

## One Health Research Project Abstract

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Wildfires are increasingly extending into the wildland-urban interface (WUI) in the US, burning a unique combination of vegetation, structures, and vehicles. WUI fire emissions pose significant risks to the environment, public health, and local ecosystems, which have not been well characterized. Firefighters are a high-exposure group for WUI fires, exposed both through inhalation and dermal contact to chemicals produced by the fires, similar in nature to animals living in close proximity to these fires. While firefighting is a class 1 carcinogen as determined by the International Agency for Research on Cancer (IARC), epidemiologic evidence for this determination was based predominantly on exposure to structural fires, and the cancer risk of specific WUI fire exposure is not known. We propose to leverage existing WUI pre- and post-fire urine samples collected from a firefighter-led cohort study in collaboration with the Los Angeles County Fire Department (LACoFD) and Orange County Fire Authority (OCFA) to evaluate fire challenges facing firefighters, and to evaluate health risks induced by WUI fire exposures. These urine samples have already been analyzed for metabolites of exogenous exposure which provide a unique perspective on the chemicals produced from these fires and released into the environment, and for metabolites of endogenous metabolites produced by the effect of the exposures on the human body. However, to understand these results requires an arduous process of identifying individual features which are present only in the post-fire urine samples. If funded, we also proposed to evaluate urine metabolomics in mice exposed to wood smoke and compare these results to those of the firefighters. Information gleaned from the proposed study could therefore inform risk evaluation for the environment, communities, and animals exposed to combustion products of WUI fires.

**Aim 1. Identify environmental contaminants produced by WUI fires through metabolic changes from pre- to post-exposure in firefighters.** In this aim we will evaluate environmental exposures by using untargeted metabolomic profiles to capture changes from baseline urines to post-fire exposure urines of firefighters. We will conduct a literature review and scrape biomarker databases, e.g., Exposome Explorer, to identify urinary biomarkers of environmental toxicants introduced by fire exposure. These markers will then be mapped to existing urinary metabolic profiles of FFCCS firefighters to evaluate the effect of fire exposure on metabolic changes in firefighters. We expect to see multiple exogenous metabolites in firefighters' metabolic profiles and significant changes in their levels when comparing pre and post WUI fire samples.

**Aim 2. Evaluate endogenous metabolic changes after WUI exposures.** In this aim we will evaluate biological effects by using untargeted metabolomic profiles to capture changes from baseline urines to post-fire exposure urines. Using existing urinary metabolomics data from 87 participants in the Firefighter Cancer Cohort Study, we will compare pre-post fire exposure samples and conduct statistical tests (Welch two sample test) to determine metabolic profile changes. We will use a significance level of 0.05 for individual tests and FDR/Bonferroni adjusted significance level of 0.05 for multiple tests. Our hypothesis is that multiple metabolites will change significantly when comparing pre and post WUI incident samples.

**Aim 3. Evaluate metabolic changes after smoke exposure in animals.** In this aim we will evaluate the effect of wildfire smoke on metabolic profile change in mice. For both pre- smoke exposure and post-

smoke exposure, we will collect urine samples and measure the metabolic profiles in ~64 mice (5 pooled groups: 1 pre-exposure group and 4 post-exposure groups based on mice exposure durations) using high-performance liquid chromatography-mass spectrometry (HPLC-MS), and then characterize the difference in the metabolic profiles comparing pre-post smoke exposure. We will identify differentially expressed urinary metabolites in mice using statistical tests (Welch two sample test) and a significance level of 0.05 for individual tests and an adjusted level of 0.05 for simultaneous tests. We expect to see an overlap of altered metabolite levels after smoke exposure in mice with known untargeted metabolic changes in firefighters after fire exposure for at least some of the environmental toxicants. Information gathered in this aim will facilitate extrapolation from toxic effects in mice to humans. (This aim will be depending on previous funding of the animal pilot One Health proposal.)