Sepsis – A battle between humans and bacteria

Sepsis is a growing problem in the western world with mortality rates ranging from 30-50% depending on the severity of the disease and number of dysfunctional organs. Complications are caused by microbes (bacteria in most cases) infiltrating the circulatory system, resulting in an exaggerated inflammatory response which is harmful to the host. Heiko Herwald, professor at the Division of Infection Medicine, has been studying the coagulation and immune systems in relation to sepsis. His research is focused on how to better understand the involving molecular mechanisms in these two systems during disease progression and how to combat infectious agents to prevent the adverse events which lead to sepsis.

One of the current focuses in Heiko Herwald’s research is on a small endothelial protein called p33. This protein is believed to bind to damage-associated molecular pattern (DAMP) molecules also known as alarmins in order to down-regulate pro-inflammatory signaling from growing too strong. This interaction is enabled due to charge differences in the proteins; p33 is very negatively charged whereas DAMPs have positive net charge. As opposites attracts each other p33 is able neutralize the activity DAMPs. As this interaction is probably not highly specific, p33 has the ability to bind to more than one type of DAMP.

Despite learning more about the host’s response during a sepsis, the ideal goal would be to prevent the sepsis from occurring in the first place. Skin infections are known to be one type of infection prone to cause sepsis. A recent method of dealing with bacterial surface infections is by using cold plasma: UV-light irradiating molecules (oxygen, nitrogen) at 37°C to generate radicals which are applied to the site of infection. In scratch assays, Heiko Herwald’s team has applied the kINPen® instrument to investigate the effect of cold plasma on M1 protein, a streptococcal pro-inflammatory virulence factor.

In scratch assays, keratinocytes are grown on plates and either exposed to M1 protein or cold plasma treated M1 protein. The M1 protein is known to cause a halt in cell proliferation and that was also the case after keratinocytes exposed to M1 protein had been scratched. However, when cold plasma treated M1 protein was added to keratinocytes, cell proliferation was detected again. The next step in this project is to use mass spectrometry to identify which amino acids in the M1 proteins have been affected by the cold plasma.

Treating the patients with severe infections is only possible if they can be identified as soon as possible. Heiko Herwald underlines the importance of finding a rapid way of diagnosing patients with sepsis, since the disease progresses quickly. In addition to the immune system getting compromised, the coagulation system is either hyperactivated or depleted during sepsis, increasing the risk of micro-clots or bleedings. There is currently no well-defined way of diagnosing sepsis in patients, but Heiko Herwald suggests a precision medicine approach to the issue.
A diagnostic system capable of separating sepsis patients into groups based on the status of their inflammatory and coagulation system would be necessary. From there, treatments which either suppress or boost the immune and coagulation systems can be administered. To this end, reliable biomarkers which represent the different states of the immune and coagulation systems have to be identified. Finding these biomarkers and constructing a reliable diagnostic system is one of the next big challenges in the field of infection medicine, but Heiko Herwald believes that this goal can be achieved.

- Bacteria have fought against anti-microbial agents for over a hundred thousand years, whereas we humans entered the battlefield merely a hundred years ago. We can’t win this battle using traditional antibiotics, we need to find alternatives which can do the same job, only better, says Heiko Herwald.

- Joakim Hising