Cigarette smoking is a risk factor for chronic obstructive pulmonary disease (COPD) and cardiovascular disease (CVD). Apo- deficient mice are prone to developing premature atherosclerosis and emphysema making it an ideal model in which both pathologies can be assessed simultaneously. We evaluated the effects of cigarette amine (CS) from a conventional cigarette (3R4F) and from THS 2.2, a modified risk tobacco product (MRTP). Apo- mice were exposed for up to 8 months to an aerosol from 3R4F or from THS 2.2; respirator studies. A battery of markers of disease progression were investigated including atherosclerotic plaque formation, pulmonary inflammation (cell infiltration, cytokine levels), pulmonary function and lung emphysema. Exposure to CS induced time-dependent molecular, physiological and inflammatory responses in the lungs of Apo- mice consistent with emphysema and atherosclerotic plaques. The size of atherosclerotic plaques measured in the aortic arches was higher in CS-exposed animals compared to both sham and MRTP-exposed animals at all time points examined. A network-based approach to quantifying the impact of biologically active substances, Drug discovery today, 17, 413-418.


Boue, S., et al. (2013) Cigarette smoke induces molecular responses in respiratory tissues of ApoE-/- mice that are progressively deactivated upon cessation or aerosol exposure from a prototypic modified risk tobacco product, Food and chemical toxicology : an international journal published for the International Life Sciences Institute - North America, 63, 111-118.

These data collectively indicate a halting or regression of the disease genesis of cigarette smoke (CS) from a conventional cigarette (3R4F) and from THS 2.2, a modified risk tobacco product, THS2.2, a candidate MRTP, THS2.2, a prototypic modified risk tobacco product, Food and chemical toxicology : an international journal published for the International Life Sciences Institute - North America, 63, 111-118.

3R4F reference cigarettes

418

The candidate MRTP, THS2.2,

3R4F reference cigarettes

TEST ITEMS

Systems toxicology analysis of cardiovascular and respiratory endpoints from Apo- mice showed similar effects after switching to a candidate modified risk tobacco product, THS 2.2, or to smoking cessation

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<tr>
<th>TEST ITEMS</th>
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<td>3R4F</td>
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<td>THS2.2</td>
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<td>Cessation</td>
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**CONCLUSIONS**

- The exposure to 3R4F cigarette smoke resulted in significant levels of pulmonary inflammation, decline in pulmonary function, and histopathological changes. These phenotypic changes were coherent with the molecular data.
- Chronic exposure to an aerosol from the THS2.2 resulted in very little difference in all measured parameters related to COPD and CVD when compared to the filtered air-exposed animals.
- The biological response to switching to a THS2.2 aerosol or filtered air following 2 months of 3R4F cigarette smoke exposure were very similar between the conditions across the spectrum of endpoints assessed, and showed a generally positive effect.
- Differential gene expression profiles associated with 3R4F exposure returned to nearly filtered air-like levels following either switching to a THS2.2 aerosol or filtered air.
- Histopathological assessment also showed a marked effect of switching, in which a partial or complete (depending on the inflammatory cell type) reversal of pulmonary inflammation was observed.
- These data collectively indicate a halting or regression of the disease genetics following switching from conventional tobacco to 3R4F aerosol in Apo- mice.