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Project Summary (Abstract)
The recommendation for environmental control measures as key components in the management of asthma stems in part from previous research that found exposure to mouse allergen may contribute greatly to the burden of inner-city asthma, especially in the Northeast. This group has shown that mouse-targeted integrated pest management (IPM) successfully reduces residential mouse allergen levels by greater than 75%. Evidence also suggests that reduction of allergens may result in immune modulation that could influence favorably the future course of disease. This proposal focuses on determining such molecular mechanisms. This project will collaborate with an NIAID funded randomized, controlled trial to assess the efficacy of IPM in children with moderate to severe asthma who live in homes with high levels of mouse allergen (1U01AI083238). Epigenetic alterations in genes associated with asthma are believed to occur following exposure to environmental toxicants, including allergens. We propose to determine whether remediation of mouse allergen is associated with changes in epigenetic marks and expression of genes important to the regulation of allergic airway disease, and whether these are associated with improvement in asthma. We will investigate multiple key steps in this pathway by collecting and analyzing measures of 1) allergen levels, 2) buccal DNA methylation levels of asthma regulatory genes under epigenetic control: interferon (IFN)γ and Forkhead box P3 (Foxp3), 3) levels of gene expression, and 4) asthma symptoms prior to and following mouse allergen-targeted IPM or control intervention. We hypothesize that 1) Reduction in indoor mouse allergen levels will be associated with changes in buccal cell DNA methylation of asthma counter-regulatory genes important to Th cytokine production (IFNγ) and T cell regulation (Foxp3), 2) Changes in DNA methylation of asthma genes will be associated with a reduction in asthma symptoms after completion of a mouse allergen intervention among n=200 moderate to severe asthmatic children. If the aims are achieved, we will develop research that helps define a 'molecular footprint' of mouse allergen exposure and its remediation on DNA methylation. This new direction may result in novel biomarkers that could inform us about the efficacy of interventions against environmental toxicants important to asthma, and its immune modulation, addressing a critical clinical and public health problem.

Home visits will be conducted every 3 months to assess settled dust mouse allergen levels and other evidence of infestation. Symptom data will be collected every 3 months either during clinic visits or telephone calls. Buccal specimens will be collected at screening, 6 months (following IPM at 0.5, 1.5 months, and if necessary 3 months) and 12 months. Analyses will control for the appropriate covariates. This proposed study would be the first to study environmental epigenetic regulation in the context of a randomized environmental intervention.
