Psoriasis is an autoimmune inflammatory skin disease associated with aberrant activation of T and B lymphocytes. Recently, there has been increasing evidence to indicate that T helper 1 (Th1) and Th17 lymphocyte subsets play key roles in the immunopathogenesis of the disease. Thus, Th1/Th17 cell subsets produce pro-inflammatory cytokines and chemokines and promote the production of prostaglandin E2 (PGE2) and nitric oxide (NO). Further, activated Th1/Th17 cells interact with keratinocytes leading to their proliferation and hyperplasia. In addition, Th1/Th17 cells promote angiogenesis; another characteristic feature of psoriasis immunopathology.

Our studies are focused on developing new approaches for targeted therapy for psoriasis. In this respect, our recent studies have examined the potential therapeutic effects of compounds extracted from the ginger species *Zingiber officinale* Roscoe (var. *rubrum* Theilade), which has known anti-inflammatory effects, on the pathogenic mechanisms involved in psoriasis. The therapeutic effects of selected fractions and compounds were assessed for their ability to suppress the production of pro-inflammatory mediators and the interaction between immune cells and keratinocytes. Initial experiments identified four fractions, F5, F6, F7 and F10 that had potent suppressive effects on NO and PGE2 production. The fractions had higher potency than L-NAME, a specific inhibitor of iNOS, suppressing NO production. Furthermore, the fractions/compounds had comparable effects to inhibition of PGE2 production by indomethacin. F6 had particularly potent inhibitory effects on inhibiting NO and PGE2 production and suppressed iNOS gene transcription by 82.3±3.73% at 20 μg/ml. Three major compounds were isolated from F6 and shown to have potent inhibitory effects on NO production and iNOS gene transcription. Paradoxically, however, quantitative PCR analyses revealed that the fractions and compounds upregulated *tnfa* gene transcription. In view of the potentially-beneficial effects of the fractions in suppressing mediators of inflammation, this data suggests that TNFα could be involved in negative regulatory circuits involved in terminating inflammation once the initial need for an inflammatory response is achieved (1). Current experiments are focussed on identifying the active therapeutic compounds and mechanisms of their therapeutic effects in psoriasis.

References