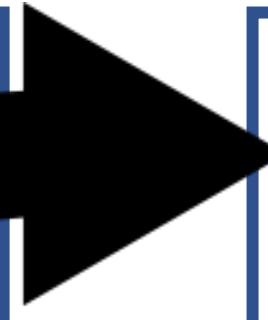


Biological origin of Volatile Organic Compounds

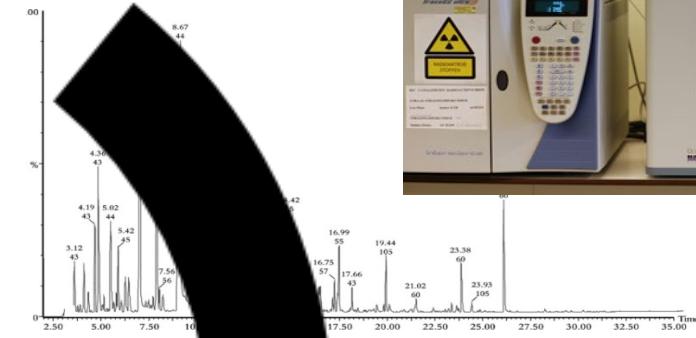
Dr. Rianne Fijten

1

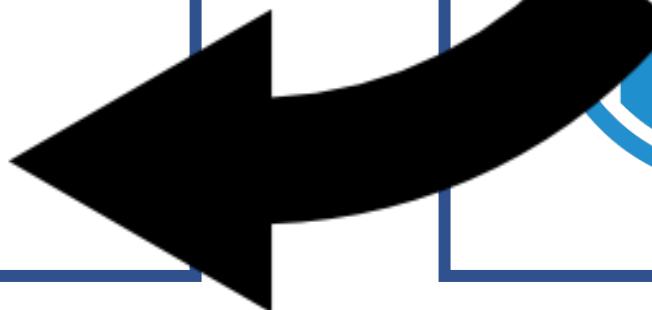
CLINICAL TRIAL



2



4

