tubular cells and imparting phenotypes.

First, using GC-MS analysis of trimethylsilyl sugars from the glycosphingolpid receptor of SEB we identified this compound to be digalactosylceramide in human kidney proximal tubular cells. Next, we observed that the SEB peptide 191-220 was bound to these cells with the highest affinity and this was markedly inhbited by the presence of digalactosylceramide and upon the use of endoglycoceramidase which can specifically cleave off the glycome from the cognate receptor. We have also developed an ELISA-based assay to diagnose the presence of SEB in human fluids and food.Following binding SEB peptide used peptide 130-160 (containing a highly conserved sequence KKKVTAQEL) to inhibit cell proliferation via inducing apoptosis via the ceramide-neutral sphingomyelinase pathway. In contrast, peptide 130-160 was most effective at inhibiting SEB induced proliferation in human T lymphocytes. Thus, the residues surrounding KKKVTAQEL may be critical in SEB induced T cell proliferation and could be useful for neutralizing serum to SEB. The significance of this study is that SEB recruits a glycosphingolipid to bind to kidney cells and therefore provides a novel target to mitigate the toxic effects of this toxin.

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