Increased serum levels of IL-22 in patients with nickel contact dermatitis

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Nickel can elicit both Th1-type and Th2-type responses *in vitro* (1) in patients with nickel allergic contact dermatitis, but this complex cytokine cascade has still to be clarified. The recently discovered Th17 subset, which has crucial functions in host defence against infections and has been implicated in the development of autoimmune diseases (2), has been supposed to play an important role in some inflammatory and autoimmune skin disorders, such as contact hypersensitivity (3) and psoriasis (4), respectively. Th17 cells are characterized by expression of interleukin (IL)-6, tumour necrosis factor-α, granulocyte–macrophage colony-stimulating factor, IL-17A, IL-17F, IL-21, IL-22, and IL-26 (5).

Among these cytokines, IL-22, a member of the IL-10 cytokine family, described as having proinflammatory activities on liver, pancreas, intestine, and skin (reviewed in 6), has been demonstrated to have a crucial function in the development of dermal inflammation and epidermal acanthosis induced by IL-23 in mice (4). Moreover, IL-22 seems to be involved in the pathogenesis of psoriasis in humans, as demonstrated by the high serum levels showed by psoriatic patients and the high levels produced by T cells isolated by psoriatic skin (6), where the IL-22 receptor is expressed on a variety of epithelial tissues (4). However, no data are available on the possible role played by IL-22 in nickel contact hypersensitivity in humans, thus we measured the circulating levels of this cytokine in patients with allergic nickel contact dermatitis.

We enrolled 31 female patients affected by allergic contact dermatitis to nickel (mean age 31.9 years; range 17–64 years) diagnosed following patch testing in accordance with the International Contact Dermatitis Research Group guidelines. Blood samples were collected after patch testing during a period of clinical remission 1 month after nickel contact avoidance.

15 sex- and age-matched blood donors, with no contact dermatitis and negative patch tests, were recruited as controls. Each subject gave previously used written, informed consent to the study.

Serum IL-22 was measured using an enzyme-linked immunosorbent assay kit (R&D System Europe, Abingdon, UK). All samples were analysed in duplicate.

Differences in IL-22 blood levels were assessed by the Student's *t*-test for unpaired comparison, assuming unequal variances. Data were expressed as mean ± standard deviation. A P value <0.05 was considered to be significant.

IL-22 serum levels were significantly higher in patients affected by contact dermatitis compared with controls (17.10 ± 9.50 pg/ml versus 8.61 ± 7.25 pg/ml, $P = 0.002$) (Fig. 1). No correlation between IL-22 levels and age was found.

About 10 years ago, it was demonstrated that nickel-specific CD4 T cells expressing the cutaneous lymphocyte-associated antigen skin-homing receptor can synthesize and release IL-17 and that IL-17 modulates various proinflammatory functions of keratinocytes, especially when acting together with interferon-γ and IL-4 (7). Zheng et al. have recently demonstrated that the injection of IL-23 (a Th17-inducing cytokine) into mice ears induces a model of psoriasis-like lesions characterized by epidermal acanthosis with inflammatory cellular infiltration mediated by IL-17 and IL-22. These features decrease in IL-22-deficient mice (4), and the administration of IL-22 neutralizing autoantibodies reduces acanthosis, inflammatory infiltrates, and expression of Th17 cytokines (8). However, the histological features found in these murine models are not exclusively characteristic of psoriasis but of allergic contact dermatitis as well.

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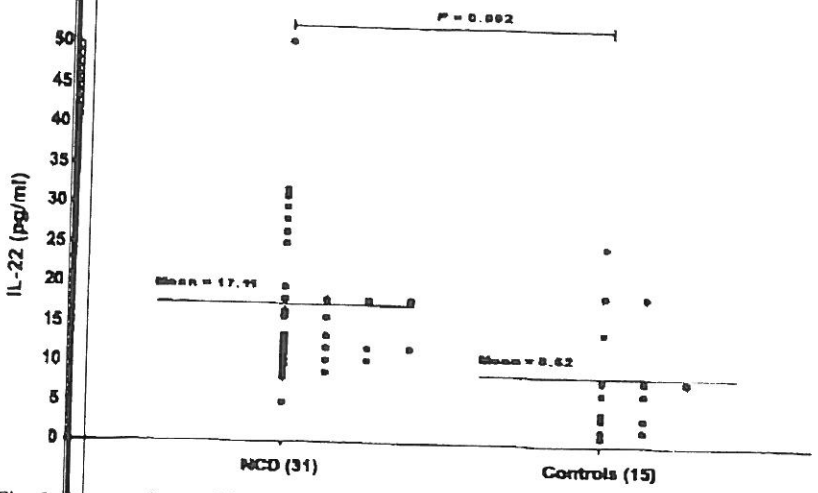

Fig. 1. Comparison of interleukin-22 serum concentration in patients affected by nickel allergic contact dermatitis and in controls. NCD, nickel contact dermatitis.

Our data suggest a possible involvement of IL-22 in the pathogenesis of human allergic contact dermatitis. Therefore, as hypothesized for psoriasis, IL-22 could be of potential interest as a therapeutic target for the treatment of the disease, but further studies are needed to clarify the cross-talk between the immune system and epithelial cells.

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