

Metabolomic strategy to identify markers of exposure and toxicity of electronic cigarettes, heated tobacco products and tobacco cigarettes

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Conflicts of interest

The authors have no conflicts of interest to disclose
concerning the presentation

Electronic cigarettes or

e-cig



Heated Tobacco Products (HTP)

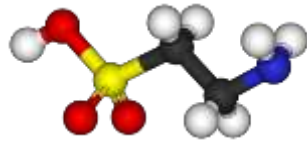


IQOS® (Philip Morris)

New, less harmful alternatives to



Chemical composition



Short-term effects:
in vitro experimental models

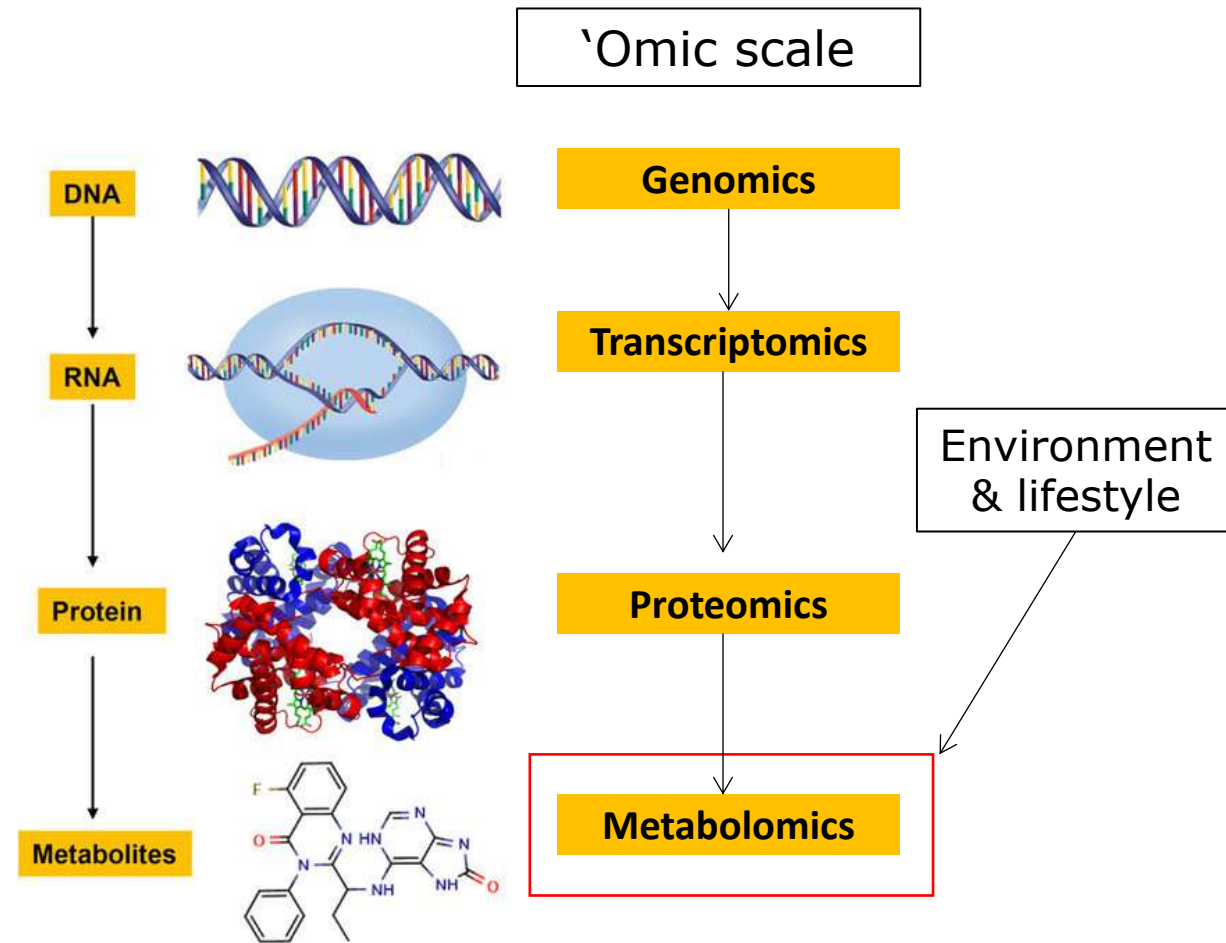


Long-term effects:
in vivo experimental models



Metabolomic strategy

- Systematic identification and quantification of the metabolome of a biological system
- Down the stream of a genome
- Amplified and dynamic measure of changes resulting from processes involving the genome, physiological and pathological processes and the environment
- Well correlated to a phenotype



Yu L. & al., *Oncotarget*. 2017; 8: 115774-115786.



**Targeted
metabolomics**

Investigation of a relatively limited and specific number of metabolites. Accurate determination of known metabolites.



**Non-targeted
metabolomics**

Investigation of all metabolites detectable in the test samples. Maximize the number of metabolites detected and thus provide the opportunity to observe unexpected changes.

