'WAVE1' identified as key protein in sepsis

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Sepsis is a feared complication in bacterial infections. Despite treatment with antibiotics this uncontrolled systemic inflammation is linked to a very high mortality rate because there is no treatment that could bring the inflammatory reaction under control. In a publication, which has just been published, researchers from the MedUni Vienna belonging to the working group under Sylvia Knapp identify the "WAVE1" protein as a significant factor in these inflammatory processes.

In their study, Ulrich Matt and Omar Sharif from the working group under Sylvia Knapp (head of the Laboratory for Infection Biology at the University Department of Internal Medicine 1), describe how uncontrolled inflammations can block the innate immune system: oxygen radicals are produced to defend against bacterial infections. These kill the pathogens, but at the same time damage the body's own structures such as cell membranes. If these phospholipid membranes are oxidised, they interfere in the inflammatory process and block phagocytosis, the mechanism in which harmful bacteria are removed by phagocytes.

A key protein in this mechanism is the "WAVE1" protein which binds with actin, the cell's structural protein. If WAVE1 is missing, oxidised lipids can no longer affect the engulfing of bacteria and thus the defence against infection is once more intact. Consequently, a sepsis caused by the common pathogen Escherichia coli is more survivable.

In addition, the researchers found out that oxidised lipids also occur in the peritoneal dialysates of patients with kidney failure, and that these lipids can also block the phagocytosis of bacteria – but only when the

WAVE1 protein is present. This knowledge is interesting due to the fact that patients with long-term kidney damage exhibit a raised risk of infection for various, mostly unexplained reasons.

"A targeted blocking of inflammatory molecules, which interfere negatively in the body's defence mechanisms, appears attractive," says the author of the study, Ulrich Matt: "The new insights do at any rate expand our understanding of the innate immune response in the defence against bacteria and highlight a potentially interesting approach for treatment to take." Further studies are now ongoing to examine to what extent a therapeutic intervention via WAVE1 would make sense. "Before the clinical application of an immunomodulating treatment can occur there is still quite a way to go," is how Sylvia Knapp sums up the position.

More information: Matt, U. et al. WAVE1 mediates suppression of phagocytosis by phospholipid-derived DAMPs, *Journal of Clinical Investigation*, 2013;123(7). doi:10.1172/JCI60681.

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