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Novel mechanisms of adjuvanticity implied from *in vitro* studies with bacterial toxins

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Enterotoxigenic *E. coli* secrete two heat-labile toxins of LT-I and LT-II. Each toxin is composed of a catalytic A-subunit and a binding B-subunit. The B-subunits of LT-I (LT-IB) and LT-IIa (LT-IIaB) are strong non-toxic adjuvants that bind to cell-surface receptors, including gangliosides GM1 and GD1b, respectively. LT-IIaB also binds toll-like receptor 2 (TLR-2) in a complex with GD1b. LT-IB and LT-IIaB have multiple stimulating effects on antigen presenting cells (APCs), T cells and their products. Thus, very small or minute amounts of the holotoxins or their B-subunits adjuvant immune responses to other antigens and induce long-term immunological memory. The stimulating effects on the APCs by very small doses of the B-subunits could not solely explain, however, their remarkable adjuvant properties. We demonstrate that the co-incubation with the B-subunits induces significant clustering of B cells after only 4 hrs, and B and T cells in 24 hrs. Clustering was dependent on intact B-subunits, but not on the TLR-2 binding activity of LT-IIaB, indicating it was ganglioside-mediated. Treatment of B cells with LT-IB, but not LT-IIaB, caused a delay in T cell division following ovalbumin endocytosis. B cell receptor-mediated uptake in presence of each treatment caused an arrest, but with increased production of IL-2. Further treatments differentially increased the proportion of macrophages expressing MHC class-II. These results suggest that cell clustering and the delay/arrest in T cell division orchestrated by some bacterial toxins mimic conventional adjuvants.

Biography

Rawah Faraj is a PhD student at Tuskegee University, Tuskegee, USA. She earned her degrees in Veterinary Medicine and Master of Science in Genetic Engineering and Biotechnology at Baghdad University, Iraq. She also taught Physiology, Molecular Biology and Medical Microbiology at Middle Technical University, Baghdad, Iraq. Her research interest is in zoonotic diseases. Her current PhD project involves construction of recombinant chimeras made of heat-labile enterotoxins and the *Leptospira* proteins. She has 8 publications.

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