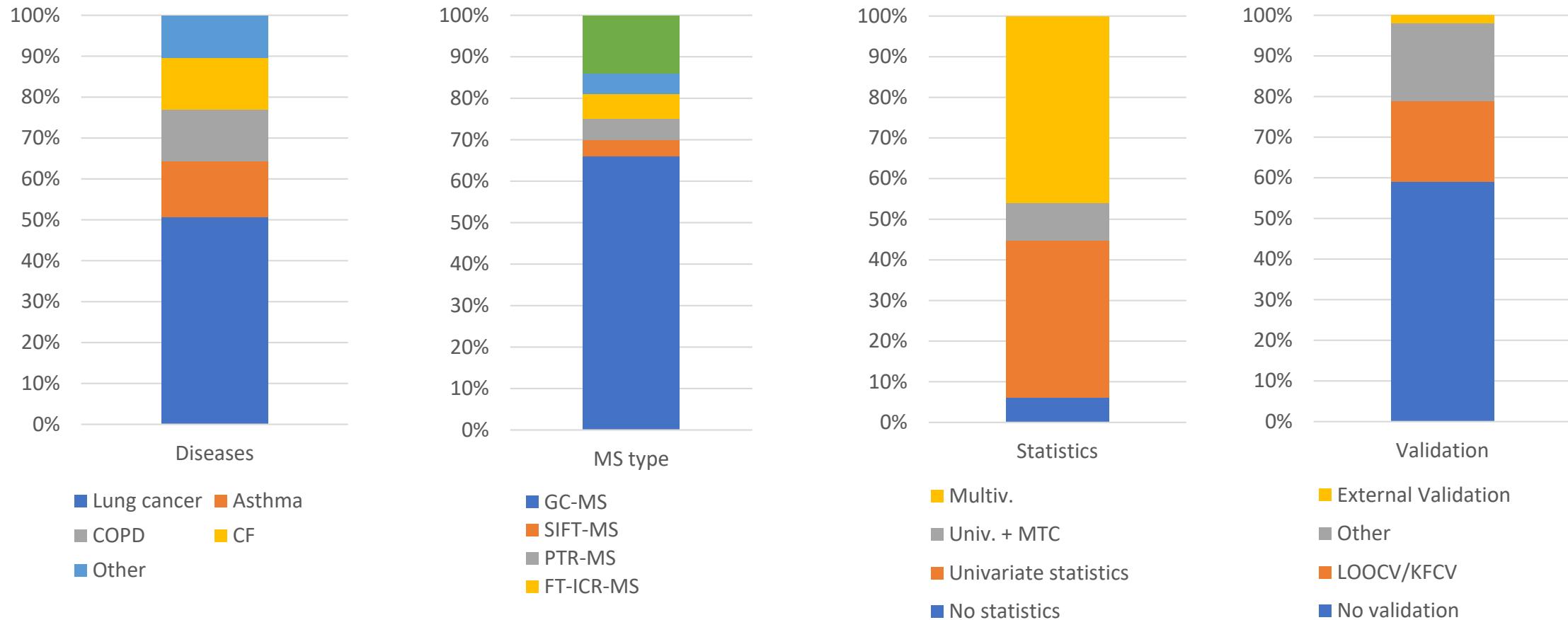


3



AUC: 0.84
PPV: 0.74
NPV: 0.80

88 MS-based exhaled breath research in lung disease



Concerns in exhaled breath research

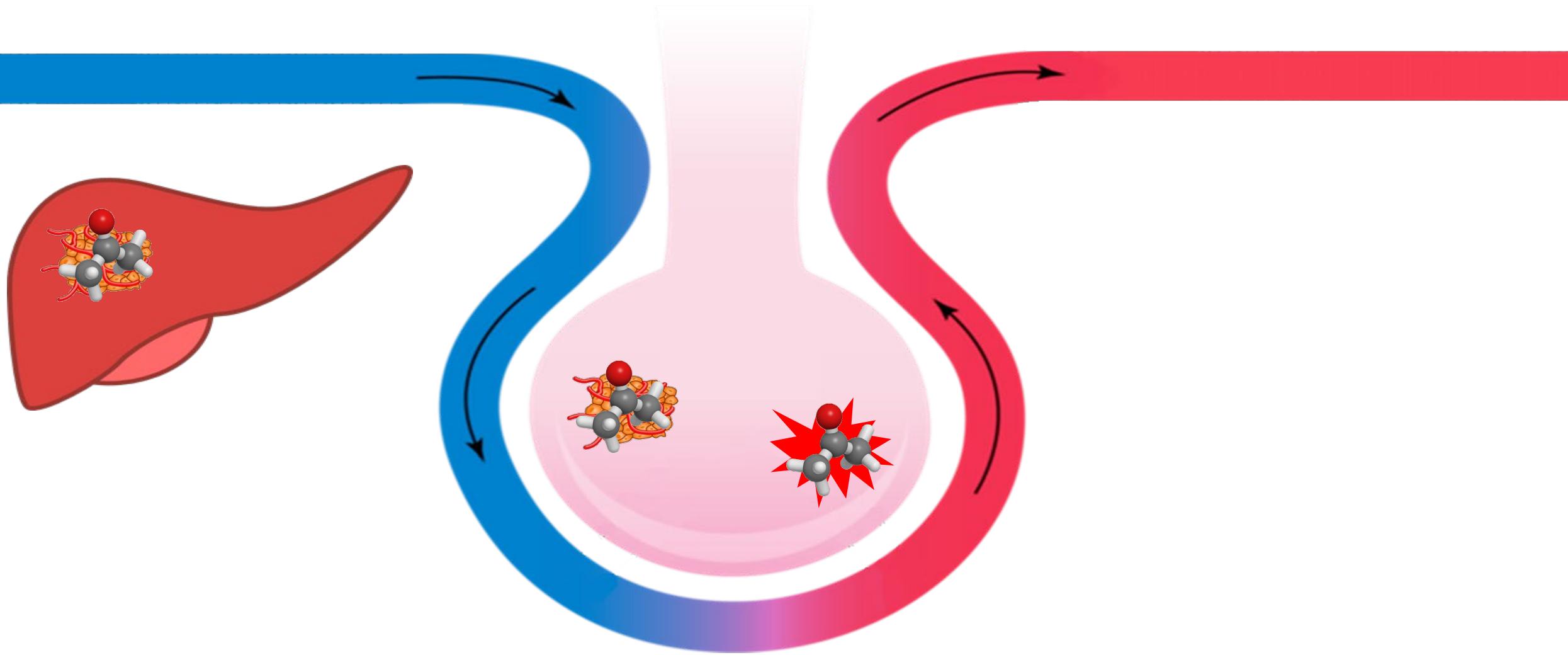
Table 5. List of the alcohols identified in studies

