Abstract

Air pollution is a critical risk factor in the development and exacerbation of lung diseases, especially asthma.However, the molecular mechanisms directly involved in air pollution-induced asthma are not fully understood. Previous studies have established that exposure to diesel exhaust particles (DEP), a major component in traffic-related air pollution (TRAP), promotes airway inflammation and oxidative stress. DEP also exacerbates lung function impairment and disease severity in both asthma patients and asthmatic animal models. Our preliminary studies suggest that Tet1 (Ten-eleven translocation methylcytosine dioxygenase 1), a protein that initiates cytosine demethylation, may play a protective role in response to TRAP. We hypothesize that Tet1 protects against DEP-induced lung inflammation by epigenetically promoting AhR signaling and inhibiting neutrophil and pro-Th17 response in airway epithelium. I will explore this premise through two main objectives: 1) To determine the role of airway epithelial Tet1 in DEP-induced lung inflammation, I will use *in vitro* and *in vivo* models to examine the effects when Tet1 is lost and also when Tet1 is reactivated. 2) To determine the molecular mechanisms by which Tet1 controls gene expression to regulate the response to DEP, I will use omics approaches to assess gene expression, chromosome accessibility and transcription factor binding.