A study of cigarette smoke-induced COPD in C57BL/6 mice: 
The changes in lung epigenome and proteome after smoking cessation or switching to aerosol from a prototypic modified risk tobacco product

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In this study, the impact of inhalation of aerosol from a reference cigarette (3R4F) or a prototypic modified risk tobacco product (pMRTP), was evaluated in the lung methylome and proteome of C57Bl/6 mice, a model for cigarette smoking-induced chronic obstructive pulmonary disease (COPD). Mice were exposed to aerosol from 3R4F, pMRTP or filtered air for up to 7 months. After 2 months of exposure to 3R4F, switching and cessation groups were exposed to pMRTP or filtered air, respectively.

Differences in lung DNA methylomes analyzed with whole genome bisulfite sequencing showed that continuous exposure to 3R4F presented a larger increase in the amount of hypermethylated CpG sites over time than continuous exposure to a pMRTP, smoking cessation or switching to a pMRTP.

Changes in protein expression levels were detected with isobaric tags for absolute and relative quantification (iTRAQ®). Exposure to 3R4F induced up-regulation of biological functions such as xenobiotic metabolism. Animals exposed to pMRTP exhibited negligible changes, and smoking cessation and switching to a pMRTP resulted in a reduction of changes close to control group levels.

These data demonstrate that exposure to a pMRTP resulted in a response similar to fresh air-exposed animals, while smoking cessation and switching to a pMRTP resulted in the reversal or stabilization of parameters assessed. These results complement those obtained from other endpoints such as transcriptomics or lipidomics, and further establishes the foundation of our systems biology approach to assess the impact of conventional and modified risk tobacco products on biological systems.