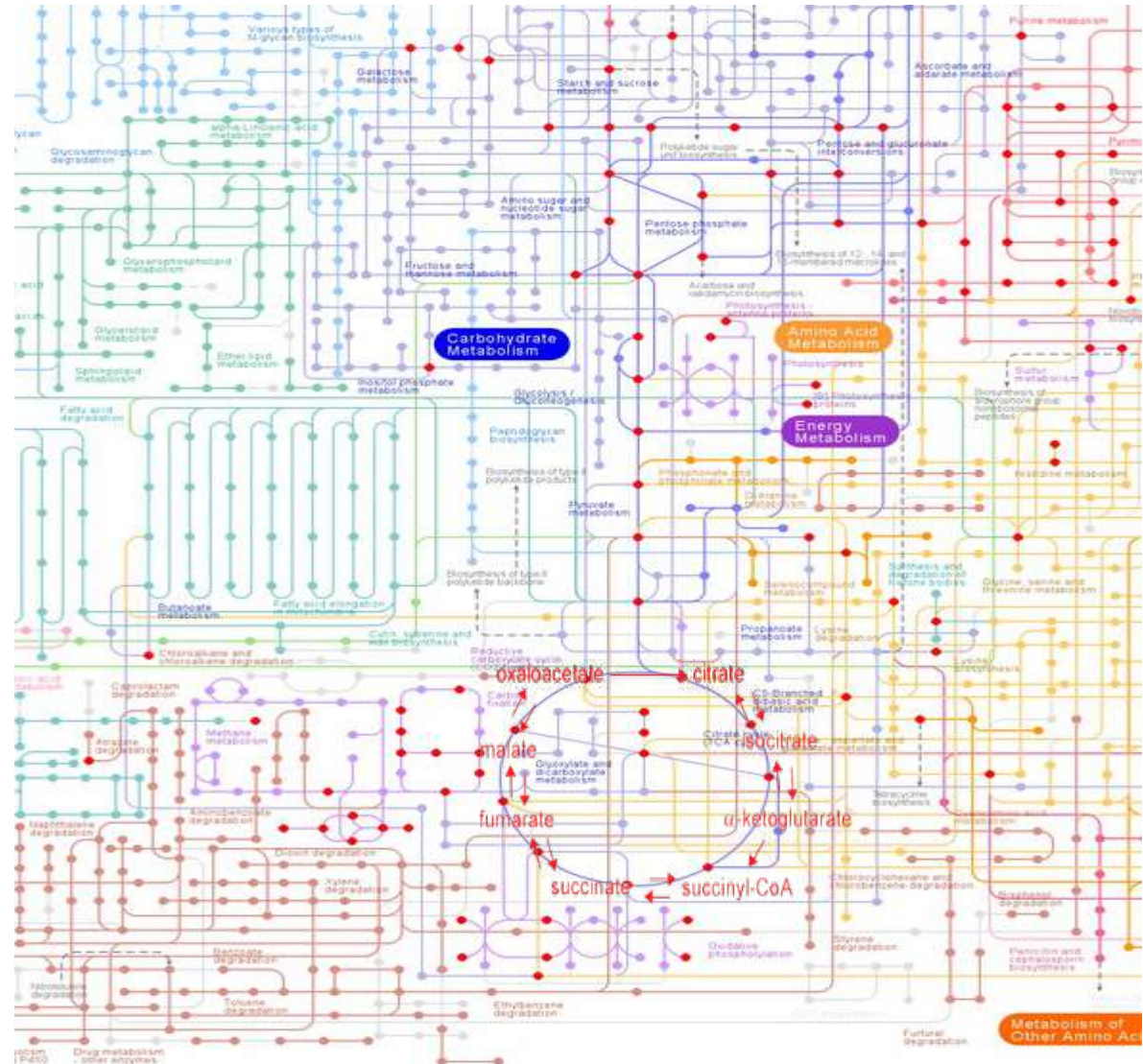
Limit = identification



Targeted metabolomics



Non-targeted metabolomics



Electronic cigarettes or

e-cig



New, less harmful
alternatives to
cigarettes?

Heated Tobacco
Products (HTP)



