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Systems toxicology analysis of cardiovascular and respiratory endpoints from ApoE-/- mice showed similar effects when switching to a candidate modified risk tobacco product, THS2.2 or ceasing smoking

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Cigarette smoking is a risk factor for chronic obstructive pulmonary disease (COPD) and cardiovascular disease (CVD). ApoE-/- 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 smoke (CS) from a standard reference cigarette (3R4F) and aerosol from Tobacco Heating System 2.2 (THS2.2), a candidate modified risk tobacco product (cMRTP). ApoE-/- mice were exposed for up to 8 months to the test aerosol for 3 hours/day, 5 days/week to a target nicotine concentration of 30 µg/l. After 2 months of exposure to CS, cessation and switching groups were further exposed for up to 6 months to fresh air, or THS2.2, respectively. Multiple markers of disease progression were investigated including atherosclerotic plaque formation, pulmonary inflammation, pulmonary function and lung emphysema. Exposure to CS induced time-dependent molecular, physiological and inflammatory pulmonary responses in ApoE-/- mice consistent with emphysematous changes. The area and volume of atherosclerotic plaques measured in the aortic arches were higher in CS-exposed animals compared to both sham and cMRTP-exposed animals at all time-points. Significant changes in the lung transcriptome and proteome of ApoE-/- mice were observed in response to CS-exposure compared to sham-exposed mice. Smoking cessation and switching to THS2.2 resulted in lower activation levels compared to continuous exposure to CS. Both the cessation and switching groups showed similar effects on the histopathological and molecular endpoints, indicating significant reduced effects in comparison to the continued exposure to CS.

Biography

Xia W has earned his Bachelor and PhD degrees from National University of Singapore. He has worked in Takeda and GSK prior to joining PMI and has profound expertise in using preclinical *in vivo* models to evaluate products/compounds and to understand the mechanism of action.

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