

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

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Psoriasis is a noncontagious, arytomatous-squamose dermatitis 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 (PKC ϵ) 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 PKC ϵ in the pathogenesis of the autoimmune disease Hashimoto's thyroiditis (3). PKC ϵ 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 PKC ϵ 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 PKC ϵ 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 RoRyT. Moreover, PKC ϵ overexpression significantly increases STAT3 and phosphorylated STAT3 levels, suggesting that PKC ϵ boosts Th17 polarization. Thereafter, we sought to investigate PKC ϵ expression in CD4 $^{+}$ lymphocytes obtained from peripheral blood of psoriatic patients and we observed that PKC ϵ expression levels are significantly higher compared with healthy donors. Intriguingly, we observed a closely correlation of PKC ϵ expression with PASI index, suggesting an involvement of the kinase with the severity of the disease. Collectively these data suggest that PKC ϵ 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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