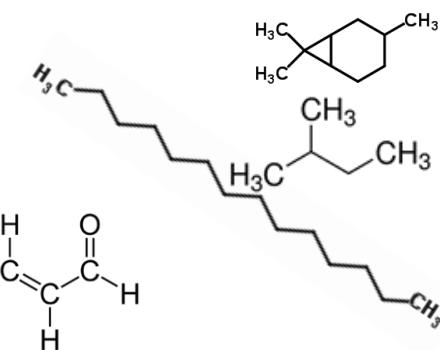
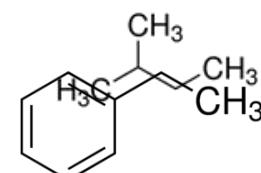
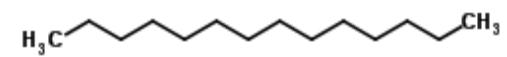
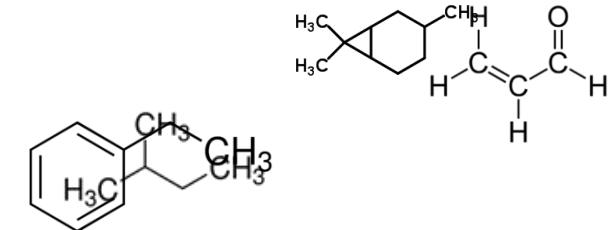
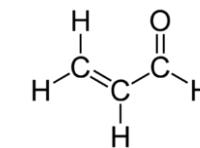
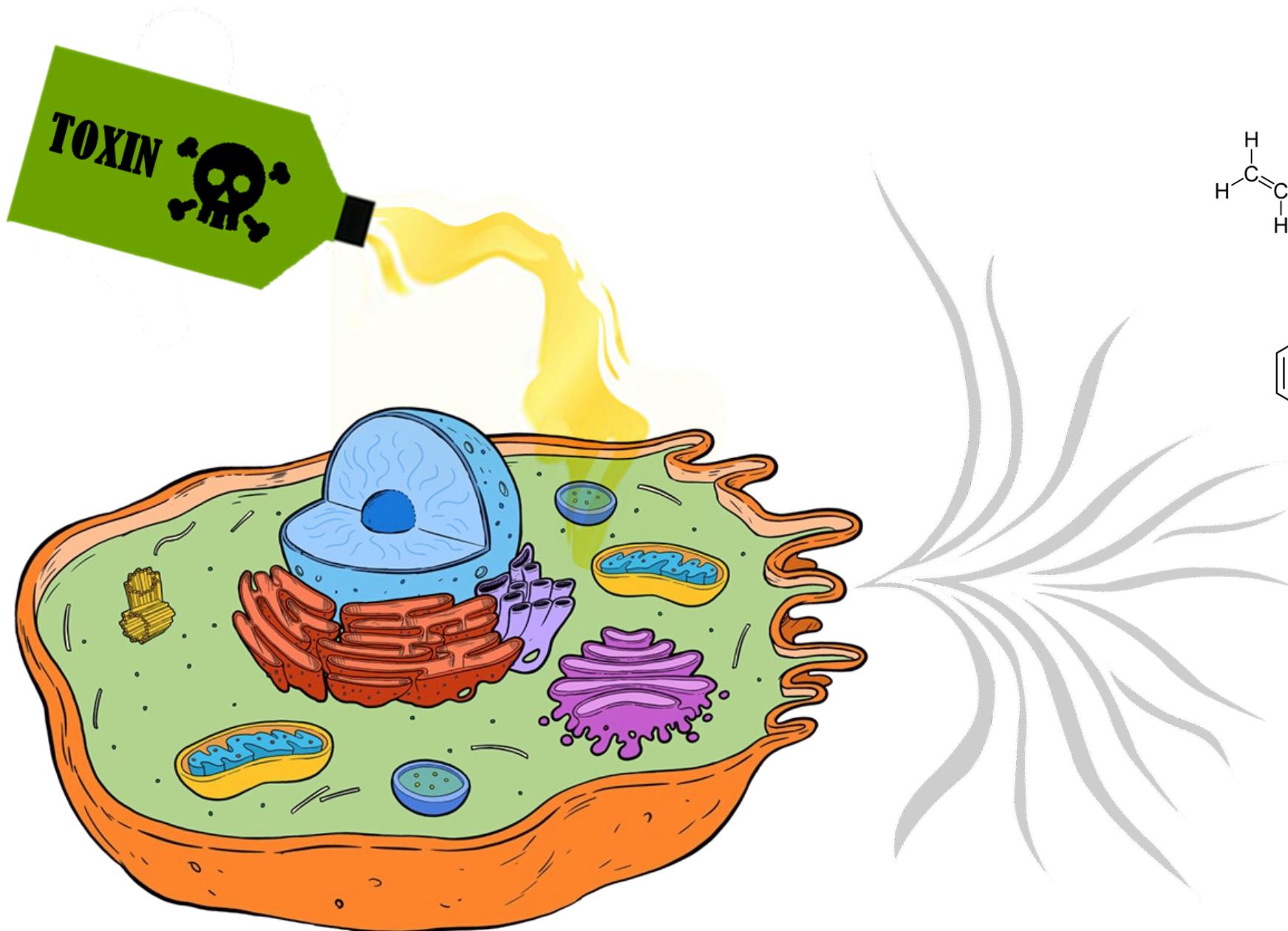
Compounds	[Ref.]									
	[24]	[25]	[26]	[27]	[28]	[29]	[30]	[31]	[32]	[33]
p-menth-1-en-8-ol	X									
Isopropyl alcohol	X									
5-Isopropenyl-2-methyl-7-oxabicyclo[4.1.0]heptan-2-ol	X									
2,2,4-Trimethyl-1,3-pentanediol	X									
diisobutyrate										
9,10-Anthracenediol, 2-ethyl-	X									
4-Penten-2-ol	X									
Isopropanol		X	X							
Ethyl alcohol		X	X							
2-Ethyl-1-hexanol			X					X	X	
2-Ethyl-4-methyl-1-pentanol			X					X	X	
2-Propyl-1-pentanol			X							
Methanol			X							X
1-propanol										

