Toxic shock: immune system's anthrax link

August 23 2007

Artist's impression of the perforin-like protein Plu-MACPF. Australian scientists have found that this protein belongs to an ancient and lethal toxin family previously only found in bacteria. (Acrylic on canvas). Credit: Carla Chinni

Human immune proteins crucial for fighting cancer, viruses and bacterial infections belong to an ancient and lethal toxin family previously only found in bacteria, Australian researchers have found. These proteins, called perforins, are related to bacterial toxins that cause diseases such as anthrax, gas gangrene and scarlet fever. The discovery was made by a team led by Professor James Whisstock and Dr Michelle Dunstone from Monash University's School of Biomedical Sciences.

Professor Whisstock, winner of the 2006 Science Minister's Prize for Life Scientist of the Year, said the team was stunned when it became clear that the bacterial toxins and perforins had a common ancestor.

"Over millions of years of evolution bacteria developed these proteins as weapons of attack," he said. "But animals have evolved these proteins for defence against that attack. It's a molecular arms race and there's still no clear winner."

Professor Whisstock said perforins were so-called because they kill bacteria, virally-infected cells and cancerous cells by punching tiny holes that perforate them. "People who lack one of these perforins can develop a serious blood disease called hemophagocytic lymphohistiocytosis and may be predisposed to develop cancer," he said.

"Perforins are also dangerous molecules. They can create absolute havoc in the immune system if they're not controlled properly. By understanding how they work we can find ways to control them in infectious diseases and areas such as transplantation rejection."

Using X-ray crystallography, the team worked out the structure of a perforin called Plu-MACPF, which, due to its similarity to the bacterial toxins, told them how the whole perforin family worked. Their findings are published today in the international journal *Science*.

Dr Dunstone said the findings were the culmination of nine years of research. "Now we finally know what perforins look like and how they work, we can use this knowledge to develop new ways to fight disease," she said.

Professor Whisstock said certain perforins were not only important for defending humans against attack by bacteria and viruses, but also important for propagating the human species because of their role in

embryo implantation. “It is ironic that we fear diseases such as anthrax yet from the same family of toxins comes a protein that is involved in reproduction,” he said.

The research team included scientists from the National Health and Medical Research Council’s protease systems biology program, the Australian Research Council’s Centre of Excellence in Structural and Functional Microbial Genomics and the Peter MacCallum Cancer Centre. The X-ray data was collected at the Advanced Photon Source in Chicago.

Source: Monash University