# Poultry Dust Exposure and Lung Inflammation

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## *Background & Rationale*

- Poultry production in the United States has increased rapidly in recent years, and the combined value of poultry production was valued at $ 38.1 billion in 2011.
- Workers in poultry concentrated animal feeding operations (CAFOs) are exposed to airborne dust and are at risk of developing respiratory symptoms and lung diseases.
- Interleukin-8 (IL-8), a pro-inflammatory cytokine, is involved in the pathogenesis of acute and chronic lung diseases.
- Despite the high prevalence and severity of acute and chronic respiratory symptoms and diseases in poultry workers, and the rapid expansion and economic impact of poultry production there is little information on lung inflammatory responses to poultry dust.
- A better understanding of inflammatory responses to poultry dust is essential to develop new preventive measures and treatments for agricultural dust-induced lung diseases.

## *Specific Aims*

1. **Characterize changes in the expression [profiles of airway and alveolar epithelial cells in response to broiler dust.** Hypothesis: Broiler dust induces unique changes in the expression of RNAs and proteins in airway and alveolar epithelial cells.
2. **Determine the molecular mechanisms of interleukin-8 (IL-8) induction by broiler dust in airway and alveolar epithelial cells.** *Hypotheses: Components of broiler dust such as endotoxin, □-glucan, peptidoglycan, and proteases modulate IL-8 levels. Broiler dust induces IL-8 expression by transcriptional and posttranscriptional mechanisms.*
3. **Determine the role of oxidants and protein kinase signaling pathways in the induction of IL-8 levels by broiler dust in airway and alveolar epithelial cells.** *Hypothesis: Broiler dust induces reactive oxygen species (ROS) and activates protein kinase C (PKC) and mitogen activated protein kinase (MAPK) enzymes to induce IL-8 levels.*
4. **Determine the in vivo effects of broiler dust on lung inflammatory responses and lung mechanics. Determine if inducers of transcription factor Nrf2, such as the triterpenoid CDDO-Im attenuate broiler dust induced lung inflammation in mice.** *Hypotheses: Broiler dust induces lung inflammation and disrupts lung mechanics. Induction of Nrf2, a master regulator of antioxidant response attenuates dust induced inflammation and disruption of lung mechanics.*

## *Activities/Outputs*

1. Gottipati K, Bandari S, Nonnenmann MW, Levin JL, Dooley GP, Reynolds SJ, and **Boggaram,V.** Transcriptional and protein kinase signaling mechanisms mediate organic dust induction of IL-8 expression in lung epithelial and THP-1 cells. Am J Physiol Lung Cell Mol Physiol 308: L11-L21, 2015.
2. **Boggaram V,** Loose DS, Gottipati K, Natarajan K, and Mitchell C T. Gene expression profiling of the effects of organic dust in lung epithelial and THP-1 cells reveals inductive effects on inflammatory mediators. Physiol Genomics 48(4): 281-289, 2016.
3. Natarajan K, Gottipati K, Berhane K, Samten B, Pendurthi U, and **Boggaram V.** Proteases and oxidant stress control organic dust induction of inflammatory gene expression in lung epithelial cells. Respiratory Research, 2016, accepted for publication.
4. Mitchell, CT et al. Poultry dust induced lung inflammatory responses in mice. Manuscript under preparation, 2016.

## *Outcomes/Impact*

1. Bandari S. (2012). Regulation of interleukin-8 (IL-8) gene expression in THP-1 cells by organic dust (Master's thesis in Biotechnology), Stephen F Austin State University, Nacogdoches and University of Texas Health Science Center, Tyler.
2. Gangam K. (2013). Regulation of surfactant protein gene expression by organic dust (Master's thesis in Biotechnology), University of Texas Health Science Center, Tyler.
3. Mitchell CT. (2015). Organic dust induced lung inflammatory responses in mice (Master's thesis in Biotechnology), University of Texas Health Science Center at Tyler.