Meningitis bacteria dress up as human cells to evade our immune system

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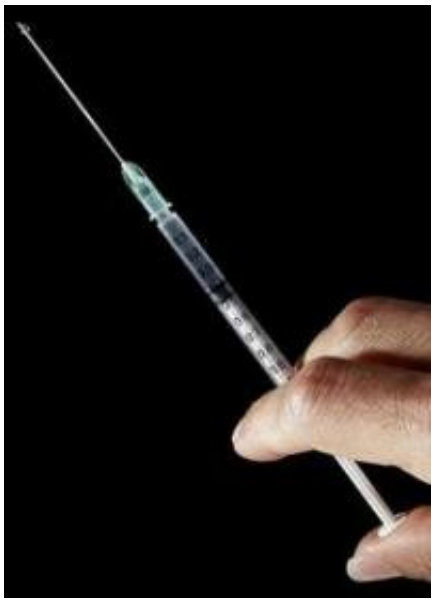

ThisOxford research suggests new vaccines could be tailored to fight Meningitis B.

(PhysOrg.com) -- The way in which bacteria that cause bacterial meningitis mimic human cells to evade the body's innate immune system has been revealed by researchers at the University of Oxford and Imperial College London.

The study, published in *Nature*, could lead to the development of new vaccines that give better protection against meningitis B, the strain which accounts for the vast majority of cases of the disease in the UK.

Meningitis involves an inflammation of the membranes covering the brain and the spinal cord as the result of an infection. The infection can be due to a virus or bacteria, but bacterial meningitis is much more serious with approximately 5% of cases resulting in death. The disease mainly affects infants and young children, but is also often found in teenagers and young adults. The disease is frightening because it can strike rapidly, with people becoming seriously ill within hours.

The bacterium Neisseria meningitidis is the most common cause of bacterial meningitis. It comes in different forms, causing different strains of the disease. With vaccines against strains A and C, group B now accounts for around 90% of cases in the UK. While there is still no vaccine available for strain B, two vaccine candidates are in clinical trials.

The Oxford and Imperial research team, funded by the Wellcome Trust and Medical Research Council, looked at how one protein in the outside coat of *Neisseria meningitidis* enables the bacteria to avoid being attacked and killed by the complement system, part of the body's innate immune system.

The complement system is designed to attack all foreign bodies that come into contact with the blood. We have particular sugar molecules on the surface of our own cells that flag them as being part of our body and stop them from being attacked and killed. This system works through factor H, a molecule that circulates in the blood and binds to the sugars on the surface of our cells, preventing any immune response.

Critically, the protein on the outside of Neisseria bacteria also binds factor H. Called factor H binding protein, it makes the bacteria appear like human cells and so prevents any attack from the innate immune system.

The researchers, led by Professor Susan M. Lea of the Sir William Dunn School of Pathology at the University of Oxford and Professor Christoph M. Tang of the Centre for Molecular Microbiology and Infection at Imperial College London, determined the structure of human factor H attached to factor H binding protein on the meningitis bacterium.

They found that the protein in the bacterial coat mimicked the sugars on the surface of human cells precisely, enabling the bacteria to bind factor H in the same way as human cells.

"It's like the bacteria have stolen someone's coat and put it on in an effort to look like them," says Professor Lea of Oxford University, who led the work. "This protein enables the meningococcal bacteria to pass themselves off as human cells, and the disguise is good enough to fool the immune system."

"Meningitis B can be a devastating disease and there is an urgent need to create an effective vaccine against it. We hope our new findings will help with this work. Our study gives us a clearer understanding of how meningococcal bacteria shield themselves from the immune system and it suggests that we could tailor new vaccines to fight this important human pathogen," added Professor Tang, from the Centre for Molecular Microbiology and Infection at Imperial College London.

The two vaccines against meningitis B that are currently in clinical trials, which have been developed by different pharmaceutical companies, both use factor H binding protein as part of the vaccine formulation. The aim is to generate an immune response that will protect against any subsequent infection.

These results suggest that on injection, the bacterial protein used in the vaccine will immediately get bound up by factor H in the blood and may no longer be able to generate an optimal immune response. The researchers at Oxford and Imperial believe that the bacterial protein could be modified so that it did not bind factor H, making it likely that a much stronger immune response could be elicited to protect against the disease.

"We are looking to use the knowledge gained from this study to work with pharmaceutical companies in the design of improved, smarter vaccines that give better protection against meningitis B," says Professor Lea.

Source: Imperial College London