Medical Xpress

Study reveals a genetic signature of autoimmune disease

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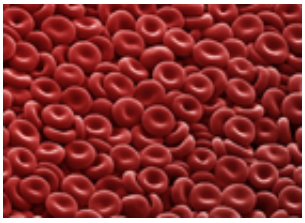

Red blood cells. Credit: Annie Cavanagh, Wellcome Images

(PhysOrg.com) -- Researchers have identified a cellular genetic signature that predicts prognosis in two different autoimmune diseases. It is hoped the findings could one day help to guide therapy and might also reveal new therapeutic targets.

Autoimmune disease is caused when the immune system mistakenly attacks and destroys healthy body tissue. Currently the only way to treat these diseases is with drugs that switch off the immune system in general, which have toxic side-effects and leave patients susceptible to opportunistic infections. Being able to tailor drug treatment to the severity of disease would help to reduce these debilitating side-effects.

The research, led by Kenneth Smith from the Cambridge Institute of Medical Research, looked at patients with two types of autoimmune disease: a type of vasculitis characterised by inflammation of the blood vessels known as AAV, and lupus, a disease caused by antibodies acting

against the body's own tissues.

The team took blood samples from patients before treatment and isolated the different populations of immune system cells, including T cells, B cells and neutrophils. By looking at gene expression in each of the different types of cells, they were able to get a snapshot of which cell types might be contributing to disease.

Their first analysis revealed distinct patterns of gene expression in each cell type, but it was the T cell population that captured their attention. When they looked at a specific subgroup of T cells, known as CD8+ T cells, they found that the patients could be separated into two distinct groups based on their long term prognosis, with one group having more disease relapses or 'flares' than the other.

CD8+ T cells from patients with relapsing disease had higher levels of expression of genes involved in promoting T-cell activity - including the T-cell receptor, which controls activation of the T cell, and the receptor for IL-7, a chemical that drives T-cell survival. CD8+ T cells from these patients also showed the hallmarks of having been activated already - so-called 'memory T cells' that are poised to react faster and stronger.

The study does not explain how the CD8+ T cells contribute to the severity of disease, or why these particular genes might be switched on in patients with poor prognosis, but by identifying a genetic signature that predicts poor disease outcome, it is hoped that doctors may one day be able to use this information to tailor drug therapy according to the individual patient.

More information: McKinney EF et al. A CD8+ T cell transcription signature predicts prognosis in autoimmune disease. Nat Med 2010 [Epub ahead of print]. www.nature.com/nm/journal/vaop … nt/full/nm.2130.html

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