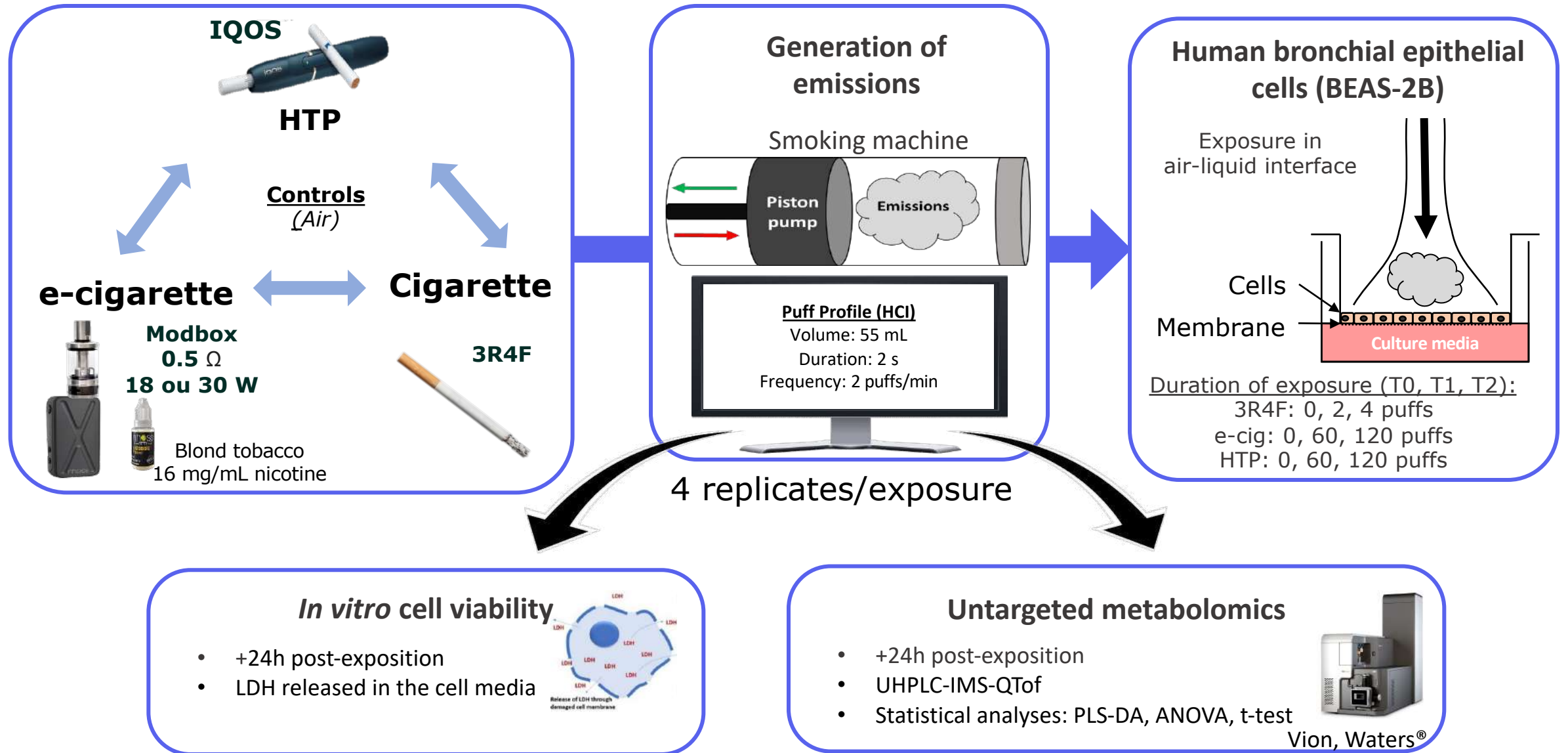
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