House dust mite-induced atopic dermatitis: pharmacological and immunological approach

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House dust mite (HDM) has been implicated in the etiology and exacerbation of atopic dermatitis (AD). Diverse factors contribute to HDM allergenicity through the activation of innate immunity. We investigated whether *Dermatophagoides farinae* extract (DFE) allergens mediate innate immune activation through specific Toll-like receptors (TLRs) in epidermal keratinocytes, DFE-induced murine AD model and human AD lesions. DFE activated the expression of TLR1, TLR6, interleukin (IL)-25, and IL-33 in *HaCaT* cells. Knockdown of TLR6 inhibited DFE-induced upregulation of IL-25 or IL-33 in *HaCaT* cells. In addition, the suppression of TLR1 inhibited the release of IL-33. DFE induced the expression of IL-25 and IL-33 by upregulation of IRAK1, TAK1, IKK, and NF-κB pathways in *HaCaT* cells. $TLR6^{-/-}$ mice did not show DFE-induced upregulation of IL-25 and IL-33. Furthermore, DFE-induced upregulation of IL-25 was not induced in $Tlr1^{-/-}$ mice. We also identified increased expression of TLR1, TLR6, IL-25 and IL-33 in human AD skin lesions with high HDM sensitization. We found that DFE-induced activation of TLR1 and TLR6 may cause polarization towards a Th2 immune response via the release of IL-25 and IL-33. Thus, therapeutics targeting TLR1 and TLR6 may be efficacious in the treatment of severe or recalcitrant AD showing high HDM sensitization.