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IL-34 suppresses *Candida albicans* induced TNF- α production by M1 macrophages through down-regulation of dectin-1 and TLR2 expression

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Introduction: *Candida albicans* is a commensal fungal microorganism, which does not normally trigger inflammatory responses by resident macrophages such as Langerhans cells in skin. An immune tolerance of skin Langerhans cells to *C. albicans* challenges has been suggested, however, the mechanism(s) of such tolerance has not been elucidated. IL-34 is a recently discovered cytokine, which is constitutively expressed by keratinocytes in epidermal skin. In skin, the key function of IL-34 is to maintain Langerhans cell expansion. Resident macrophages exhibit plasticity and can be transformed into inflammatory M1 macrophages for immunity and anti-inflammatory M2 macrophages for tissue repair.

Aim: To investigate the role of IL-34 in regulating macrophage response following *C. albicans* challenge. We have previously demonstrated that inflammatory M1 macrophages produce higher levels of the inflammatory cytokine, TNF α , in response to *C. albicans* stimulation; this is not evident with anti-inflammatory M2 macrophages.

Method: Mouse bone marrow macrophages were cultured with 10 ng/ml GM-CSF for 7 days to drive M1 macrophage maturation. Increasing concentrations of recombinant mouse IL-34 (R&D Systems) were added in the presence of GM-CSF for different periods of culture. The production of TNF α was then determined for M1 macrophages stimulated with heat killed *Candida* (HKC). Expression of Toll-like receptor 2 (TLR2) and C-type lectin receptor (Dectin-1), which are key pattern recognition receptors (PPRs) for β -glucan in the yeast wall, was also determined.

Results: 1. IL-34 was found to inhibit HKC induced TNF α production in M1 macrophage in a dose dependent manner. 2. Both expression of Dectin-1 and TLR2 was significant reduced in M1 macrophage following treatment with IL-34.

Conclusion: IL-34 suppressed HKC induced TNF α production in inflammatory M1 macrophage by down regulation of dectin-1 and TLR2 expression. This could indicate that immune tolerance of Langerhans in skin might be maintained by constitutive expression of IL-34 by keratinocytes. From a clinical perspective, neutralisation of IL-34 function in skin may have therapeutic benefit in the treatment of *Candida* mucosal infection; it may also have value for promoting immune responses following vaccination.

Biography

Rong Xu has completed her Master degree of Sciences in China at the age of 27 years from Peking Union Medical College and currently is carrying on her research fellowship study in Dental School of Cardiff University. Her research project is under Dr. Xiao-Qing Wei's supervising on a project of study cytokine biology in human health and diseases.

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