The medicine of the future against infection and inflammation?

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Researchers at Lund University in Sweden, have in collaboration with colleagues in Copenhagen and Singapore, mapped how the body's own

peptides act to reduce infection and inflammation by deactivating the toxic substances formed in the process. The study is published in *Nature Communications* and the researchers believe their discovery could lead to new drugs against infection and inflammation, for example in wound healing.

The toxins that are neutralised, known as lipopolysaccharides (LPS), come from the bacterial cell walls and generate an inflammatory reaction. The reaction is a necessary part of our immune defence system in which our bodies respond quickly and fight invasive bacteria. However, it can be over-activated and become harmful, as observed in infected skin wounds, infections in various organs, or in the case of bacteria spreading to the blood, which can lead to sepsis.

"We know from previous studies what the task of these peptides is but now we have mapped how they proceed in gradually reducing an inflammatory reaction", says Artur Schmidtchen, professor of dermatology and venereology at Lund University and consultant physician at Skåne University Hospital in Lund.

"By use of advanced biophysics such as nuclear magnetic resonance analysis, combined with molecular modelling and biological studies we show that these peptides form a C-shaped structure which enables the capturing and inactivation of LPS. They also simultaneously interfere with receptor-mediated inflammatory responses", adds Rathi Saravanan, senior research fellow at Lee Kong Chian School of Medicine at Nanyang Technological University, Singapore, and first author of the study.

"Currently, most drugs aim to more or less completely block a target, such as a receptor. But that risks a deactivation of the immune defence system which can be detrimental and downright dangerous. The body's own defence mechanisms proceed with greater caution in what is known

as a transient manner: the peptides act on their target for a short time to reduce an inflammation towards normalisation. It is the natural functions of these peptides that we want to develop into new drugs", says Artur Schmidtchen, who has been researching the field of innate immunity for over 20 years.

In addition, the peptides present in thrombin, a common blood protein, are multifunctional and can attack several targets, unlike current drugs.

The dermatology researchers now want to develop a peptide gel for improved wound healing in patient studies.

"That is the primary goal, but we will also be looking at the possibility of developing new drugs against infections in the eyes and various internal organs. This will become a new way of preventing both infection and inflammation without using antibiotics."

More information: Rathi Saravanan et al. Structural basis for endotoxin neutralisation and anti-inflammatory activity of thrombin-derived C-terminal peptides, *Nature Communications* (2018). DOI: 10.1038/s41467-018-05242-0

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