Tick saliva may offer a path to new therapies for inflammatory diseases

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A recent study by Monash University has found that proteins found naturally in tick saliva, called evasins, can be modified to block the activity of important proteins in human inflammatory diseases such as

arthritis, asthma and multiple sclerosis.

The study, conducted at the Monash Biomedicine Discovery Institute, showed it was possible to modify evasins so that they bind to the exact group of disease-promoting human proteins (chemokines), helping to suppress inflammation.

This new discovery opens the door to the development of much needed new therapies for inflammatory diseases. The findings have now been published in the *Proceedings of the National Academy of Sciences (PNAS)*.

Inflammatory diseases, such as atherosclerosis, arthritis, psoriasis, asthma and multiple sclerosis, all involve the same underlying phenomenon in which the body's white blood cells attack certain tissues. The white blood cells are attracted to these tissues by a class of proteins (chemokines) that are produced in the affected tissues (e.g. blood vessel wall in atherosclerosis, joints in arthritis). By targeting chemokines, evasins block the movement of white blood cells and the resulting tissue damage.

Typically, each tick species secretes a cocktail of evasins, thereby accomplishing broad-spectrum suppression of the host inflammatory response, presumably enabling the tick to feed for extended periods while not alerting the host to the tick's presence.

However, some chemokines are involved in inflammatory diseases while others are needed for the body's normal immune function. Therefore, for therapeutic applications, it is essential to modify the evasins so they only target the disease-causing chemokines.

Co-lead author Professor Martin Stone says the study has identified the structural basis of chemokine recognition and establishes a foundation

for engineering evasins.

"We've shown that it is possible to engineer an evasin with superior ability, giving us a novel structural model by which proteins can achieve binding selectivity," said Professor Stone.

Dr. Ram Bhusal, who co-leads the project, says: "To date, there are no anti-inflammatory therapeutics targeting the chemokine system, which makes this work of paramount significance as it opens up a whole new avenue for anti-inflammatory research. However, future work is still needed to ensure that these biomolecules avoid off-target effects."

More information: Structure-guided engineering of tick evasins for targeting chemokines in inflammatory diseases, *Proceedings of the National Academy of Sciences* (2022). DOI: 10.1073/pnas.2122105119.

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