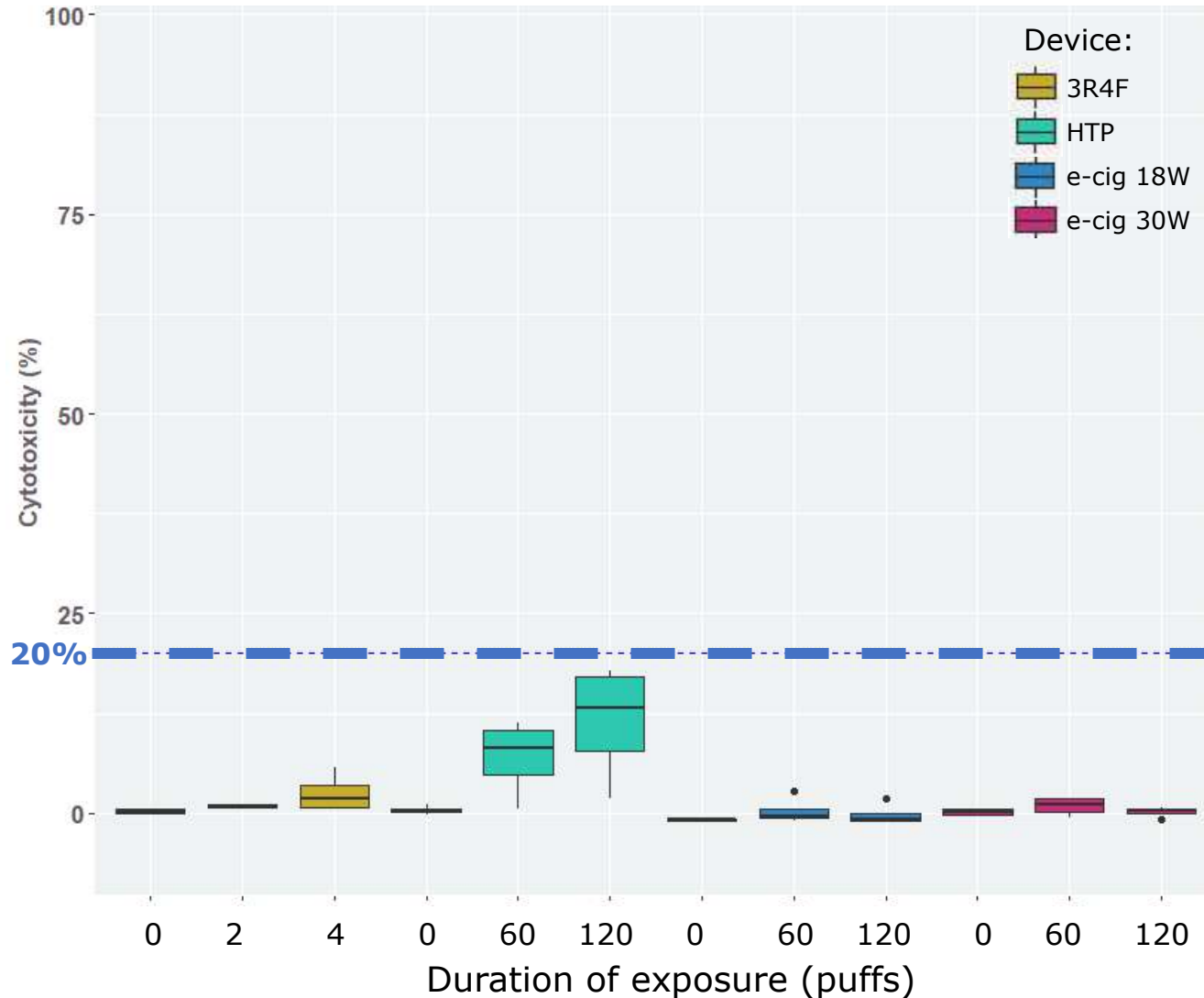


