MedicalXpress

Genetic differences that make some people susceptible to meningitis revealed in major new study

August 8 2010

Genetic differences that make some people susceptible to developing meningococcal meningitis and septicaemia, and others naturally immune, are revealed in a new study of over 6,000 people, published today in *Nature Genetics*.

The research, led by Imperial College London and the Genome Institute of Singapore, is the largest ever genetic study of meningitis and septicaemia caused by meningococcal bacteria. It suggests that people who develop these diseases have innate differences in their natural defences that leave them unable to attack meningococcal bacteria successfully.

Although several different bacteria and viruses cause meningitis, meningococcal bacteria cause one of the most devastating forms of the disease - meningococcal meningitis, which is fatal in approximately one in ten cases. Meningococcal septicaemia is a type of blood poisoning that often accompanies this form of meningitis.

Meningococcal meningitis and septicaemia most commonly affect babies, young children, teenagers and young adults. The diseases are frightening because they can strike rapidly, with people becoming critically ill within hours.

There are vaccines available against some strains of meningococcal

bacteria but not others. The researchers hope that their new findings will boost the development of effective vaccines to combat the group B strain of the bacteria, for which there is currently no vaccine. Every year, this strain causes thousands of deaths in children and adults across the world.

Most people carry the meningococcal bacteria in their throat intermittently during their lives without ever developing the disease. Prior to today's study, it has not been known why some people in the population develop meningococcal meningitis and septicaemia while others appear to be naturally immune to the bacteria.

Today's study compared the genetic makeup of 1,500 people who developed meningococcal meningitis, from the UK, Holland, Austria and Spain, with over 5,000 healthy controls from the Wellcome Trust Case Control Consortium. It was supported by the Wellcome Trust, Meningitis Research Foundation UK and the European Society for Paediatric Infectious Diseases.

Researchers looked at half a million common genetic variants scattered across each person's genome, and searched for differences between the patients with meningococcal disease and healthy controls. The results revealed that those who had developed meningococcal meningitis had genetic markers in a number of genes involved in attacking and killing invading bacteria.

Professor Michael Levin, from the Department of Paediatrics at Imperial College London, who led the international research effort, said: "Although most of us have carried the meningitis bacteria at some point, only around one in 40,000 people develop meningococcal meningitis. Our study set out to understand what causes this small group of people to become very ill whilst others remain immune. Our findings provide the strongest evidence so far that there are genetic factors that lead to people

developing meningitis."

Dr Victoria Wright from the Department of Paediatrics at Imperial College London, who co-ordinated patient recruitment for the study across four European countries, added: "Meningococcal disease is a terrible illness as it strikes healthy children and adults suddenly, and can kill in a few hours. Improving our understanding of why some people get the disease and not others will help to identify those at risk and develop better vaccines. The success of the study was due to the willingness of patients and families to contribute their DNA for analysis, and it could not have been achieved without international collaboration."

The variations uncovered in the study were around the genes for Factor H and Factor H-related proteins. These proteins regulate a part of the body's immune system called the complement system, which recognises and kills invading bacteria.

Normally, Factor H and Factor H-related proteins ensure that the complement system does not cause excessive damage to the body's own cells. However, meningococcal bacteria can hijack the body's Factor H and use it to ensure that the body does not recognise the bacteria as foreign. The bacteria effectively use Factor H as a 'Trojan Horse,' enabling them to evade the body's defences and preventing the immune system from killing them.

The researchers are now keen to investigate precisely how the genetic variations that they have uncovered affect the activity of Factor H and Factor H-related proteins.

This study involved collaboration between researchers at Imperial College London and clinicians at Imperial College Healthcare NHS Trust, as part of the Academic Health Science Centre (AHSC), a unique kind of partnership between the College and the Trust, formed in

October 2007. The AHSC's aim is to improve the quality of life of patients and populations by taking new discoveries and translating them into new therapies as quickly as possible.

Other institutions involved in the study were the Alder Hey Children's Hospital, the Genome Institute of Singapore, and other children's centres in the UK, Holland, Austria and Spain.

More information: "Genome-wide association study identifies variants in the CFH region associated with host susceptibility to meningococcal disease" Nature Genetics, Sunday 8 August 2010.

Provided by Imperial College London