Acta Derm Venereol (Stockh) 1994; Suppl. 186: 43

## ABSTRACT

# Potential Mechanisms of Action of Vitamin D and Analogues in Psoriasis

OLE BAADSGAARD

*Department of Dermatology, University of Copenhagen, Gentofte Hospital, Denmark*

Psoriasis is an inflammatory skin disease characterized by increased numbers of proliferating keratinocytes, vascular expansion and leukocytic infiltration. These changes may be caused by a primary defect in keratinocyte growth and/or cytokine release, or as a phenomenon secondary to the release of cytokines from activated leukocytes.

The immune hypothesis, which has received increasing attention, is supported by associations with certain HLA types, the clinical efficacy of the immunosuppressant cyclosporin, and the ability of growth factors released from T cells from psoriatic lesions to directly stimulate keratinocyte growth.

Calcipotriol (Daivonex®) is a vitamin D analogue having demonstrated efficacy in psoriasis. In the circulation, vitamin D is bound with highest affinity by an alpha-2 globulin called the GC-globulin. It binds to the vitamin D receptor, a 50–60 kD intercellular protein related to the steroid, thyroid and retinoic acid receptor superfamily. The receptor complex is thought to interact with DNA sequences regulating synthesis of mRNA involved in cell growth and differentiation. The receptor is expressed by many cells involved in the pathogenesis of psoriasis, including keratinocytes, monocytes, macrophages and activated T cells.

*In vitro*, vitamin D and its analogues induce differentiation of resting monocytes, and demonstrate inhibitory effects on activated monocytes, causing impaired accessory cell function and decreased release of IL-1α, TNF α and IL-6. They also have a direct effect on T cell activation, resulting in decreased proliferation and release of cytokines including IL-2, interferon gamma, GM-CSF, TNF β and IL-6. Furthermore, in cultural human keratinocytes, vitamin D enhances transglutaminase activity and the formation of cornified envelopes. Simultaneously there was an inhibition of keratinocyte proliferation. *In vivo*, vitamin D and its analogues inhibit T cell mediated responses in animals, including allograft rejection and the development of autoimmune diseases. The effects of vitamin D in psoriasis may be twofold, since it demonstrates direct effects on both the immune system and on keratinocytes.