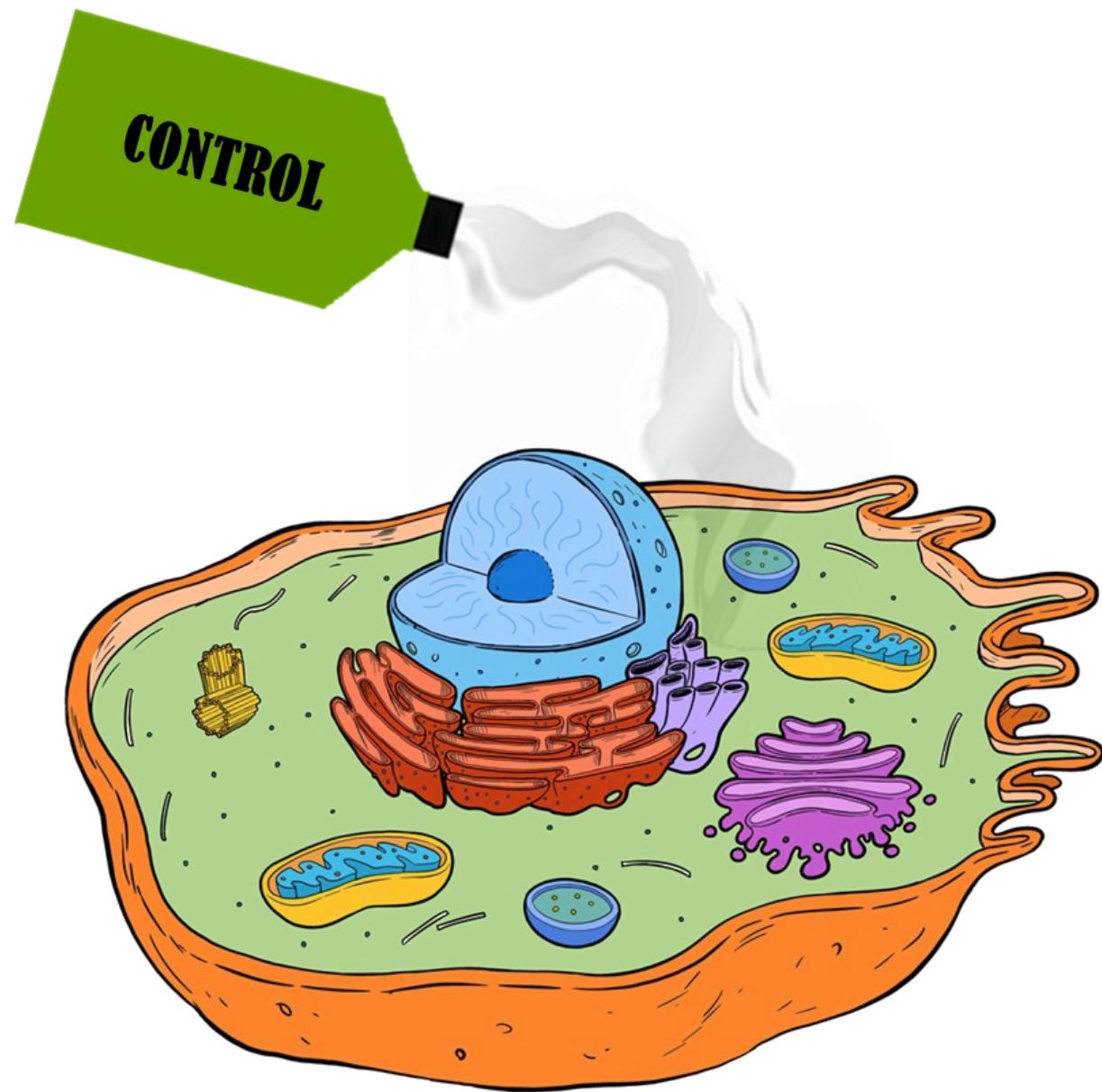
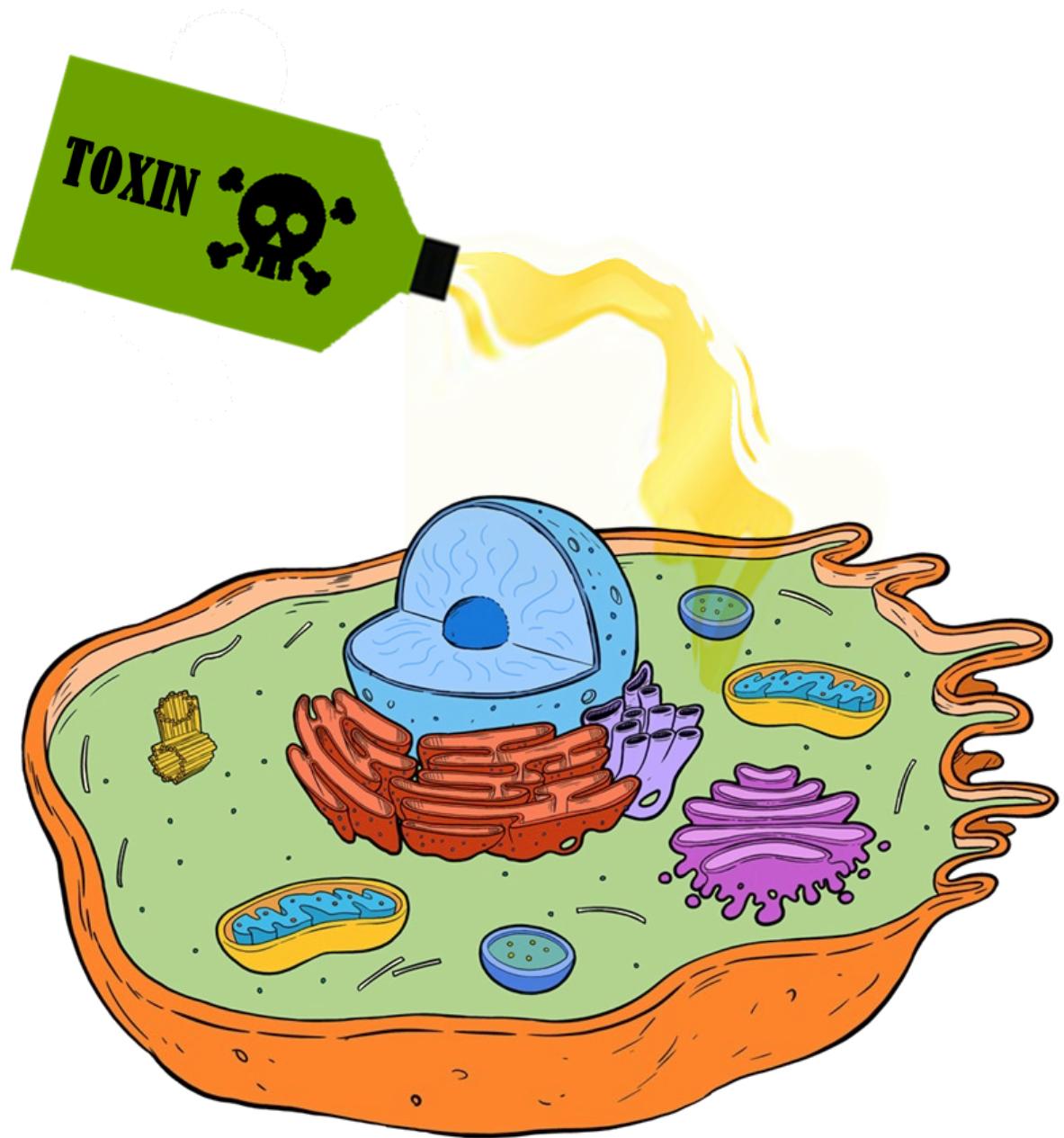
Volatile organic compounds were identified in breath except in [31–33] which were concerned with the headspace of cancer cell cultures.

