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PKC epsilon involvement in Th17 in vitro differentiation: implications in psoriasis pathogenesis

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Psoriasis is a noncontagious, arytematous-squamose dermatitits affecting both sexes and all races. Although its exact etiology is largely unknown, it is now recognized as one of the most common immune-mediated disorders and several studies demonstrate an impairment of regulatory T-cells (Tregs) function and an up-regulation of IL-17 levels produced by T-helper 17 lymphocytes (Th17)(1,2). Protein kinase C epsilon (PKCε) is a serine/threonine kinase which plays a key role in the proliferation and differentiation of epidermal cells. We have previously demonstrated a role for PKCε in the pathogenesis of the autoimmune disease Hashimoto's thyroiditis (3). PKCε is over-expressed in CD4+ T lymphocytes isolated from PBMC fraction in patients affected by this pathology and its forced down-modulation primed the TGF-mediated in vitro Treg polarization of human T CD4+ cells. Since it has been demonstrated that PKC-signalling is altered in psoriatic keratinocytes (4), we investigated the involvement of PKCε in Th17 in vitro differentiation and its potentially implication in immune response correlated to psoriasis. Using western blot and real time PCR, we have observed that PKCε protein levels and mRNA increase during Th17-lineage in vitro differentiation from naïve CD4+ T cells with a similar trend of Th17 markers of differentiation STAT3 and RoRγT. Moreover, PKCε overexpression significantly increases STAT3 and phosphorylated STAT3 levels, suggesting that PKCε boosts Th17 polarization. Thereafter, we sought to investigate PKCε expression in CD4+ lymphocytes obtained from peripheral blood of psoriatic patients and we observed that PKCε expression levels are significantly higher compared with healthy donors. Intriguingly, we observed a closely correlation of PKCε expression with PASI index, suggesting an involvement of the kinase with the severity of the disease. Collectively these data suggest that PKCε might be involved in Th17 differentiation, that it could be a key factor to regulate Th17 pathological expansion and therefore a potential psoriatic pharmacological target.

References

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