Metabolomic strategy to identify markers of
exposure and toxicity of e-cig, HTP and
tobacco cigarettes

- Exploration and comparison the metabolome of human lung cells exposed to emissions to highlight their specific metabolic fingerprints

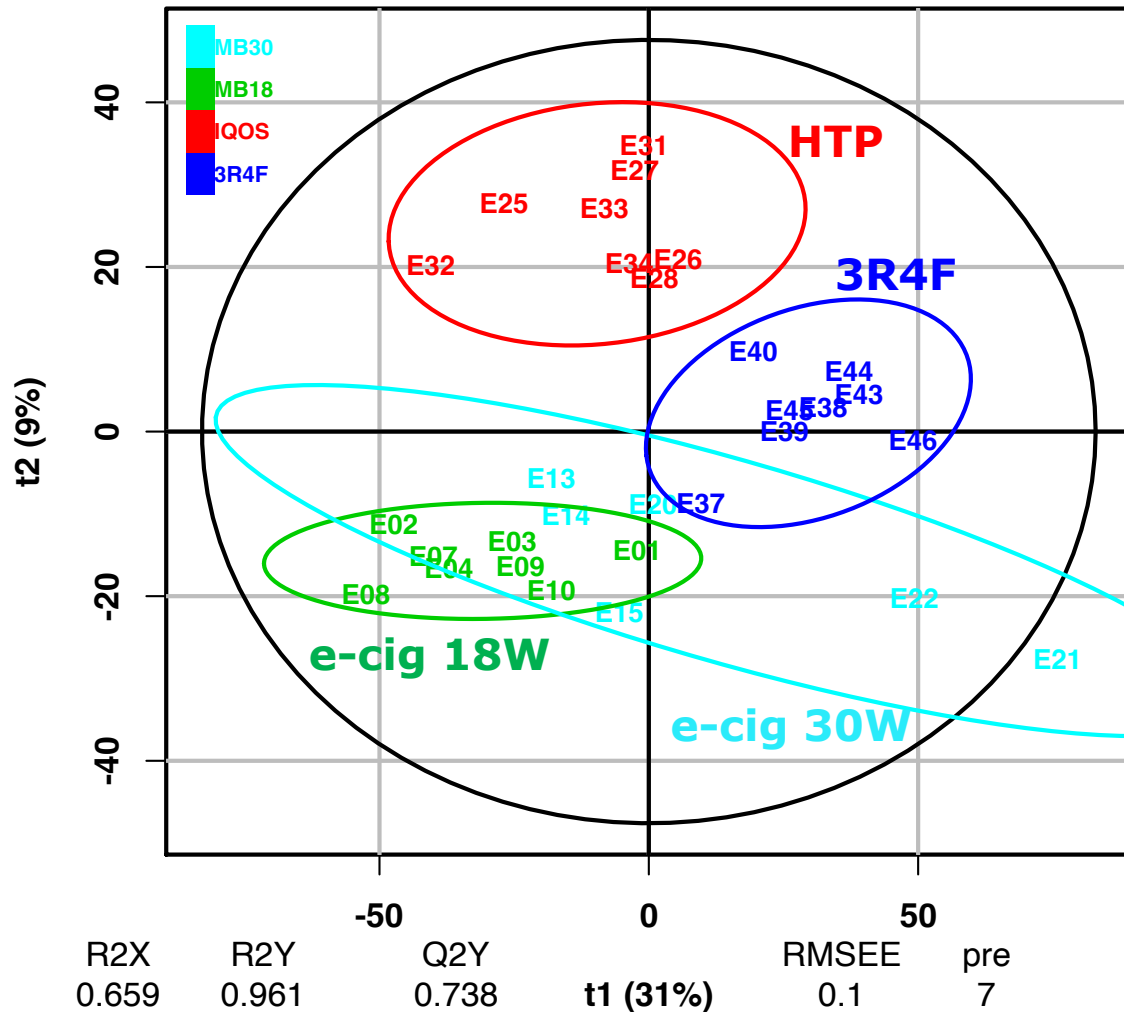
Experimental protocol





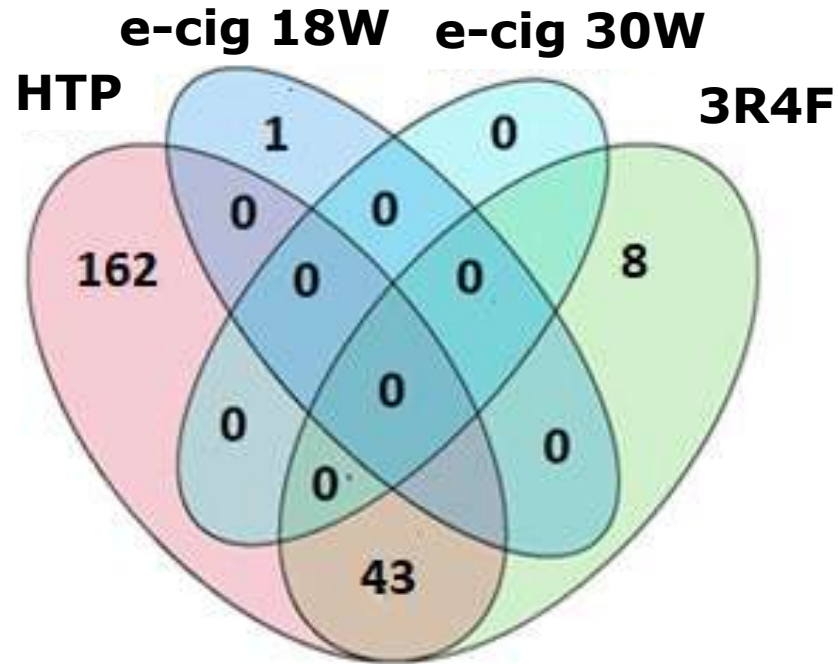
- 4 replicates/exposure
- Low cytotoxicity between the different devices (< 20%)
- In accordance with preliminary data of cell viability (ATP test)

Metabolomic variations will reflect biological changes due to exposure



- After data pretreatment : **3591 features** detected
- **PLS-DA** to discriminate exposed groups with the most discriminating variables
 - constructed with both timepoints
 - validated by permutation tests

Samples exposed to tobacco products (HTP and 3R4F) were discriminated from e-cig groups using a metabolomic fingerprint that includes discriminant features

