

## IL-23 encapsulated PLGA micro-particles has a strong adjuvant effect in Pertussis vaccine

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**Objective:** Pertussis still remains endemic worldwide and is an important public health problem. There has been a resurgence of reported pertussis cases in many regions of the world where the acellular pertussis vaccine (ACV) vaccination coverage in young children is high. Ten infant deaths were reported in California in 2010. The epidemic was not confined to California, with similar reports from Michigan, Ohio and Oklahoma and in other countries, including Australia and Ireland. More recently, 5 neonate deaths in UK and 9 deaths in Washington in 2012 have been reported. This resurgence of pertussis may be, in part, associated with escape from immunity owing to antigen variation and/or poor or short-lived adaptive immunity induced by the ACV when compared with the whole cell pertussis vaccine (WCV) that they replaced. Currently, ACV are administered with alum as the adjuvant which favours the induction of Th2 cells and antibodies. Studies have shown that WCV or natural infection induce relatively high levels of protection and promote Th1 responses. Given the increasing incidence of pertussis in vaccinated populations, strategies to raise the efficacy and longevity of the protection induced by ACV to that of the original WCV should be investigated taking cognisance of recent discoveries on the mechanism of vaccine-induced immunity, especially the role of T-cell and CMI response.

New nanotechnology has merged in recent years in drug/vaccine delivery fields. Bio-degradable PLGA nanoparticles have been reported to easily penetrate through dermal skin into lymphoid tissue to initiate T and B cell responses. This method has been used to deliver antigen for vaccination successfully together with TLR agonist which effectively induced dendritic cell maturation and dramatically enhanced cellular immunity. IL-12 family cytokines e.g. IL-23 and IL-27 have been reported to play an important role in generation of high Th1 response and CD8+ cytotoxic T cells against virus infection and IL-23 and IL-27 have been shown synergistically with IL-12 inducing Th1 responses. IL-23 is also a critical cytokine to induce Th17 response which has been demonstrated to play a beneficial role in vaccination against *Staphylococcus aureus* infection. CpG alone, or in combination with alum has shown to promote both humoral and CMI responses in mice and thereby enhance protection against live bacterial challenge.

**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 EB13/p40/35 protein interaction, IL-12p70 bicistronic expression vector and EB13 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 EB13 and IL-12p40 for IL-12p35 binding, which was confirmed by IL-12p40/p35 and EB13 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 graduated in medicine in Medical School of Peking University in Beijing, China. He has also completed his Ph.D. in Immunology Department of University of Glasgow and studied the role of cytokine, IL-15, IL-18 and IL-35 in infection and immunity as a research fellow in University of Glasgow in UK. He is a lecturer in Immunology in Cardiff University currently. He has published 60 papers in reputed journals and serving as an editorial board member of some immunology journals. He has awarded honorary professorships in 4 medical universities in China and currently working closely with his collaborators in China and UK in cytokine and skin DC research.

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