Scientists map structure of key complex in the immune system

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Leicester scientists have mapped the "bouquet-like" structure of a key part of the body's immune system responsible for neutralising bacteria and viruses.

A team from the University of Leicester's Departments of Infection, Immunity, and Inflammation and Biochemistry led a project which has mapped the structure of complement component C1 - a large complex of the immune system.

The C1 complex is a protein which is responsible for spotting foreign agents in the blood which can cause disease - known as pathogens.

When it comes across bacteria, viruses, fungi and other objects, it sets off a process called the complement system.

This stimulates the body's immune system including the activation of membrane attack complex (MAC) proteins which attack and kill the foreign cells.

Although the C1 complex was first identified more than 50 years ago, the way it works has been poorly understood until now.

The three-year project was funded by the Medical Research Council and the Wellcome Trust.

Working with colleagues at Warwick Medical School, the University of

California, San Diego, and the Hungarian Academy of Sciences, Budapest, the Leicester researchers have revealed the constituent parts which make up the C1 complex.

This is extremely useful for helping us understand our own immune system - and could help us develop treatments to prevent the complement system from going wrong.

In some instances - including following a heart attack or stroke - the complement system attacks our own tissues, preventing the body from recovering.

Understanding the structure of the C1 complex could help scientists develop inhibitors to prevent the complement system from working against us in these cases.

The research reveals how the C1 complex is formed from constituent parts called C1q - the subcomponent responsible for recognising targets - and C1r and C1s, which activate further developments in the complement process.

Dr Russell Wallis, of the University of Leicester's Departments of Infection, Immunity and Inflammation and Biochemistry, who led the project, said: "We have determined the structure of part of a large complex (called complement component C1) of the immune system. It recognises pathogens and neutralises them by triggering a reaction pathway called complement.

"Our study reveals for the first time how the complex is assembled from its constituent proteins and suggests how it activates the complement cascade.

"We were able to piece together the structure of the full-size complex

from the structures of a series of overlapping segments. It looks like a bouquet of flowers. Our study has shown how the C1q, C1r and C1s proteins fit together.

"This finding helps us to understand how the immune system prevents disease and over the longer term may facilitate the development of new therapeutics.

"For example, the complement system attacks our own tissues in a number of disease states such as following a heart attack or stroke. Under these circumstances, use of inhibitors of complement could prevent this damage from occurring and allow the body to recover."

More information: The paper can be found at: www.pnas.org/content/110/34/13916.full

Provided by University of Leicester