

ABSTRACT

RECOMBINANT PROTEINS AND PEPTIDES FOR ENDOTOXIN BIOSENSORS, ENDOTOXIN REMOVAL, AND ANTI-MICROBIAL & ANTI-ENDOTOXIN THERAPEUTICS

Recombinant fragments of Factor C are disclosed. These proteins and peptides show great potency in recognizing, binding to, neutralizing, and removing endotoxin. These molecules can thus be used for anti-microbial, anti-endotoxin, and anti-sepsis therapy. SSCrFCES is a 38 kDa protein representing the LPS-binding domain of Factor C. The ability of SSCrFCES to bind lipid A was analyzed using an ELISA-based assay as well as surface plasmon resonance. Surface plasmon resonance similarly carried out for SSCrFC-sushi-1,2,3-GFP, SSCrFC-sushi-1GFP, and SSCrFC-sushi-3GFP confirmed their superior affinity for endotoxin. The 50% endotoxin-neutralizing concentration of SSCrFCES against 200 EU of endotoxin is 0.069 μM , suggesting that SSCrFCES is an effective inhibitor of LAL coagulation cascade. Although partially attenuated by human serum, as low as 1 μM of SSCrFCES inhibits the LPS-induced secretion of hTNF- α and hIL-8 by THP-1 and human peripheral blood mononuclear cells with a potency more superior than polymyxin B. SSCrFCES is non-cytotoxic, with a clearance rate of 4.7 ml/minute. The LD₉₀ of SSCrFCES for LPS lethality in mice is achieved at 2 μM . These results demonstrate the endotoxin-neutralizing capability of SSCrFCES *in vitro* and *in vivo*, as well as its potential for use in the treatment of endotoxin-induced septic shock. Also embodied in this application is the use of the sushi peptides and their mutant derivatives as potent antimicrobials. Further embodied in this application is the use of sushi peptides or sushi recombinant proteins to remove endotoxin from liquids.

Figure 15 of the Drawings is to accompany the Abstract when published.



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