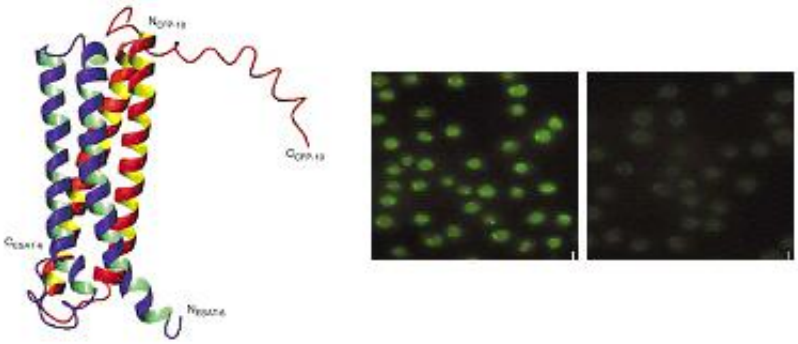
Scientists seek to disarm TB's 'molecular weapon'

March 6 2008



Left: The structure of the ESAT-6/CFP-10 complex. Note the 'long arm' on the right side of CFP-10. When this is intact, it allows the complex to attach to the outside of host white blood cells (central, the intense green shows a high amount of the complex binding). When the long arm is cleaved off, the complex shows greatly reduced attachment (right). © University of Leicester

Scientists at the University of Leicester are claiming a new advance in their fight against the resurgence of TB in Britain.

They have isolated the molecular ‘weapons’ of the bacterium and are now assessing ways to make the bacterium impotent.

Scientists in the University’s Department of Biochemistry are focusing on two proteins in the TB bacterium which, it is thought, allows it to thrive in white blood cells.

They are particularly examining a ‘long arm’ in a molecule of the bacterium which is thought to be used to bind onto white blood cells. The scientists are also seeking to identify which part of the white blood cell is being targeted.

Dr. Mark Carr, from the Department of Biochemistry said: “If you were to ask most people about TB, they would have most likely told you it was no longer a threat, merely a memory of a Britain with an undeveloped healthcare system.

“But TB is on the rise around the world with the number of new reported cases nearly doubling in the past 25 years. The World Health Organisation reported 8,500 instances in the UK in 2005.

“At the University of Leicester, our aim is to take the molecular ‘weapons’ of TB and isolate them, to understand their function and hopefully find a way to minimise their effects.

“One of the most important of these molecular weapons is known as the ESAT-6/CFP-10 complex. These are two proteins that bind together to become a functional unit, and it is thought that they may be needed to allow the bacteria to thrive inside white blood cells, as happens during the initial infection. Removal of the genes for this complex from the TB genome renders the bacteria unable to cause disease, exposing how important this particular weapon is to the bacteria.

“Similarly, studies of the structure of the protein complex have shown that removal of a ‘long arm’ from the molecule prevents the complex’s ability to bind to the outer surface of human white blood cells. This data has provided us with a potential insight into the important components of this complex.”

Dr. Carr added: “Current work is attempting to identify the exact

components of the human white blood cells that this complex is targeting. Once found, this should give us a greater knowledge of the action of these molecular weapons of TB and give us the edge in the war against an ancient, reawakened foe."

Source: University of Leicester