

INTERVIEW about

Extracellular adherence protein of *Staphylococcus aureus* with

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How can *Staphylococcus aureus* evade the host immune response?

Triantafyllos Chavakis: *Staphylococcus aureus* (*S. aureus*) has developed several mechanisms to evade the immune response of the host, thereby surviving in the host tissues. Major components of the anti-inflammatory arsenal of *S. aureus* are a) factors that block the complement system and thereby opsonophagocytosis

and b) anti-chemotactic factors. The latter group comprises two different molecules, the chemotaxis inhibitory protein of *S. aureus* (CHIPS), that blocks chemotaxis of leukocytes and the extracellular adherence protein (Eap), that blocks the adhesion of leukocytes to the endothelium.

What is known about extracellular adherence protein of *Staphylococcus aureus*?

Triantafyllos Chavakis: Eap is a 60-70 kD secreted protein that is found in 97% of *S. aureus* strains. Although it is secreted a portion of it binds back to the bacterial surface. Eap has the propensity to bind to several extra-

cellular matrix components, such as fibronectin, fibrinogen, prothrombin, thrombospondin, osteopontin, and vitronectin. Thus, it was originally thought to enhance the adhesion of the bacteria to the host tissues.

How does Eap block leukocyte-endothelial interactions?

Triantafyllos Chavakis: 4 years ago we published (Chavakis et al., Nat Med, 2002) the observation that Eap blocks the adhesion of leukocytes to different proteins of the extracellular matrix. Moreover, we found that Eap specifically interacts with the receptor ICAM-1 on endothelial cells, thereby specifically inhibiting the binding of leukocyte LFA-1 to

ICAM-1. Thus, we could show Eap to potently block adhesive events of leukocytes important for their recruitment to the site of inflammation or infection. As a consequence we found that infection with an Eap-negative strain resulted in a much higher host inflammatory response as compared to infection with the wildtype Eap-positive *S. aureus* strain.

What are the consequences of the anti-adhesive functions of Eap?

Triantafyllos Chavakis: As we could demonstrate in the original publication 4 years ago Eap may promote the survival of

the bacteria in the host tissue by blocking the host inflammatory response. Furthermore we could recently prove that

the anti-inflammatory Eap is responsible for the delayed healing of *S. aureus* infected wounds, so called “non-healing” wounds (Athanasopoulos et al.,

BLOOD, 2006). These findings explain the common clinical observation that *S. aureus* infection may strongly delay wound healing.

How can Eap inhibit autoimmune disease in mice?

Triantafyllos Chavakis: After having shown that Eap blocks the host immune response in favor of the bacteria, we thought to use purified Eap in order to block host leukocyte recruitment and thereby the immune response in autoimmune disease. The adhesive and migratory mechanisms of

autoimmune T cells also involve the LFA-1-ICAM-1 interaction. By using different forms of Eap we could prevent the development of experimental autoimmune encephalomyelitis (EAE) in mice, which is the mouse model of human multiple sclerosis (Xie et al. J Exp Med 2006).

Could Eap be a feasible treatment for human multiple sclerosis?

Triantafyllos Chavakis: Although it would be too early to make any prediction towards this direction, the first findings indicate that Eap-based therapies might be beneficial in MS. The fact that we found

that intervention with Eap after the onset of EAE completely suppressed the disease is very encouraging. However, the potency of Eap as a treatment of MS should be assessed in future studies.

REFERENCES

1. Chavakis T et al. Nat Med 8, 687, 2002
2. Athanasopoulos AN et al. Blood 107, 2720, 2006
3. Xie C et al. J Exp Med 203, 985, 2006