27th ECCMID Vienna, Austria 22 – 25 April 2017

The congress of ESCMID

Session: OS066 Host-pathogen interactions provide opportunities for novel therapy

Category: 9b. Host-pathogen interaction

23 April 2017, 12:06 - 12:16
OS0332

The peptide SET-M33 as novel agent to neutralize and remove LPS in patients with sepsis

Leila Quercini[1], Chiara Falciani[2], Jlenia Brunetti[1], Bracci Luisa[1], Giulia Roscia[1], Chiara Ambrosini[1], Alessandro Pini*[3]

[1]*University of Siena*

[2]*University of Siena; Department of Medical Biotechnology*

[3]*University of Siena; Medical Biotechnology*

Background: The synthetic antimicrobial peptide SET-M33 has strong activity against bacterial infections due to Gram-negative bacteria. It is currently in preclinical development as a new drug to treat infections caused by Gram-negative bacteria. Here we report its strong activity in neutralizing LPS from P. aeruginosa, K. pneumoniae and E. coli, thus reducing in vitro and in vivo expression of a number of cytokines, enzymes and signal transduction factors involved in sepsis. We also describe the construction of a new SET-M33-based device for the selective removing of LPS from blood of patient with sepsis.

Material/methods: RT-PCR, immunoblotting and luminex technologies have been used to verify and quantify cytokines' reduction in cells stimulated with LPS, and in vivo in bronchoalveolar lavage (BAL) of mice challenged via aerosol with LPS and treated with SET-M33. Then, the construction and use of a specific device based on a resin conjugated with SET-M33 for the removal of LPS from biological fluids is described.

Results: Sixteen cytokines and other major agents involved in inflammation and sepsis were analyzed in cells after stimulation with LPS and incubation with SET-M33. A number of these proteins showed up to 100% reduction in expression. LPS neutralization was also demonstrated in vivo by challenging BAL of SET-M33-treated mice with LPS, which led to a sharp reduction of cytokines with respect to non SET-M33-treated animals.

Conclusions: SET-M33 showed strong activity in vitro and in vivo in modulating cell response to the inflammatory stimuli (LPS), thus reducing the main sepsis signs. The same molecule was used to

construct a new medical device for selective removal of LPS form blood, to be used in the severest cases of sepsis.