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

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The B-subunits of heat-labile enterotoxins 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 can adjuvant immune responses to other antigens and induce long-term memory by a number of routes, including the mucosae. However, the stimulating effects on the APCs by very small doses of the B-subunits could not solely explain their remarkable adjuvant properties. We demonstrate that the co-incubation with the B-subunits induce 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 alone, 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 could form an additional and novel mechanism of adjuvanticity orchestrated by some bacterial toxins. Moreover, the differential effects between LT-IB and LT-IIaB on IL-2 production and MHC class-II expression on macrophages highlight the outcomes of interplay between signals involving different receptors.

### Biography

Toufic O Nashar has completed his PhD from University of Bristol, UK and Post-doctoral studies at University of Bristol and University of Kent, UK and Albany Medical College, NY, USA. He held the post of Research Affiliate at Wadsworth Research Center, NY, USA. He is currently Assistant Professor of Immunology/Virology at Tuskegee University, Alabama. He has more than 25 publications including peer-reviewed articles in reputed journals, review articles and book chapters. His research work is focused on mechanisms of immune modulation by bacterial toxins towards vaccine development against viral and bacterial diseases.

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