POLLUTANTS MODULATE INNATE IMMUNE RESPONSE VIA EXTRACELLULAR VESICLES

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Background: (max 50 words)

Pollution can perturb immune function through chronic activation or suppression. We showed that flame retardant BDE-47 modulates macrophage innate immune responses *in vitro* [1-4] and *in vivo* [5]. Little is known about BDE-47's effects on macrophages derived extracellular vesicle (EV) biogenesis, cargo content, and their effects in bystander cells.

Methods and Results: (max 100 words)

EVs were purified from BDE-47-treated M(LPS) THP-1 macrophages by d(UC) method ($sEVs^{PBDE+LPS}$). Their concentration, size distribution and specific markers were determined by DLS, NTA and western blots analyses. EVs miRNA profile was characterized by microarrays and cytokine and surface markers by qPCR and flow cytometry, respectively. We observed that BDE-47 affects EVs biogenesis and interferes with their miRNA cargo. Indeed, $sEVs^{PBDE+LPS}$ can modulate naïve M0 THP-1 to make immunological synapses and present antigens. Finally, $sEVs^{PBDE+LPS}$ can modulate the expression of tight junction and cytokines genes in epithelial A549 cells cultured in ALI conditions.

Conclusions and Significance: (max 50 words)

Our studies demonstrate that BDE-47 exerts direct immunotoxic effects on a macrophage cell line, impairing the proinflammatory response and modulating sEVs biogenesis and miRNA cargo. Purified sEVs modulate cellular activities in naïve macrophages and heterologous cell lines suggesting the potential relevance of EVs in toxicology and exposure science.

Keywords: (max 5)

innate immune response, macrophages, extracellular vesicles, flame retardants, miRNAs

References: (max 5 relevant references from the Authors in the following format:

full authors list, title, year, journal, vol.: pages)

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