Summary

The Toll like family of receptors, among other pattern recognition receptors (PRR), are expressed by various cells of the innate immune system, such as monocytes, macrophages, neutrophils, and dendritic cells. Because TLRs are key players in the innate response to pathogens, the expression of TLRs at sites of host-pathogen interaction is critical for host defense. Given that the skin is a crucial interface for host encounters with microbial invaders, it seems appropriate that the skin expresses TLRs to allow for recognition of pathogens before they invade the bloodstream or the tissues of internal organs. Recognition of microbial components by TLRs initiates signaling transduction pathways that induce gene expression. These gene products regulate innate immune responses and further develop an antigen-specific acquired immunity.

As TLR are instrumental in both launching innate immune responses and influencing adaptive immunity, regulation of TLR expression at sites of disease such as in leprosy, acne, and psoriasis may be important in the pathophysiology of these diseases. In some cases, as in leprosy, modulation of TLR expression and activation may be protective and lessen the severity of disease. TLR activation, however, may also promote excessive inflammation and apoptosis contributing to the pathology such as the nerve damage seen in leprosy patients. Additionally, the recognition of P. acnes, a commensal bacterium, through TLR2 induces inflammatory cytokine production that may play a role in the pathogenesis of the disease. Thus, TLR are vital players in infectious and inflammatory diseases, making them potential therapeutic targets.

Indeed, the ability of TLR to combat disease has already been harnessed through the development of drugs that act as TLR agonists.To date, synthetic TLR agonists such as imiquimod have found utility in treating viral pathogens and skin cancers. Therefore, it seems possible that in the future there may be drugs capable of blocking TLR-dependent inflammatory responses, and thus new treatment options for inflammatory diseases such as acne and psoriasis.

The discovery of TLR and the development of drugs that act through them are beginning to have an impact upon our understanding and treatment of several cutaneous diseases. In spite of their importance, however, relatively few studies have addressed the role of TLR in skin. The expression of TLR on keratinocytes and their potential differential expression across the layers of the epidermis is still unclear. Also, in addition to their role in infectious skin diseases, TLR may play important roles in inflammatory skin diseases such as acne, psoriasis, atopic dermatitis, lichen planus, and lupus erythematosis, leaving this promising area of study open for future investigations.