Centers for Disease Control and Prevention

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Antimicrobials and Allergic Disease: Identifying Novel Biomarkers and Mechanisms of Action

Updated July 12, 2021

NIOSH Dataset RD-1017-2021-0 July 2021

Introduction

Occupational immune diseases are some of the most common illnesses that affect workers in the United States. The Healthcare and Social Assistance Sector (HCSA) has one of the highest incidence of allergic disease compared to other industrial sectors. Individuals in this sector are frequently exposed to a variety of high-level cleaners and disinfectants along with antiseptics for the purposes of sterilization of surfaces, medical and surgical instruments, and reducing the incidence of nosocomial infections. The range of specificity and effectiveness of these agents is very diverse based on the type of chemical used. Commonly used antimicrobials include: alcohol, chlorine, iodine based agents; phenols; hydrogen peroxide; and quaternary ammonium compounds (QAC). While the importance of these kinds of chemicals is understood, many of these agents are also known to directly contribute to allergic disease. Antimicrobials including disinfectants and antiseptics are unique in that they have been identified to cover all classes of immune action related to allergic disease (irritants, sensitizers and adjuvants). In addition, new chemicals are constantly being synthesized for specific antimicrobial purposes or as potentially less toxic alternative, and these may also present unique burdens on the immune system. While the primary routes of exposure to these chemicals are the skin and lung, in the health care setting exposures to multiple chemicals present in individual products or exposures to multiple products, often occur presenting the opportunity for complex mixed exposures. In addition, while dermatitis and asthma are often thought a direct consequence of respective skin or lung exposure, the role of the skin in both dermal and respiratory sensitization is increasingly being recognized. Worker exposure leading to sensitization can often be asymptomatic in nature until subsequent exposure elicits a response in the sensitized individual. Therefore, knowledge about how the skin regulates allergic disease is extremely important because protection from sensitization and other factors that influence this process will prevent disease. Due to the increasing development of and uses for antimicrobials, it is imperative to analyze the immunotoxicological effects of these compounds. Results of these studies will provide the necessary tools to develop a hazard-based approach to investigate the role of antiseptics and disinfectants used in HCSA on allergic disease. As new occupational hazards continue to emerge it is critical that we understand the immunological mechanisms that exacerbate immune mediated respiratory and dermal diseases. Specific understanding of these mechanisms has direct implications in exposure assessment and the development of appropriate intervention and prevention strategies.

Download Data

- Tissue specific S100A8 and ATP expression [XLS – 4 KB]
- Tissue specific Opa1 and Drp1 expression [XLS – 2 KB]
- Tissue specific Inflamasome expression [XLS – 5 KB]
- Tissue specific IL-1beta expression [XLS – 5 KB]
- Tissue specific chemokine expression [XLS – 17 KB]
- Mitochondrial morphology [XLS – 796 B]
- Immune phenotyping in the skin [XLS – 6 KB]
- immune phenotyping in the lymph node [XLS – 8 KB]
- Evaluation of mitochondrial activation [XLS – 3 KB]

- Data Dictionary [PDF – 92 KB]
- Methods [PDF – 126 KB]

Data Collection Methods

1. Animal Exposures
    - Female BALB/c mice (7-8 weeks at start of study)
    - Triclosan (0-3%) or acetone on dorsal surface of ear for up to 4 days
2. Tissue Collection
    - Ears (2 per mouse; split into ventral and dorsal halves) were collected in RPMI and either used intact or processed into single cell suspensions prepared by incubating with a 0.25 mg/ml Liberase-TL Research grade (Roche) enzymatic digestion for 90 min at 37°C in RMPI with 100 µg/ml DNase I.
    - Right and left auricular draining lymph nodes (dLNs) collected in 2 ml sterile phosphate-buffer saline (PBS) (pH 7.4) and single cell suspensions (2 nodes/animal) were prepared by mechanical disruption of tissues between frosted microscope slides
3. Caspase-1 inflammasome activation
    - Ear and dLN caspase-1 activation was assayed via Promega Caspase-Glo 1 Inflammasome kit according to manufacturer's instructions.
4. Cytokine production (Gene and protein)
    - Real-time PCR (Applied Biosystems 7500 RT-PCR System.
    - Mouse IL-1β Quantikine ELISA Kit (R&D Systems)
    - Capillary western immunoassay performed according to the ProteinSimple Wes user guide for a 12-230 kDa Separation Module and the Anti-Rabbit detection module.
5. Extracellular ATP assay
    - ATP production was assayed via Promega ToxGlo kit.

6. Immune Cell Subsets
    - Flow cytometry using BD LSRII Flow Cytometer and data was analyzed using FlowJo software.
7. Mitochondrial Evaluation
    - Mitochondrial membrane potential was measured via MitoProbe JC-1 Assay Kit (ThermoFisher Scientific) according to manufacturer's instructions.
    - Mitochondrial mass, single cell suspensions of dLN were resuspended in 100 µl of 200 nM MitoTracker Green dye for 20 mins at 37°C/5% CO_2.

Mitochondrial ROS, single cell suspensions of dLN were resuspended in 100 µl of 5 µM MitoSOX Red dye for 20 mins at 37°C/5% CO_2.

8. Transmission electron microscopy (TEM)
    - Ultrastructural changes were evaluated using a JEOL JEM-1400Plus transmission electron microscope (JEOL, Tokyo, Japan).

Citations

Dzubak L, Shane H, Friend S, Lukomska E, Baur R, Anderson S [2020]. Topical application of the antimicrobial agent triclosan induces NLRP3 inflammasome activation and mitochondrial dysfunction. Toxicol Sci. Jul 1;176(1):147-161

Acknowledgements

This work was supported by NIOSH CAN 993909NZ

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Page last reviewed: July 12, 2021