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A dysregulation of LPS-induced inflammatory response by mitotoxic Trimethyltin Hydroxide and Triethyltin Bromide

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When a eukaryotic body incurs trauma or infection, immune cells are prompted to orchestrate both defensive and curative inflammatory responses. Macrophage cells are implicated in inflammatory processes essential for elimination of pathogens and required for homeostatic restoration. Mitochondrial dysfunction may represent a biological process and pathway by which environmental chemicals can modify the macrophage inflammatory response. Multiple organic tin compounds have been established as mitochondrial and neuronal toxicants by the NTP Tox21 program. Acute exposure to these chemicals can result in severe skin irritation, chronic neurological effects and death. Although commonplace usage of these compounds has been prohibited in most developed nations, risks of occupational exposure are still relevant in many undeveloped industrial settings and antiquated infrastructures. In order to evaluate how macrophage inflammatory response may be modulated by mitochondrial dysfunction, we employed two organotin compounds: Trimethyltin Hydroxide (TMT OH) and Triethyltin Bromide (TET Br). In this study, we explored how 6-hour pre-exposure to TMT OH or TET Br in murine RAW 264.7 macrophages may alter the basal LPS-driven inflammatory response. We saw TET Br pre-exposure elicit a mRNA blunting effect for both pro- (TNF- α, IL-1β and IL-1α) and anti-inflammatory (IL-10) cytokines, where TMT OH did not. The inhibitory effect on cytokines of both natures may imply a holistic dysregulation of the inflammatory process within macrophages. In addition to these results, we saw a significant deviation in arginase II and TLR4 message levels in TET Br-dosed cells. Following this, a Mito Stress analysis revealed that TMT OH exposure did not significantly impact the oxygen consumption rate at any point during the experiment. However, in contrast, TET Br exhibited a significant difference from both the control and TMT OH groups during the period of basal respiration, ATP production and maximum respiration. The reduction in maximal respiration also suggests a decreased spare respiratory capacity for TET Br-exposed cells.

Biography

Caroline Reed is currently a fourth-year student studying Environmental Health and Biology at the University of North Carolina at Chapel Hill. In addition to this, Caroline is a NSCP scholar, conducting research under GJean Harry at the National Institute of Environmental Health Sciences. She has been accepted to and will matriculate into the Environmental Sciences and Engineering MPSH program within UNC-CH's Gillings School of Global Public Health following her undergraduate graduation in May. Her research interests include environmental toxicology, developmental epigenetics and cell biology.

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