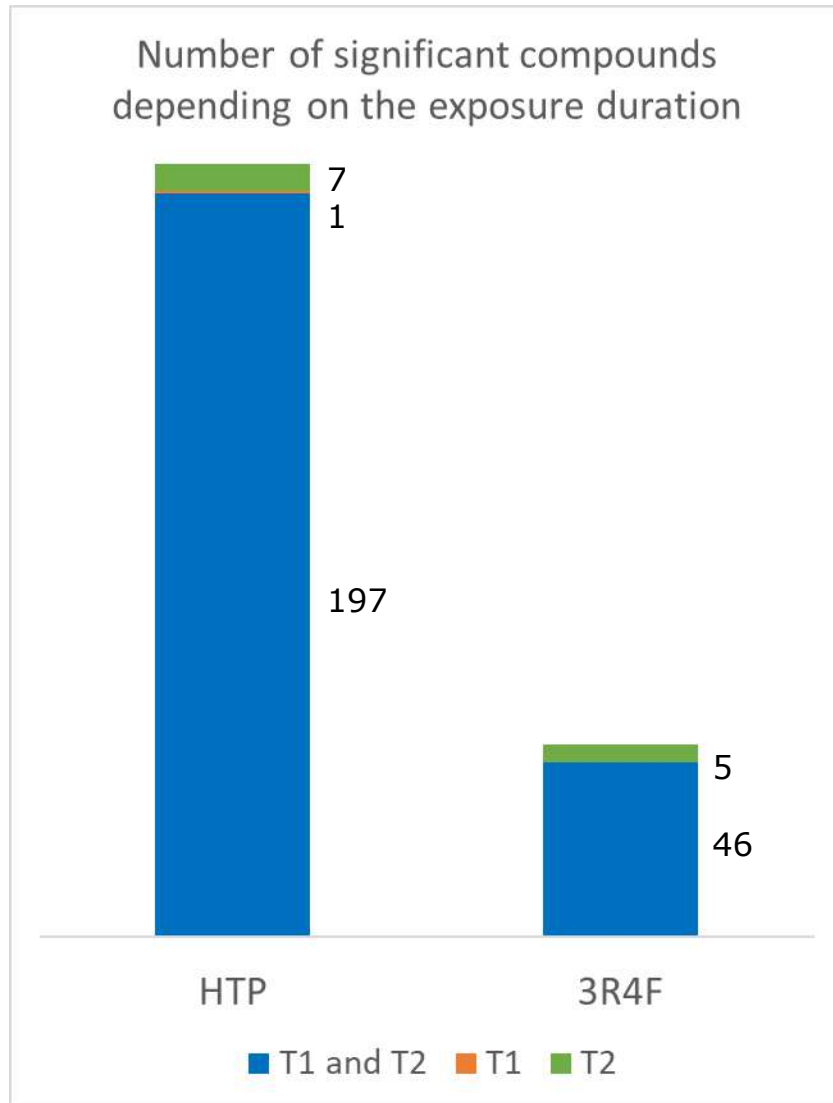


ANOVA reveals compounds allowing to discriminate the exposure times

214 significant features

- HTP : 205 metabolites deregulated
54% were up-regulated after HTP exposure
- 3R4F : 51 metabolites deregulated
51% were up-regulated 3R4F exposures
- e-cig 18W : 1 metabolite deregulated
- e-cig 30W : No metabolite deregulated

Both 3R4F and HTP emissions significantly affected metabolome, whereas no difference was observed after e-cig exposures, compared to controls



214 significant features

- t-test to compare each time of exposure
 - HTP: T1 = 60 puffs ; T2 = 120 puffs
 - 3R4F: T1 = 2 puffs ; T2 = 4 puffs
- Increasing the duration of exposure sparsely impacted the metabolite profile
- Weak time-dependent effect

Significant metabolites were considered to be the metabolomic signature resulting from exposure

Electronic cigarettes or e-cig



Heated Tobacco Products (HTP)



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Metabolomic strategy

Exploration and comparison the metabolome of human lung cells exposed to emissions

- Samples exposed to tobacco products were discriminated from e-cig groups
- Both 3R4F and HTP emissions significantly affected metabolome, whereas no difference was observed after e-cig exposures, compared to controls
- Weak time-dependent effect
- Significant metabolites were considered to be the metabolomic signature resulting from exposure

