Molecular and cellular discoveries in inflammatory dermatoses
Report from Dr Vassili Soumelis – Paris, France

In 1991, researchers focused on the specific characteristics of lymphocytic infiltrates of atopic dermatitis, accompanied by the secretion of cytokines such as IL-4, IFN-gamma, TNF-α, IL-6 and GM-CSF.

25 years later, published phase 3 trials on dupilumab in atopic dermatitis show the most therapeutic promise. Cytokine plasticity and functional pleiotropy are important elements: one cytokine can have several functions and play a role in several diseases.

TSLP

Vassili Soumelis has done a great deal of work on thymic stromal lymphopoietin (TSLP): several important functions have been identified recently for this cytokine, both in humans and in mice. It is produced by the epithelial and stromal cells, and plays a key role in regulating physiological processes such as lymphocyte homoeostasis, or certain inflammatory allergic reactions. TSLP is expressed in skin with atopic dermatitis (Soumelis, 2002). It is a cytokine derived from epithelial cells, triggering a proallergic immune cascade (Soumelis, 2002): activation of dendritic cells, Th2 profile for T-cells, production of IgE from B lymphocytes, degranulation of mast cells and the final immunological response. TSLP targets dendritic cells and innate lymphoid cells in atopic dermatitis. TSLP is a new, non-histamine mediator of pruritus.

It causes the activation of dendritic cells, ILC2 and pruritus. It plays a role in atopic dermatitis and other diseases such as HPV-induced tumours and psoriasis. The TSLP protein is overexpressed in psoriasis skin lesions. It is expressed at similar levels in psoriasis and atopic dermatitis. Researchers recently studied the effects of an anti-TSLP antibody on allergen-induced asthmatic responses.

Psoriasis

The pathogenesis of psoriasis plaques involves TNF-α, IL-23, IL-17A/F and IL-22. An anti-IL-23A monoclonal antibody was also studied for the treatment of moderate-to-severe psoriasis.

What are the inflammatory pathways for psoriasis?

- TNF/IL-17 for chronic plaque psoriasis. A therapeutic solution can use a TNF, IL-23 and IL17/17R inhibitor.
- IL-36/IL-1 for pustular psoriasis (generalised or palmoplantar). In generalised pustular psoriasis, possible therapies are cyclosporine, infliximab, retinoids, methotrexate; IL-1, IL-36 inhibitors?
- IFN-α for acute psoriasis (unstable, erythrodermic or inverse). Possible therapies using cyclosporine, UV, topical corticosteroids, vitamin D, IFN/pDC inhibitors.

Inflammasomopathies

These include familial Mediterranean fever, CAPS, TRAPS, hyper IgD syndrome, PAPA and Blau syndrome.

Inhibition of the IL-1 pathway is very promising, with molecules including:

- Anakinra: recombinant IL-1 receptor antagonist, administered once a day.
- Rilonacept: fusion protein: IL-1 receptor + IL-1 accessory protein, administered once a week.
- Canakinumab: monoclonal antibody targeted at IL-1 beta. Administered every month or every other month.