MedicalXpress

Lupus gene finding prompts call for more DNA samples

December 2 2007

Wellcome Trust researchers have identified a key gene involved in the disease Lupus, which affects around 50,000 people in the UK, mostly women. The lead researcher behind the study has called for more patients to volunteer DNA samples to enable them to further study the underlying causes of the disease.

Lupus – or Systemic Lupus Erythematosus (SLE) – is an autoimmune disease which frequently causes skin rash, joint pains and malaise, but can also lead to inflammation of the kidneys and other internal organs. The risk of death in SLE is increased fivefold over that of the general population. However, because the symptoms are often non-specific, diagnosing the condition can be difficult. There is currently no cure for the disease, which can be triggered by viral infections, sunlight, trauma or stress, as well as puberty and childbirth.

In research published online today in the journal *Nature Genetics*, Professor Tim Vyse from Imperial College London, and colleagues in the US and Canada, have identified a new genetic variant, OX40L, which increases the risk of developing Lupus. The variant, which is carried by one in six people in the UK, increases the risk of developing the disease by 50% per copy.

"Lupus can be a very serious condition, but because its symptoms are often similar to those of other illnesses, it can be difficult and take time to diagnose," says Professor Vyse, a Wellcome Trust Senior Fellow from Imperial College. "Although it appears to have a number of

environmental triggers, we are now beginning to get a clearer picture of the role that genetics also plays in the disease."

OX40L is a gene that is important in several different types of cells in the immune system. The work, carried out by members of Prof Vyse's laboratory, shows that the genetic variants in the OX40L gene that amplify the risk of lupus do so by increasing the amount of OX40L present on the surface of lymphocytes, which are key components of the immune system. They are currently studying exactly how this increases the risk of SLE.

"As well as causing problems with diagnosis, Lupus's many symptoms make it difficult to work out which are key to the disease," he says. "Identifying a specific gene will enable us to see at a molecular level what is behind Lupus and develop treatments targeted at inhibiting or blocking the action of those genes."

Prof Vyse's group and other scientists have previously discovered two other genes implicated in Lupus. IRF5 is a gene involved in regulating interferons, of which there appears to be an overabundance in Lupus. Interferons are natural proteins produced by the cells of the immune system in response to challenges by pathogens such as viruses, bacteria and tumour cells. The role of the second of the previously-discovered genes, FCGR3B, in Lupus is unclear.

Professor Vyse is very grateful to everyone who has provided DNA samples for these studies, but stresses the importance of more DNA samples from volunteers and calls for more patients to provide samples. The OX40L gene was identified by studying approximately 1.400 people with Lupus, and other members of their families in the UK and the US.

"Without DNA samples from people with Lupus, we would be unable to study the disease," he says. "Despite the disease being relatively

common, DNA samples are in short supply. I would encourage patients to discuss with their GP or consultant about providing a blood sample to help further our understanding."

Source: Wellcome Trust