

Activation of adenosine receptor by PDRN improves skin remodelling in an experimental model of psoriasis-like dermatitis.

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Psoriasis is an immune-mediated skin disease characterized by increased keratinocyte proliferation, epidermal hyperplasia, acanthosis, and alterations in fibroblast organization. The nucleoside adenosine is a small molecule that, stimulating A₂A receptor, promotes activation of downstream targets such as PKA and Epac, involved in skin remodelling. Several studies have already demonstrated the role of A₂A receptor in fibroblast activation and collagen synthesis in skin disorders.

Therefore, we investigated the effects of polydeoxyribonucleotide (PDRN), an adenosine receptor agonist, in an experimental model of psoriasis-like dermatitis.

Psoriasis-like lesions were induced by a topical application of imiquimod cream (IMQ; 62.5 mg/day) on the shaved back skin of C57BL/6 mice for 7 consecutive days. Sham psoriasis animals were challenged with vaseline cream. Sham and IMQ animals were randomized to receive PDRN (8 mg/kg/i.p.) or its vehicle (100 µl/i.p. of 0.9% NaCl). Skin of IMQ animals developed erythema, scales, thickening and epidermal acanthosis starting from day 3 following IMQ application. Treatment with PDRN produced a marked reduction of inflammatory panel and blunted epidermal thickness and acanthosis. The immunohistochemical analysis of the hyperproliferative markers cytocheratin 6 and Ki67 showed that PDRN reduced cell hyperproliferation, but promoted fibroblast proliferation and skin remodelling in dermis. In fact, animals treated with PDRN showed upregulation and downregulation respectively of cyclin D1/CDK6 and its inhibitor p15, thus demonstrating an improvement of cell cycle machinery. In addition, the activation of adenosine receptor by PDRN administration determined an increase of dermal collagen deposition.

Our data suggest that PDRN reduced epidermal hyperproliferation, restoring epidermal structure and might act as a remodelling promoter in psoriasis-like dermatitis.