

# Accepted Manuscript

Comparative systems toxicology analysis of cigarette smoke and aerosol from a candidate modified risk tobacco product in organotypic human gingival epithelial cultures: A 3-day repeated exposure study

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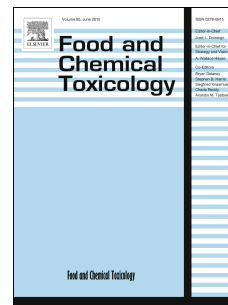
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# Graphical Abstracts

cigarette smoke

vs.

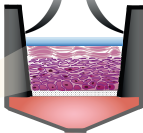
THS2.2  
aerosol

# Systems Toxicology Assessment



Gingival  
epithelium

Two concentrations  
(matched by nicotine)



*In vitro* gingival  
3D cultures

I Exposure

✓

✓

✓

✓ Histology

✓ AK cytotoxicity

✓ CYP1A1/1B1 activity

✓ Pro-inflammatory markers

✓

(✓) mRNA/miRNA

✓

Metabolomics

✓

✓

II Exposure

III Exposure

day 1

day 2

day 3

4 h

24 h after last exposure

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