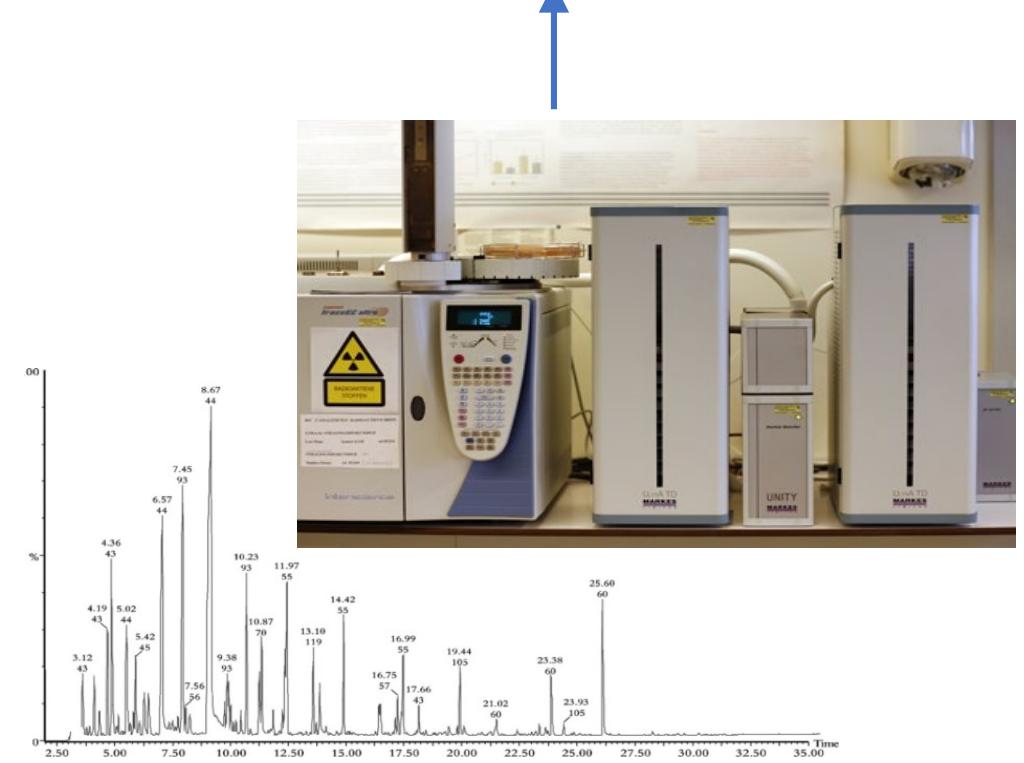
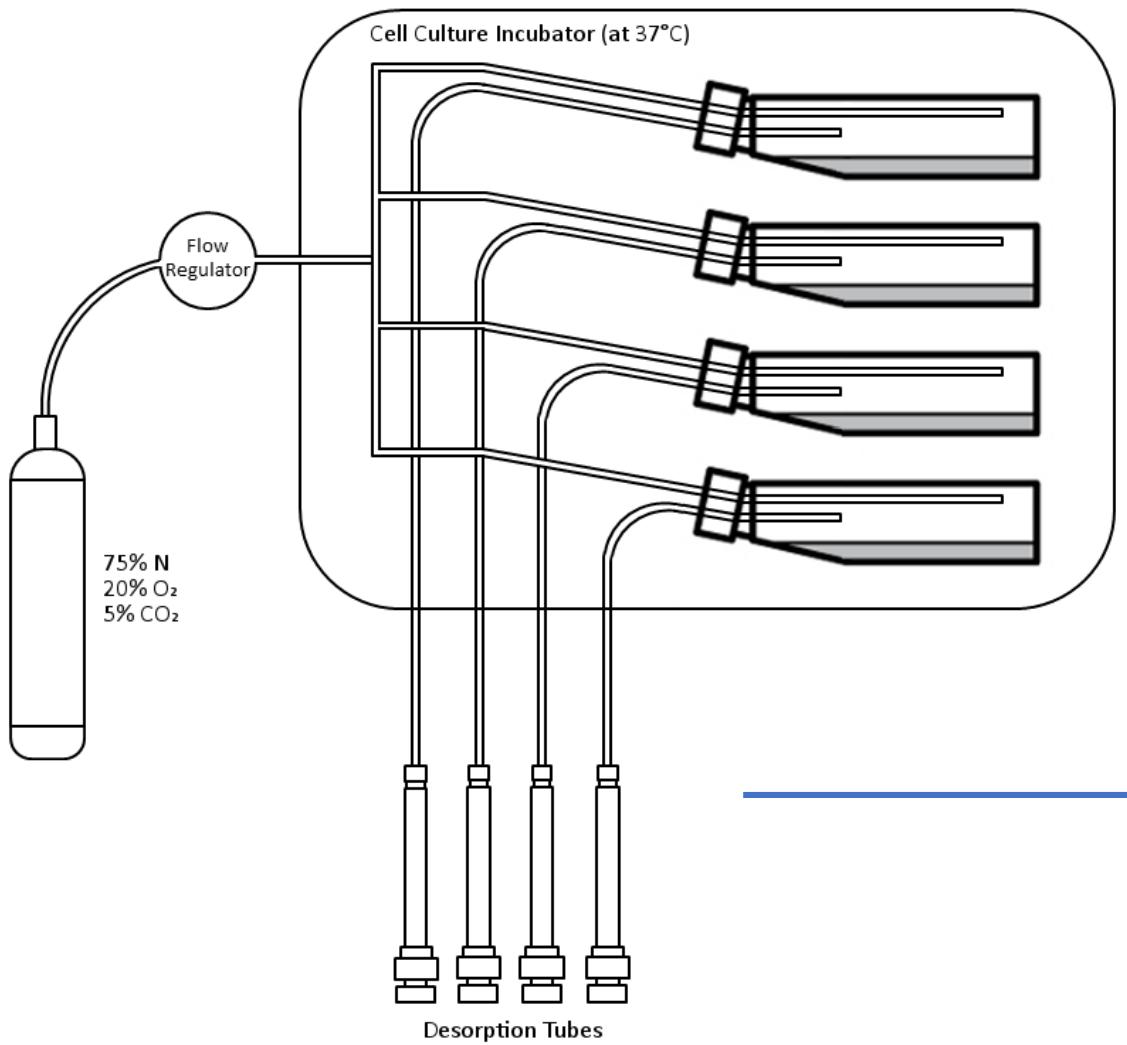
- Inter-/Intra-individual variation → SOP + devices (ReCIVA)
- Reliability of models → Multivariate statistics
- Reproducibility → External validation
- Reliability of VOCs → Biological knowledge