Metabolomic analyses
Tobacco products **»»** e-cig

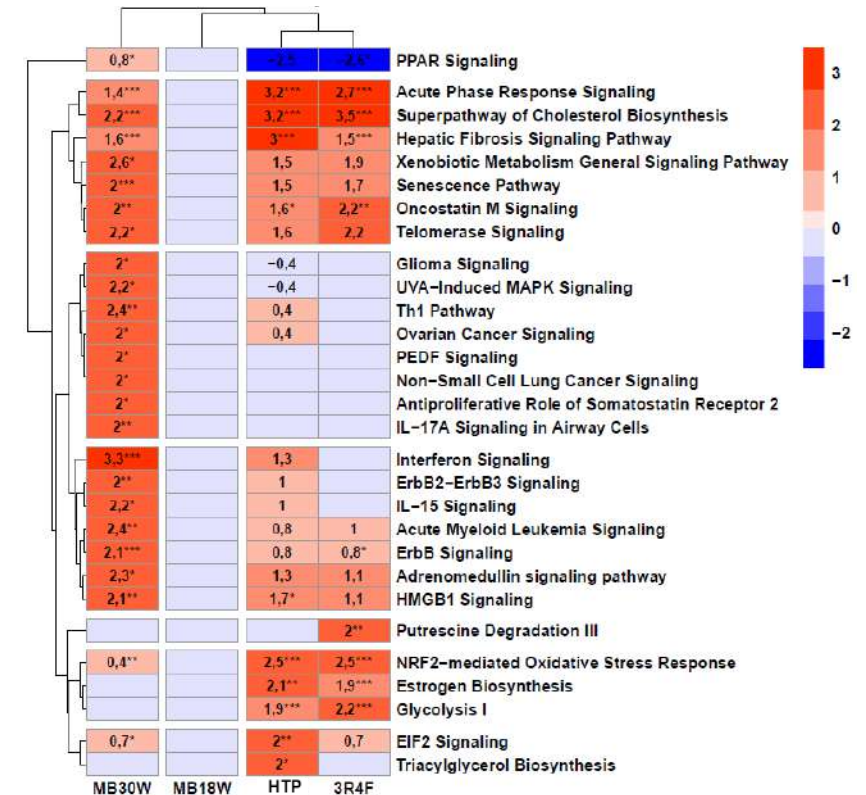
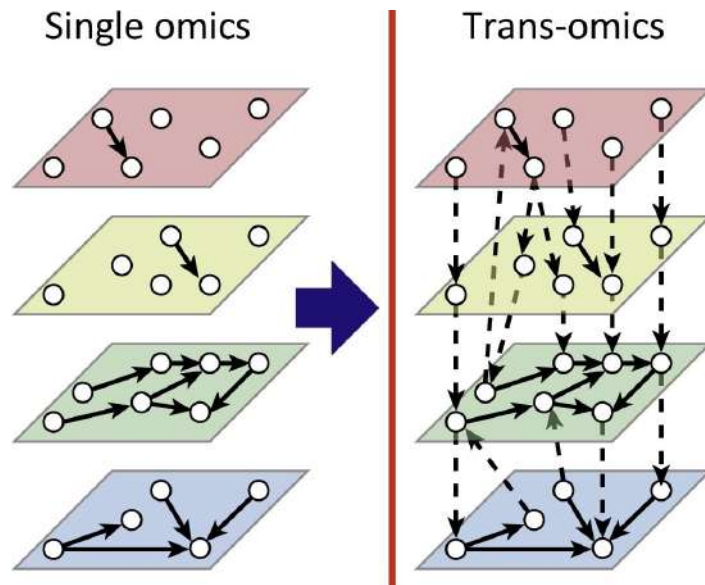


• 1. Identification of features and functional analyses

Preliminary identifications :

- \approx 10% of features with a putative identification
- Involved in different pathways : Arachidonic acid metabolism, Tryptophan metabolism, Glutathione metabolism...

• 2. Integrative biology with transcriptomic data



Thank you for your attention



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