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POSTER PRESENTATION Open Access

Atopy affects LPS responsiveness and TLR-4 expression in children peripheral mononuclear cells

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Background

Lipopolysaccharide (LPS) exposure in early life is associated with a lower incidence of atopy. We sought to determine whether atopy regulates TLR-4 expression and LPS-induced signal transduction on peripheral immune cells e.g. CD4 T 'helper' T cells, monocytes and B cells of a large pediatric cohort.

Methods

Over 350 subjects were recruited from the Pediatric Test Center of the Montreal Children's Hospital and a questionnaire was administered to determine presence of a history of atopic diseases. 3-5cc of anti-coagulated blood was taken and peripheral blood mononuclear cells were cultured for up to 24h with IL-4 (13.5ng/ml) and/or LPS (up to 5μg/ml). We conducted flow cytometric analysis for surface TLR-4 expression, along with T 'helper' lymphocyte marker CD4, pan-B lymphocyte marker CD19, monocyte marker CD14, and for intracellular phosphorylated p44/p42 and p38 signaling molecules.

Results

Non-atopic monocytes prominently internalize TLR-4 and trigger signal transduction (e.g. phosphorylation of p44/p42 and of p38) upon LPS exposure. Such LPS responsiveness was strikingly impaired in monocytes from atopic children. Compared with monocytes, reduced proportions of $CD4+^{High}$ T 'helper' lymphocytes and CD19+ B cells express TLR-4. In T cells, TLR-4 expression varies with age (it peaks between 7-17 years of age) and atopy; atopic children display reduced TLR-4 expression compared with controls. Recombinant IL-4 also interferes with LPS signaling, and was found to differentially modulate TLR-4 expression in T 'helper', B lymphocytes and monocytes.

Conclusions

Peripheral TLR-4+ CD14+ $CD4+^{Low}$ monocytes may be used to discriminate between atopic and non-atopic children based on reduced LPS-induced signaling in atopic subjects. TLR-4 expression greatly varies with age and appears to be affected by both atopic status and IL-4. Our data suggest that atopy and Th2-type immune bias may impair TLR-4-mediated innate immune function during childhood and, therefore influence allergic disease manifestations.

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