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IL-23 encapsulated PLGA nano- and micro-particles have a strong adjuvant effect in a model vaccine with *B. Pertussis* antigen

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Abstract

Objective: *B. Pertussis* (whooping cough) remains a worldwide endemic infection and an important public health problem. Of concern is that there has been a resurgence of pertussis in many regions of the world where acellular pertussis vaccine (ACV) vaccination coverage in young children is high. To highlight this, in 2010, there were 10 infant deaths reported in California, with cases also seen in Michigan, Ohio and Oklahoma and also in Australia and Ireland. More recently, in 2012 there were 14 neonate deaths in UK, and 9 deaths in Washington, USA. This resurgence of pertussis may, in part be associated with loss of immunity through antigen variation and/or poor or short-lived adaptive immunity induced by the ACV compared with whole cell pertussis vaccine (WCV), which they replaced. Currently, ACV is administered with aluminium as the adjuvant and this favours induction of Th2 cells and antibodies. Studies have shown that WCV or natural infection induces relatively high levels of protection and promotes Th1 responses. Given the increasing incidence of pertussis in vaccinated populations, strategies that raise efficacy and longevity of protection induced by ACV compared to the original WCV should be investigated. Such strategies can exploit recent discoveries concerning the mechanisms of vaccine-induced immunity, especially the role of T-cell and cell mediated immune (CMI) responses.

New nanotechnology has emerged in recent years in drug/vaccine delivery fields. Biodegradable poly (lactic-co-glycolic acid) (PLGA) nanoparticles can readily penetrate dermal skin into lymphoid tissue to initiate T and B cell responses. This approach has been used to successfully deliver antigen for vaccination with TLR agonists that effectively induce dendritic cell maturation and dramatically enhances cellular immunity. The IL-12 family of cytokines (*e.g.* IL-23 and IL-27) play an important role in the generation of high Th1 responses and promotion of $CD8^+$ cytotoxic T cell activity against virus infection. IL-23 and IL-27 also exhibit synergistic effects with IL-12 in inducing Th1 responses. IL-23 is a key cytokine in inducing Th17 responses, which are beneficial in vaccination against *Staphylococcus aureus* infection. CpG nucleotides alone, or in combination with aluminium, can also promote humoral and CMI responses in mice and enhance protection against live bacterial challenge. The aim of this study was to evaluate the potential of recombinant IL-23 encapsulated PLGA particles as adjuvants for a Pertussis vaccine.

Method: Recombinant mouse IL-23 was encapsulated in PLGA nano and micro scale particles by a double emulsion method. The particles were visualized using scanning electron microscopy (SEM). The slow releasing of IL-23 was measured by ELISA and its biological activity examined by inducing IL-17 production in mouse spleen cell cultures. To study the adjuvant effect of IL-23, we used filamentous haemagglutinin (FHA), acellular pertussis antigen as model antigen, encapsulated together with IL-23 in PLGA particles. The soluble FHA and FHA PLGA particles with or without IL-23 were injected into mice in subcutaneously. Antibody production and protection from living bacterial challenge were evaluated.

Results: IL-23 encapsulated in PLGA showed a slow accumulated release of up to 35 days. The released IL-23 also demonstrated significant biological activity, which was shown by induction of IL-17 from mouse spleen cells. The IL-23 encapsulated PLGA FHA vaccine showed highest antibody production and demonstrated greatest protection against *B. Pertussis*. Importantly, IL-23 PLGA induced higher IgG2a production, implying that IL-23 might be used as a T cell adjuvant to induce elevated Th1/17 responses in mice. This response will help build a stronger and longer immune memory against *B. Pertussis* in life.

Conclusion: IL-23 encapsulated in PLGA nano and micro-particles maintained good levels of biology activity and promoted T cell responses against pertussis in mice.

Biography

Dr. Xiao-Qing Wei graduated in medicine in Medical School of Peking University in Beijing, China. He has also completed his PhD 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.