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Letter to the Editor

Superantigens: procession of frets



Dear Editor,

Superantigens (Sags), a name devised by John Kappler in 1989 is a gang of about 40 microbial secretory proteins with a special morphology, sequence and ability to circumvent the orthodox mechanism of antigen presentation and processing.¹ Aberrant and extreme T cell activation is the central property of these proteins. Various bacteria known to produce these menacing proteins include *Staphylococcus*, *Streptococcus*, *Yersinia*, *Clostridium*, and *Mycoplasma*. While some viruses like Epstein-Barr virus, Rabies virus, and HIV are also capable to produce Sags. Systemic intoxication due to Sags develops a fatal condition known as toxic shock syndrome (TSS) which is basically caused by a cytokine tempest evolved by stimulated T cells. In general, Sags are virulence determinants which mark the adaptive immune response via immune synapses.²

A variety of microbes produce toxins which vary in morphology and expression but they are known as Sags that affirms the evolutionary trend of Sags production. Antigenic variation due to allelic variation as observed for streptococcal mitogenic exotoxin Z (SMEZ) is one of the obvious features and affirms that host immune system directs the Sags evolution. There is a school of thought which holds the notion that production of Sags facilitates the transport of microbe inside the host by corrupting the immune system. Interestingly, immune evasion elements like capsule and M protein are being regulated by the same genes which regulate the expression of Sags.³ Well, another candid question is that how Sags thwart immune elicitation against infection. Conceivably, the most probable phenomenon responsible for immune impediment is that Sags possess the skill to bring T-cell anergy into play. It seems likely that Sags steer the local IL2 deficit which results in stoppage of antigen-specific T cells expansion.³

Immunologically, Sags bind directly to major histocompatibility complex II (MHC-II) and T cell receptors (TCR) as intact proteins on binding sites other than conventional peptide-binding sites. Binding sites for Sags on TCR are V β (variable region of beta chain) while on MHC-II they may bind to alpha chain or beta chain. Subsequently to the binding, Sags trigger T-cell activation which ultimately steers the release of inflammatory mediators like TNF, IFN, and ILs. Sags are mainly associated with a dominated Th1 immune response. Moreover, activated T cells are responsible for the staffing of B and T cells to the infection site and co-activation of antigen-presenting cells (APCs), results in the release of TNF α and IL1

which ultimately give rise to the various clinical manifestations of TSS.³

Most Sags do not show significant expression level during microbial growth in culture media. On the other hand, ballooning data affirming the fact of post infection upregulation in the expression of Sags gives the impression that certain host factors may play a vital role during the course of infection. Transcription of some Sags genes like *smeZ* and streptococcal pyrogenic exotoxin J (*speJ*) has been observed during colonization stage. Transcription of Sags genes is cell density dependent because it has been observed that *speJ* is expressed at early stages of infection in low cellular density while expression of *speA* and *smeZ* is augmented during the late stages at high cellular density. The expression of *smeZ* is also related to the expression level of a special protein and inflammatory marker known as C-reactive protein. A virulence factor of *Streptococcus pyogenes* Streptococcal pyrogenic exotoxin B (SPEB) with multifunctional property is a cysteine protease which at protein level plays a vital role in regulation and expression of Sags.^{2,4}

Clinically, Sags are of supreme importance but not taken up with apprehension. TSS is the most serious consequence of Sags action. TSS is a capillary leak syndrome characterized by edema, hypotension, hypoalbuminemia and respiratory distress syndrome. Other syndromes which make the list long include Kawasaki syndrome, guttate psoriasis, rheumatoid arthritis, atopic dermatitis, eczema, and diabetes mellitus. Under special conditions Sags may enter into the body as an intact protein by crossing the epithelial lining; for example TSST-1 crosses vaginal mucosa and staphylococcal enterotoxin B (SEB) crosses intestinal mucosa. These characteristics of Sags make them a nominee of biological warfare.^{3,4}

Supportive therapy, fluid restoration, use of vasopressors and antibiotics are the central part of the schemes of action to fight Sags especially in case of TSS. Compellingly, clindamycin shut down the production of bacterial toxins at sites where other antibiotics especially beta lactam are usually fruitless. Additionally, clindamycin also cause the downregulation of penicillin binding proteins (PBPs) and M protein which ultimately result in inhibition of cell wall synthesis and phagocytosis augmentation, respectively. Other possible option to fend off Sags includes intravenous immunoglobulin and superantigen-blocking peptides and antibodies.⁵

As they say “nothing in biology makes sense except in the light of evolution” in future, if we may possibly arrange

solution to the questions that why microbes bound to evolve Sags then we may be able to devise much operational plans to fend off superantigenicity. Likewise, up to the stage researchers simply marvel about the amazing abilities of Sags but curiosity about the membrane complex composed of central components of T cell antigen recognition which include TCR, MHC class II and CD28 should be peered.

Conflicts of interest

The authors declare no conflicts of interest.

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Bilal Aslam^{a,*}, Mohsin Khurshid^b, Muhammad Atif Nisar^a, Saima Muzammil^a, Sumreen Hayat^a

^a Government College University, Department of Microbiology, Faisalabad, Pakistan

^b Government College University, Directorate of Medical Sciences, College of Allied Health Professionals, Faisalabad, Pakistan

* Corresponding author.

E-mail address: drbilaslam@gcuf.edu.pk (B. Aslam).

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