Atopic dermatitis (AD) is a chronic inflammatory skin disease predominantly mediated by T helper cells. While numerous adaptive immune mechanisms in AD pathophysiology have been elucidated in detail, deciphering the impact of innate immunity in AD pathogenesis has made substantial progress in recent years and is currently a fast evolving field. As innate and adaptive immunity are intimately linked, cross-talks between these two branches of the immune system are critically influencing the resulting immune response and disease. Innate immune recognition of the cutaneous microbiota was identified to substantially contribute to immune homeostasis and shaping of protective adaptive immunity in the absence of inflammation. Disturbances in the composition of the skin microbiome with reduced microbial diversity and overabundance of Staphylococcus spp. have been shown to be associated with AD inflammation. Distinct Staphylococcus aureus associated microbial associated molecular patterns (MAMPs) binding to TLR2 heterodimers could be identified to initiate long-lasting cutaneous inflammation driven by T helper cells and consecutively local immune suppression by induction of myeloid-derived suppressor cells further favoring secondary skin infections as often seen in AD patients. Moreover dissecting cellular and molecular mechanisms in
cutaneous innate immune sensing in AD pathogenesis paved the way for exploiting regulatory and anti-inflammatory pathways to attenuate skin inflammation. Activation of the innate immune system by MAMPs of non-pathogenic bacteria on AD skin alleviated cutaneous inflammation. The induction of tolerogenic dendritic cells, interleukin-10 expression and regulatory Tr1 cells were shown to mediate this beneficial effect. Thus, activation of innate immunity by MAMPs of non-pathogenic bacteria for induction of regulatory T cell phenotypes seems to be a promising strategy for treatment of inflammatory skin disorders such as AD. These new findings demonstrate how detailed analyses identify partly opposing consequences of microbe sensing by the innate immune system and how these mechanisms translate into AD pathogenesis as well as new therapeutic strategies.