Thymic function in inflammatory skin diseases

A measure of recent thymic emigrating T cells using the T cell receptor excision circle technique

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ABSTRACT

This PhD dissertation is based upon studies carried out at the Department of Dermatology, Marselisborg Hospital, Aarhus University Hospital, Denmark, from April 2001 to June 2005.

Inflammatory skin diseases are associated with immune activation in the peripheral immune system. Previous studies have shown decreased telomeres and increased telomerase activity both in Atopic Dermatitis (AD) and psoriasis patients, and an increased amount of CD4+CD8+ double-positive T cells in patients with AD.

The aim of this dissertation was to investigate thymic output and T cell turnover in patients with AD and psoriasis compared to healthy controls by measuring T cell excision circles (TREC) content in CD4+ and CD8+ T cells.

TREC are DNA excised during the formation of the T cell receptor. Because of its cytoplasmic localization in the cell, TREC is diluted during T cell divisions and can thus be used as a marker for recent thymic emigrants into the peripheral immune system.

Patients with AD or psoriasis were recruited from The Department of Dermatology, Aarhus University Hospital. To investigate the individual TREC variation a group of 10 patients with AD were observed over a period of six months. Healthy controls were recruited among blood donors. Blood samples (30 ml) were collected into heparin coated tubes for measurement of the TREC content in CD4+ and CD8+ T cells, respectively. SCORAD evaluations were performed on the ten AD patients who were observed over time.

We observed that men, but not women, with AD had decreased mean TREC values, and that men with atopic dermatitis had a significantly faster decline in their TREC content with increasing age compared to healthy men. In contrast, both men and women with psoriasis overall had significantly reduced TREC levels.

Regarding disease activity we observed an inverse relationship between levels of TREC and total serum IgE, diseases intensity and extent in atopic dermatitis patients. Furthermore, patients with AD had a significantly greater variation in TREC content, measured over time, compared to healthy controls.

These observations strongly support that both diseases are associated with an increased turnover of both CD4+ and CD8+T cells in the peripheral immune system. Atopic dermatitis patients, however, seem to have a compensatory emission of recent thymic emigrants.

Further research into different cell populations and with patients who have just developed AD would contribute to the understanding of the above-mentioned findings.