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## Genetic signature in TB patients sheds light on disease

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18 August 2010

Medical Research Council (MRC) scientists have uncovered a 'genetic signature' in the blood of patients with active tuberculosis (TB). This discovery could not only serve as the basis of future diagnostic tests but also sheds light on why some people go on to develop active TB disease.

A third of the world has been estimated to have been exposed to the organism *Mycobacterium tuberculosis* (MTb) which causes TB, but have no symptoms and carry the infection in its latent form. Around one in ten of these carriers will develop full blown TB over their lifetime. The latent form of the disease is currently diagnosed either by a skin test or a blood test that shows a reaction to MTb; however, these tests cannot determine which individuals with the latent form will develop active TB disease.

Dr Anne O'Garra, Head of Immunoregulation at the MRC National Institute for Medical Research (NIMR) and collaborators have uncovered a pattern of genes in the blood of patients who have active pulmonary (lung) TB, which is distinct from that in patients tested with other infectious diseases. This genetic signature in the blood reflects the extent of the disease in the lungs and disappears after successful treatment.

Results from the study showed that around 10 per cent of those with latent infection had the genetic signature for the active disease. Further research is required, but this new finding is a significant step towards the development of a blood test using this genetic signature to effectively predict which people with the latent form of the disease will go on to have active TB. This would enable thousands of people likely to progress to active TB to be diagnosed and treated earlier.

Dr Anne O'Garra, Head of Immunoregulation at the MRC National Institute for Medical Research (NIMR), who led the study said:

*"Although people have been studying TB for more than a century, there is still a desperate need for better prognostic and diagnostic tests and more information about the body's response to MTb infection, which may also help in the design of vaccines and treatments. These findings offer tools needed for monitoring success of treatment of TB."*

Tests to uncover this genetic signature were initially carried out in London, a central point for TB in the UK with over 3,500 cases diagnosed last year which represents 40 per cent of all UK cases. A comparative analysis was also carried out in Cape Town to confirm the original findings would be representative in other parts of the world. Over 400 participants took part in the study.

The study also sheds light on how the body responds to TB infection, in particular showing that white blood cells known as neutrophils and genes activated by a type of protein known as Type I Interferon, may be

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more important in the development of TB than previously thought. Type I Interferons are proteins produced by many cells of the body upon infection that are well known for fighting viral infection, but actually aggravate bacterial infections, and may make the patients sicker. These findings may eventually help researchers to design more effective vaccines or treatments to help the body fight TB.

The study was funded by the Medical Research Council (MRC) in conjunction with international partner the Baylor Institute for Immunology Research, and with additional support from the Dana Foundation. It represents an important step in the MRC's strategy to use genetics, imaging and biological indicators to understand predispositions for disease and how these factors could influence the quality and length of life. The study is published in the journal *Nature*.

Ends

Notes to editors:

For more information or to arrange an interview with one of the scientists, please contact the MRC Press Office on 020 76376011 or email [pressoffice@headoffice.mrc.ac.uk](mailto:pressoffice@headoffice.mrc.ac.uk)

1. 'An interferon-inducible neutrophil-driven blood transcriptional signature in human tuberculosis' will be published in *Nature* on 19 August.

2. Further images are available on the [MRC NIMR](#) website.

3. For almost 100 years the Medical Research Council has improved the health of people in the UK and around the world by supporting the highest quality science. The MRC invests in world-class scientists. It has produced 29 Nobel Prize winners and sustains a flourishing environment for internationally recognised research. The MRC focuses on making an impact and provides the financial muscle and scientific expertise behind medical breakthroughs, including one of the first antibiotics penicillin, the structure of DNA and the lethal link between smoking and cancer. Today MRC funded scientists tackle research into the major health challenges of the 21st century [www.mrc.ac.uk](http://www.mrc.ac.uk).

Background information on tuberculosis provided by the authors

- Around 1.7 million people worldwide die of tuberculosis each year, but there is little knowledge on why some people become sick whereas others do not when infected with MTb.
- Approximately two billion people worldwide are considered infected with the latent form of tuberculosis(TB)
- Between 10 to 20 per cent of TB carriers (individuals who have no symptoms) go on to develop the active form of TB.
  
- Although sustained and arduous treatment is usually very effective, if the disease remains undiagnosed there is a high risk of death. If treatment is not maintained, the infection can return.

