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Genes that increase children's risk of blood infection identified

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A team led by Oxford University has identified genes that make certain children more susceptible to invasive bacterial infections by performing a large genome-wide association study in African children.

Bacteraemia, bacterial infection of the bloodstream, is a major cause of illness and death in sub-Saharan Africa but little is known about whether human genetics play a part. The leading bacterial cause of death in young children worldwide is *Streptococcus pneumoniae* (*pneumococcus*), and 14.5 million episodes of serious pneumococcal disease occur in young children annually.

A global network of researchers, coordinated from the Wellcome Trust Centre for Human Genetics in Oxford, therefore carried out a genome-wide association study to identify which genes might be associated with an increased likelihood of developing bacteraemia.

Dr Anna Rautanen from the Wellcome Trust Centre for Human Genetics at Oxford, said: 'A key question is why only a proportion of individuals develop invasive disease despite widespread exposure and asymptomatic carriage of bacteria. We know that genetic differences contribute to individuals' chances of developing more serious disease. However, the relevant genes for bacteraemia susceptibility remain largely unknown.'

The study looked at DNA samples from more than 4,500 Kenyan children from the Kilifi area, where Oxford and the Welcome Trust have

a joint research centre with the Kenya Medical Research Institute, and where there is a high occurrence of bacteraemia. Just over 4000 children were healthy, while slightly more than 500 had pneumococcal bacteraemia.

The study found an area of two long intergenic noncoding RNA (lincRNA) genes that was associated with susceptibility to pneumococcal bacteraemia. LincRNAs are RNA transcripts that are longer than 200 nucleotides but are not translated into proteins. LincRNAs are still little understood, although it is believed that the human genome has more than 10,000 of them.

Dr Rautanen said: 'One of the associated lincRNA genes, called AC011288.2, is expressed only in neutrophils, cells that are known to have a key role in clearing pneumococcal disease. Although the role of lincRNAs in human infections is unknown, recent mouse studies have indicated that some lincRNAs can act in immune cells to regulate an individual's susceptibility to bacterial and viral infections.

'The genetic variants we identified are found only in African populations. This is one of only a few large scale genetic studies carried out in Africa, and the results show why such studies must be carried out in diverse populations.

'Critically, the genetic variants we have identified carry a doubled risk of developing bacteraemia when infected with the *Streptococcus pneumoniae* bacteria. This discovery therefore provides clues in the pressing search for new ways to target the disease.'

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