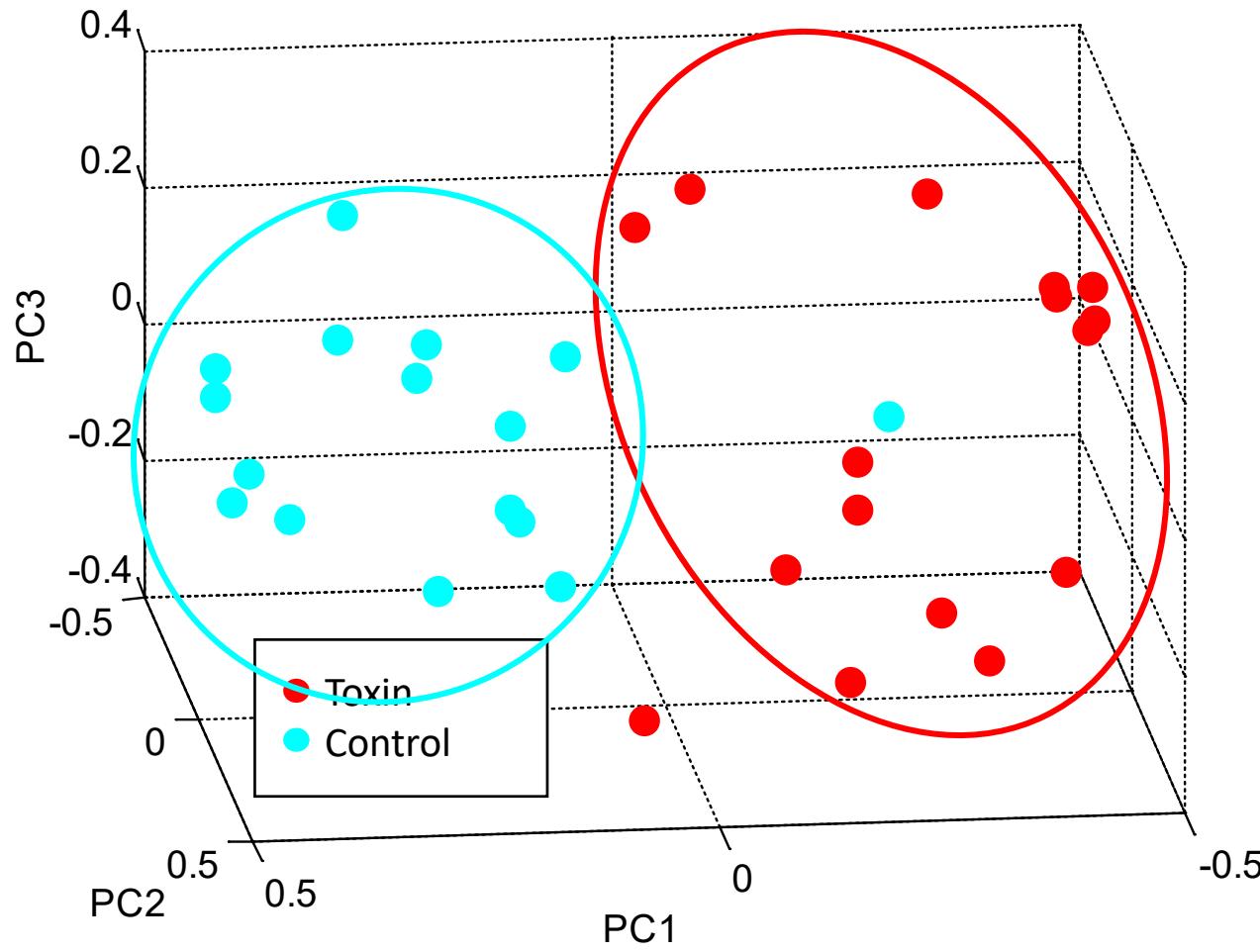
Hypothetical biological origin of VOCs











Octadecane

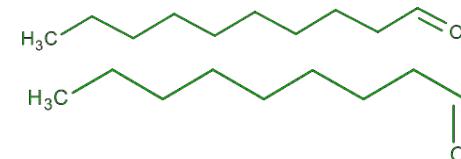
- Lipid peroxidation / oxidative stress

Unknown VOC

?

