The Roles Of CARD14 In Inflammation And Psoriasis

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Abstract
Psoriasis is a common chronic inflammatory skin disease mediated by both the innate and adaptive immune systems and affects approximately 2% of the worldwide population. The histological features of psoriasis are mainly characterized by exaggerated angiogenesis, excessive growth, aberrant differentiation of keratinocytes and brisk immune cell infiltration. However, the exact mechanisms for the initiation of psoriasis remain elusive. Genetic mutations of CARD14 (encoding CARMA2) are observed in psoriasis patients.

In our study, we showed that Card14E138A/+ and Card14ΔQ136/+ mice developed spontaneous psoriasis-like skin inflammation, which resulted from constitutively activated CARMA2 via self-aggregation leading to the enhanced activation of the IL-23-IL-17A cytokine axis. Card14/-mice displayed attenuated skin inflammation in the imiquimod-induced psoriasis model due to impaired IL-17A signaling in keratinocytes. CARMA2, mainly expressed in keratinocytes, associates with the ACT1-TRAF6 signaling complex and mediates IL-17A-induced NF-κB and MAPK signaling pathway activation, which leads to expression of pro-inflammatory factors. Together, our studies show that CARMA2 serves as a key mediator of IL-17A signaling and its constitutive activation in keratinocytes leads to the onset of psoriasis, and reveal the molecular mechanism by which psoriasis is initiated in keratinocytes and the mechanism of psoriasis development.

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