Potential new protective mechanisms for vitamin D in psoriasis

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INTRODUCTION

The skin is not only a protective layer, but also plays an important role in the transmission of stimuli, thermoregulation, synthesis and secretion of biologically active molecules. In order to fulfill such as diverse tasks the activity of skin cells is regulated in exo- and endocrine mode by a number of hormones (such as corticotropin releasing hormon - CRH) and other active molecules (e.g. vitamin D - calcitriol). As a part of the protective layer skin cells produce a fully functional analogue of HPA axis as well as other neuropeptides. Impairment of HPA axis expression has been observed in a number of skin disorders, associated with overproliferation of keratinocytes (eg. psoriasis) or immune background (eg. atopic dermatitis). The mechanism and impact of the of the HPA axis dysfunction on skin physiology and pathologies is still not fully understood. Our preliminary study showed that vitamin D may module the expression and activity of skin neuroendocrine system in human keratinocytes *in vitro*. The aim of this study is to identify potential targets for vitamin D in expression modulation of the skin analog HPA axis elements in psoriasis.

METHODS

For this study 12 unrelated patients with chronic plaque-type psoriasis and 7 adult, healthy, unrelated volunteers (mainly blood donors) without psoriasis admitted to the Dermatology Department Medical University of Gdańsk were enrolled. Briefly, the relative mRNA levels for *CRH, CRHR1* and *NR3C1* genes were investigated by quantitative polymerase chain reaction (qPCR) in matching samples (psoriatic lesion and marginal skin) and compered top control skin biopsies. Further study was conducted on *ex vivo* cultured skin biopsies obtained from patients undergoing standard surgery in Department of Surgical Oncology (Medical University of Gdańsk). For experimental investigation 6 nm skin biopsies were placed in 24-well plates (one per well) and cultured at 37°C in a minimal media of William's E media. Skin biopsies were treated with 0.1 μM $1,25(OH)_2D_3$ for 24 h. After indicated time mRNA level of selected genes (CRFR1, NR3C1) was analyzed by qPCR. The data obtained was submitted to ΔΔCt statistical analysis. Additionally, Wester Blot analysis was conducted for selected neuropeptides and their receptors. Written informed consent was obtained from all individual participants included in the study.

CONCLUSIONS

It seems that observed altered expression of CRF, CRFR1 and NR3C1 in psoriatic skin biopsies may underline the importance of the function of cutaneous HPA axis in the course of the disease. In addition, vitamin D_3 due to a number of similar properties to CRF, and well-known therapeutic effects in psoriasis, may be an important modulator of the expression of sHPA axis elements, restoring general skin homeostasis. It is worth emphasizing that the interaction between the elements of HPA axis and vitamin D has not been thoroughly investigated so far.

RESULTS

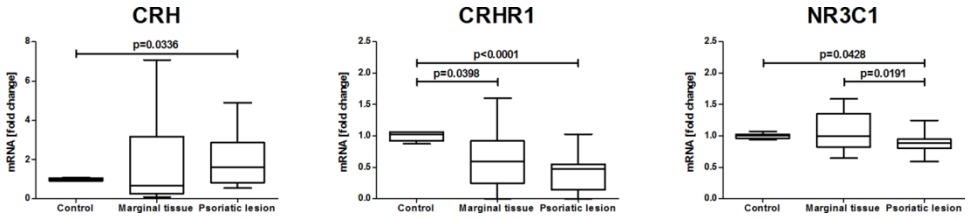

Figure 1. Changes in the expression of selected elements of the cutaneous HPA axis on mRNA levels in perilesional (n=12) and lesional psoriatic skin (n=12) compared with healthy control subjects (n=7).

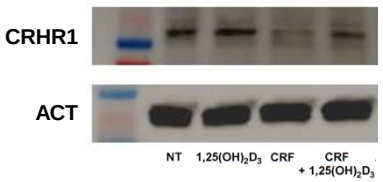

Figure 2. Western Blot analyses of CRFR1 protein level was measured in primary human epidermal keratinocytes stimulated with $1,25(OH)_2D_3$ (0.1 μM), CRF (0.1 μM), or both, for 24 h. β-Actin levels were measured as a control.

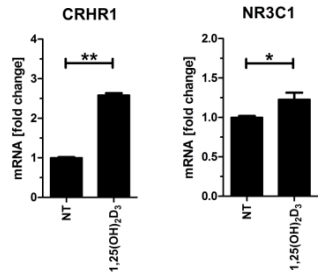

Figure 3. Skin biopsies were treated with 0.1 μM $1,25(OH)_2D_3$ for 24 h. After indicated time mRNA levels of CRFR1 and NR3C1 were analyzed by quantitative RT-PCR.

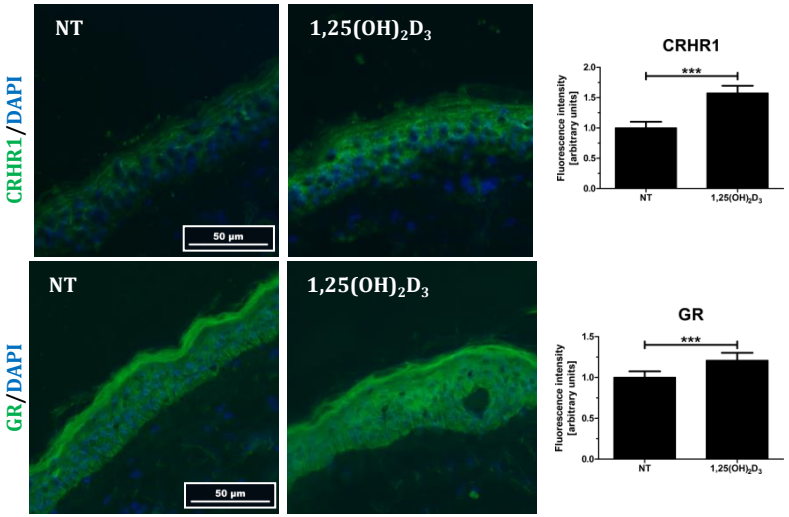

Figure 4. Skin biopsies were treated with 0.1 μM $1,25(OH)_2D_3$ for 24 h. After indicated time protein levels of CRFR1 and GR were analyzed by immunofluorescence. Graph shows fluorescence intensity of CRHR1 in skin slides.