Mon-030: Non-Target Assessment of Contributory Chemicals and In Vitro Assessment of Molecular Mechanisms of Indoor House Dust Extract-Induced Adipogenesis in 3T3-L1 Cells

Christopher Kassotis. *Duke University*

Christopher Kassotis, PhD, Kate Hoffman, PhD, P. Lee Ferguson, PhD, Heather Stapleton, PhD.
Duke University, Durham, NC.

Chemical exposures can promote triglyceride accumulation and/or increased adiposity in vitro and in various animal models, and numerous epidemiological studies have reported associations between exposure to putative “obesogens” and increased weight or adiposity in humans. We previously demonstrated that indoor house dust extracts could induce adipogenesis in vitro, and further demonstrated that the extent of triglyceride accumulation was associated with the body mass index and serum thyroid hormone concentrations of adult residents. Herein, we investigated the role of chemical mixtures isolated from house dust in child metabolic health. House dust samples (n=194) were collected from central NC households, solvent extracted, evaporated under nitrogen gas, and reconstituted in DMSO. 3T3-L1 cells were induced to differentiate, dosed with house dust extracts at 100 µg dust equivalence/well, and assayed for triglyceride accumulation and DNA content after ten days of exposure. One hundred and twenty-five dust extracts (64%) exhibited significant triglyceride accumulation at this concentration, while ninety seven (50%) of extracts exhibited significant proliferation. The fifty highest activity samples were further selected for molecular mechanism interrogation, assessing relative contributions of peroxisome proliferator activated receptor gamma activation and/or thyroid receptor inhibition to the observed activities. Preliminary statistical analyses assessed associations between the dust-induced adipogenic responses and the metabolic health of resident children. In children less than 4.5 years old, higher extract-induced proliferation tended to be associated with greater growth trajectories, and higher triglyceride accumulation with lower growth scores. In children older than 4.5, higher dust-induced triglycerides were associated with greater height and weight for age Z scores, and higher dust-induced proliferation with greater BMI Z scores. Dust extracts were also analyzed using a non-targeted analysis on an Orbitrap Fusion Lumos HRMS/MS. Preliminary differential analyses (using Compound Discoverer 3.0) between sample groups reveals three features that were significantly associated with greater extract-induced cell proliferation, respectively, seven features that were significantly associated with greater extract-induced triglyceride accumulation, and five features that were significantly higher in the homes of children who were categorized as overweight or obese. Further interrogation of these features is ongoing, though several nonionic surfactants and polyethylene glycols have been tentatively identified. Interestingly, several of these surfactants have been reported to promote adipogenesis in vitro. These results highlight the utility of non-target analysis for identifying active chemicals from complex environmental samples.

Presentation Date: Monday, March 25
Presentation Time: 1 p.m. – 3 p.m.
Location: Expo Hall