

PIGMENTATION

THE FUNCTION AND MECHANISM OF MDA5 IN THE ONSET AND PROGRESS OF VIRUS-INDUCED VITILIGO

T Zhuang⁽¹⁾ - *S Li*⁽¹⁾ - *X Yi*⁽¹⁾ - *C Li*⁽¹⁾ - *T Gao*⁽¹⁾ - *G Wang*⁽¹⁾

Xijing Hospital, Department Of Dermatology, Xi'an, China⁽¹⁾

Introduction: Virus can induce vitiligo but the mechanism is elusive. Melanoma differentiation-associated gene 5 (MDA5) functions as one of the major sensors of RNA viruses. IFIH1, which encodes the MDA5 protein, has been newly identified as a susceptibility gene in vitiligo. Nevertheless, little is known about function and mechanism of MDA5 in the onset and progress of vitiligo.

Objective: we aim to explicit how virus induce the onset and progress of vitiligo in a MDA5-dependant way.

Methods and materials: we first detected the expression of MDA5 using immunofluorescence in lesions of patients with vitiligo. The production of candidate chemokines and MDA5 was detected by performing real-time PCR, ELISA and westernblotting respectively in keratinocytes exposed to poly(I:C) which is a kind of virus nucleic acid analogue. Furthermore, the involved mediators were analyzed by using quantitative real-time PCR, western blotting, ELISA and immunofluorescence. Finally, we tested the chemotactic migration of CD8+ T cells from patients with vitiligo by transwell assay using supernatants collected from cell culture medium stimulated by poly(I:C).

Results: First of all, MDA5 expression increased and showed a positive correlation with severity of patients with vitiligo. In addition, Poly (I:C) can increase the expression of CXCL9, CXCL10, CXCL16 in a MDA5-dependant way. Further more, The poly (I:C) - induced chemokines secretion was due to the activation of MDA5-MAVS-NF-kB pathway. Finally, These chemokines produced by keratinocytes induced migration of autoreactive CD8+ T cells derived from patients with vitiligo.

Conclusion: MDA5 mediates CD8+ T-cell skin trafficking under virus infection through the section of chemokines in patients with vitiligo. This effect is caused by MDA5-MAVS-NF-kB pathway.





International League of Dermatological Societies Skin Health for the World

