

## **Editorial:**

### **Topical Macrolide Immunomodulators for Therapy of Atopic Dermatitis**

**Nidhal Abdul-Muhaimen PhD, Ahmad Hachem muhana MSc**

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#### **Introduction**

To date, tacrolimus (FK 506) and the ascomycin derivative pimecrolimus (SDZ ASM 981) are the most studied topical macrolide immunomodulators. Both of these drugs have a high specificity for inhibiting the expression of inflammatory T-cell cytokines and have shown promising results in the treatment of atopic dermatitis (AD) when applied topically <sup>(1)</sup>.

#### **Topical calcineurin inhibitors**

Tacrolimus is a topical formulation of the immunomodulatory agent FK 506 and is available as a 0.03% and 0.1% ointment. Originally used for atopic dermatitis, tacrolimus modulates immune-cell function by inhibiting calcineurin-dependent dephosphorylation- activation of specific nuclear factors and therefore preventing transcription of proinflammatory cytokines <sup>(2)</sup>.

#### **Improved therapy for atopic dermatitis**

Once AD has been diagnosed, two therapeutic strategies can be used to address the pathophysiologic abnormalities found in these patients: the first strategy is the traditional mainstay of topical treatment of atopic dermatitis is steroid ointments <sup>(3)</sup>.

Potent topical steroids have a high initial success rate in clearing an eczematous rash, but the effects tend to diminish later on, a phenomenon known as tachyphylaxis.

Long term use of these medications is associated with many potential risks, especially in infants and children, and stronger steroids are more likely to produce adverse local and systemic effects. Skin atrophy, telangiectasia, stria, secondary infection, acneiform eruption, hypopigmentation, purpura, poor wound healing can result from long-term application of topical steroids, particularly when used on face, groin, and intertriginous areas of the body <sup>(4)</sup>.

Clinically significant suppression of the hypothalamic-pituitary-adrenal axis also can result from the long term treatment of topical steroids, especially in an infant, whose body surface is large compared with his or her weight. When long-term treatment of AD is required, the adverse effects of steroids make them an unsatisfactory treatment. In addition, Colonization and infection with *Staphylococcus aureus* contributes to the severity of AD and reduce corticosteroids sensitivity. These observations suggest a role for antibiotic/corticosteroid combination or topical macrolide immunosuppressive ointment such as tacrolimus ointment in the treatment of AD. Finally, a number of patients with AD may not respond appropriately to their topical steroid due to complication by superinfection with *S. aureus* <sup>(5)</sup>.

The new immunomodulators tacrolimus and pimecrolimus represent a safer class of drugs that alter the local immune response in a more targeted fashion than do older steroids

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Dept. Medical Microbiology, College of Medicine, Al-Nahrain University.  
Address Correspondence to: Dr Nidhal Abdul-Muhaimen