INFLAMMATORY SKIN DISEASES (OTHER THAN ATOPIC DERMATITIS & PSORIASIS)

PROLYLCARBOXYPEPTIDASE – AN EMERGING PLAYER IN IMMUNE-MEDIATED INFLAMMATORY SKIN DISEASES?

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Background: Prolylcarboxypeptidase (PRCP) is s serine protease that regulates a number of hormonal pathways including the proopiomelanocortin system. Accordingly, PRCP metabolizes α-MSH (1-13) into biologically inactive α-MSH (1-12). α-MSH (1-13) has a variety of biological functions in the skin, such as regulation of pigment formation, exocrine activity, inflammatory reactions and immunomodulation.

Objective: As α-MSH has strong anti-inflammatory and immunomodulatory actions we hypothesized that PRCP due to deactivation of the biological activity of α-MSH could play role in the pathogenesis of the immune-mediated skin diseases.

Materials and Methods: We examined the expression of PRCP in various cutaneous cell types at RNA and protein level in vitro.

Results: PRCP transcripts were detected in normal human melanocytes, normal human keratinocytes and human dermal fibroblasts (HDFs) from different donors as shown by endpoint reverse transcriptase- polymerase chain reaction (RT-PCR). However, Western immunoblotting revealed expression of PRCP protein only in HDFs but not in the other cell types. Here, PRCP could be visualized as a granular cytoplasmic staining as shown by immunofluorescence analysis. As detected by liquid chromatography coupled with mass spectrometry, HDFs treated with alpha-MSH formed alpha-MSH (1-12) in conditioned media suggesting expression and secretion of functionally active PRCP. Interestingly, quantitative real-time RT-PCR analysis further revealed a time-dependent upregulatory effect of both tumor necrosis factor and ultraviolet A irradiation but not interleukin-1beta on PRCP mRNA in HDFs. However, Western immunoblotting of total cell lysates and detection of PRCP in cell culture supernatants employing ELISA did not reveal upregulation of this enzyme in HDFs exposed to these stressors. Immunohistochemical studies are currently underway to determine the expression pattern of PRCP in normal and diseased human skin in situ.

Conclusions: Our data provide first evidence of cell type-specific expression of PRCP in

human skin types. Further studies have to assess the relevance of these findings for cutaneous biology.