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LPS-induced M2 to M1 macrophage transformation for IL-12p70 production is blocked by Candida albicans mediated up-regulation of EBI3 expression

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Objective: The response of M1 and M2 macrophages to Candida albicans in the presence of LPS stimulation has not previously been reported. In this study, we examined plasticity of macrophages transforming from M2 to M1 in the presence of LPS and C. albicans impact on this transformation.

Method: Bone marrow cells extracted from C57/black mice femur bones were cultured with either 10 ng/ml rmGM-CSF or 10 ng/ml each M-CSF/IL-4 for 7 days before LPS stimulation with or without Heat-Kill Candida (HKC). Released cytokines were subsequently measured by ELISA and gene expression determined by real-time RT-PCR. In some experiments, cytokines were examined by Western blot. To confirm intracellular EBi3/p40/35 protein interaction, IL-12p70 biscistronic expression vector and EBI3 expression vector were constructed in pcDNA3.1A. CHO cells were transfected with expression vectors before detection of the protein by ELISA, Western blot (WB) and/or Immuno-precipitation WB.

Result: Mouse bone marrow derived M1 and M2 macrophages produced distinctive cytokine patterns following C. albicans stimulation. LPS converted M2 macrophages to the M1 phenotype with higher IL-12p70 production. C. albicans suppressed LPS induced IL-12p70 production in a dose dependent manner in M2. This suppression was result of competing of EBI3 and IL-12p40 for IL-12p35 binding, which was confirmed by IL-12p40/p35 and EBi3 co-expression in CHO cells.

Conclusion: This result demonstrated that Candida 'de-sensitises' tissue M2 macrophages to transform to M1 phenotype in the presence of LPS, by suppressing IL-12p70 production. This may lead to the avoidance of an unnecessary Th1 response during the resolving phase of infection.

Biography

Xiao-Qing Wei has completed his Ph.D at the age of 35 years from University of Glasgow and postdoctoral studies from University of Glasgow in UK. He is a lecturer in Immunology in Dental school of Cardiff University currently. He has published more than 50 papers in reputed journals and serving as an editorial board member of Open J. Immunology.

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