Nonanal & Decanal

- CYP450 activity



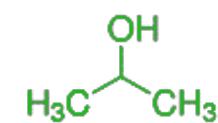
O-xylene

- Unknown

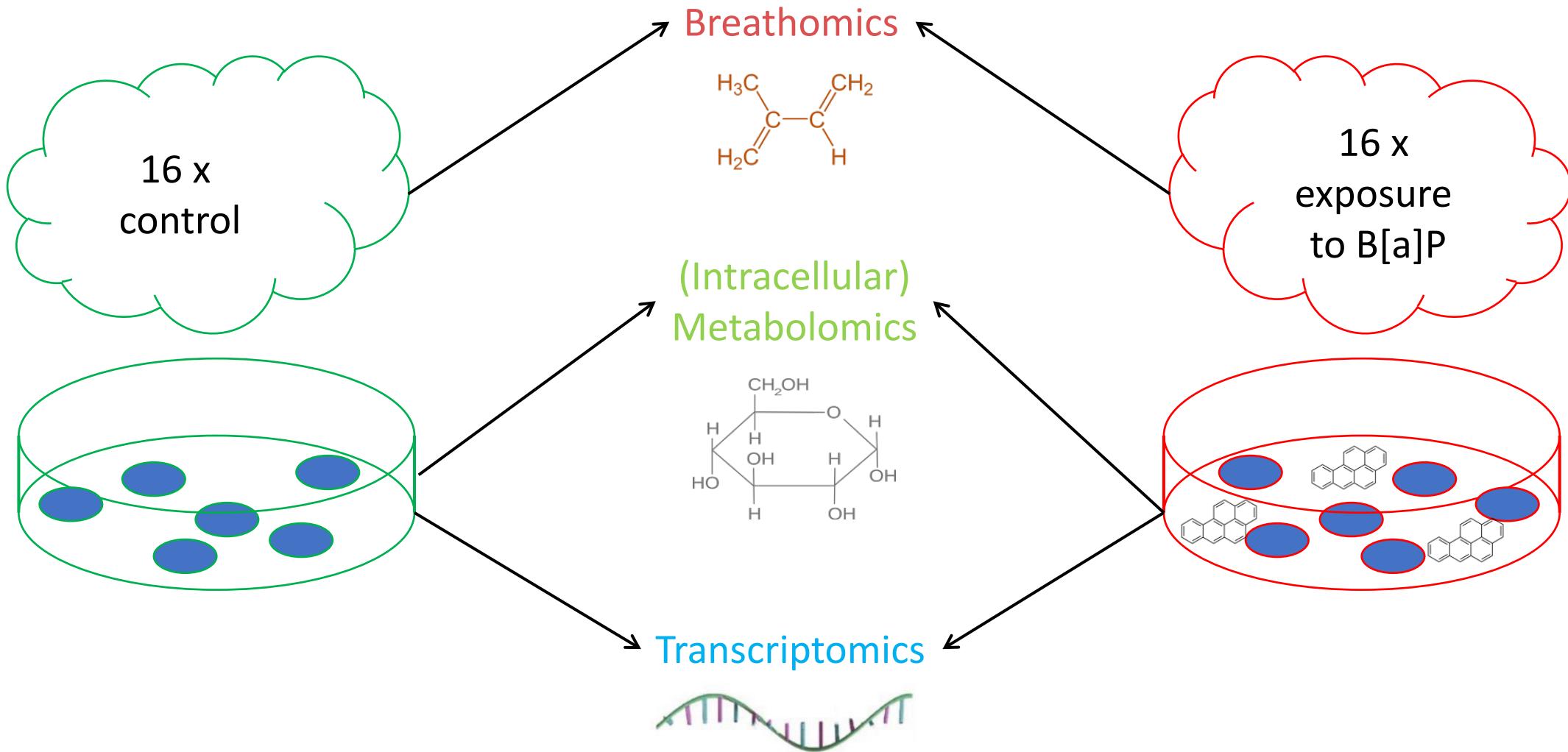


Isopropyl alcohol

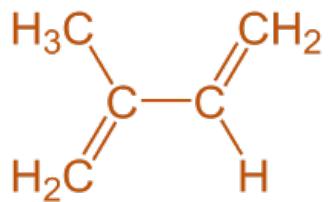
- Ketone bodies



Omics collection

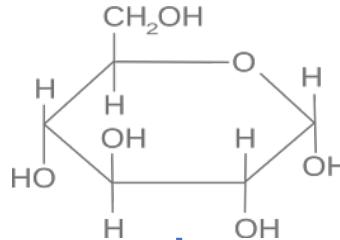


Breathomics



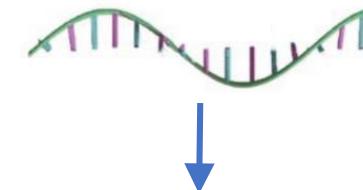
Selection of discriminatory VOCs

Metabolomics



Selection of discriminatory metabolites

Transcriptomics

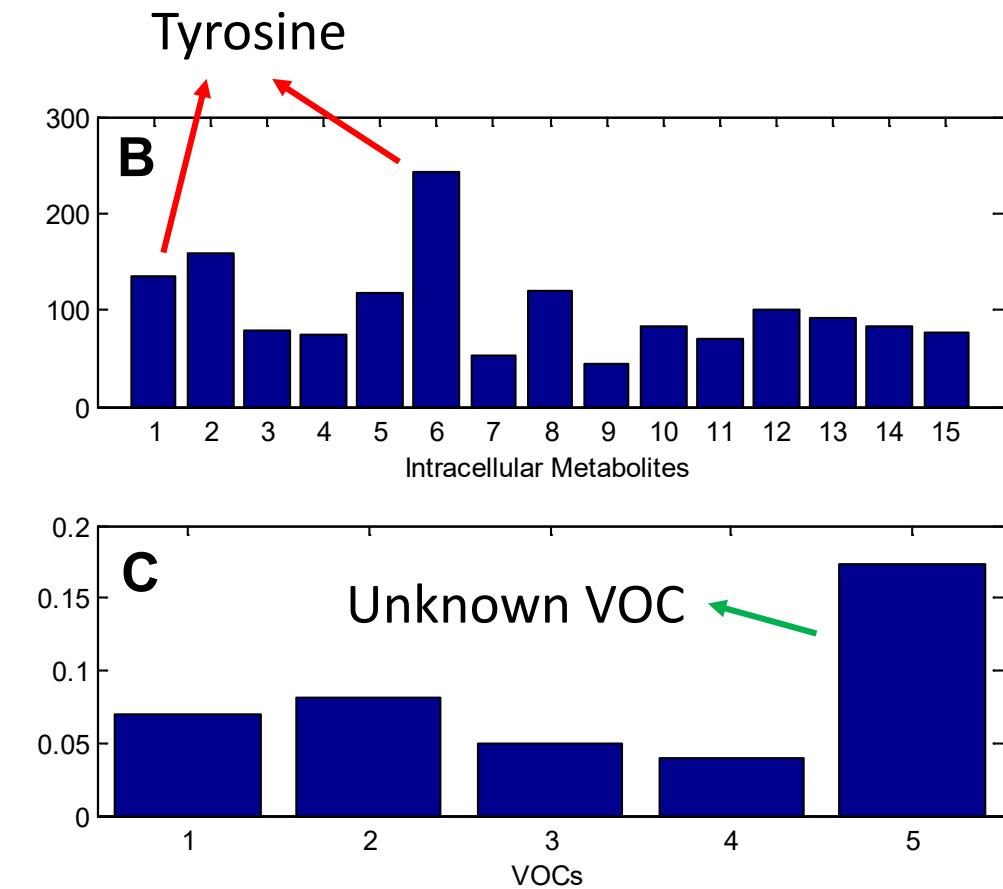
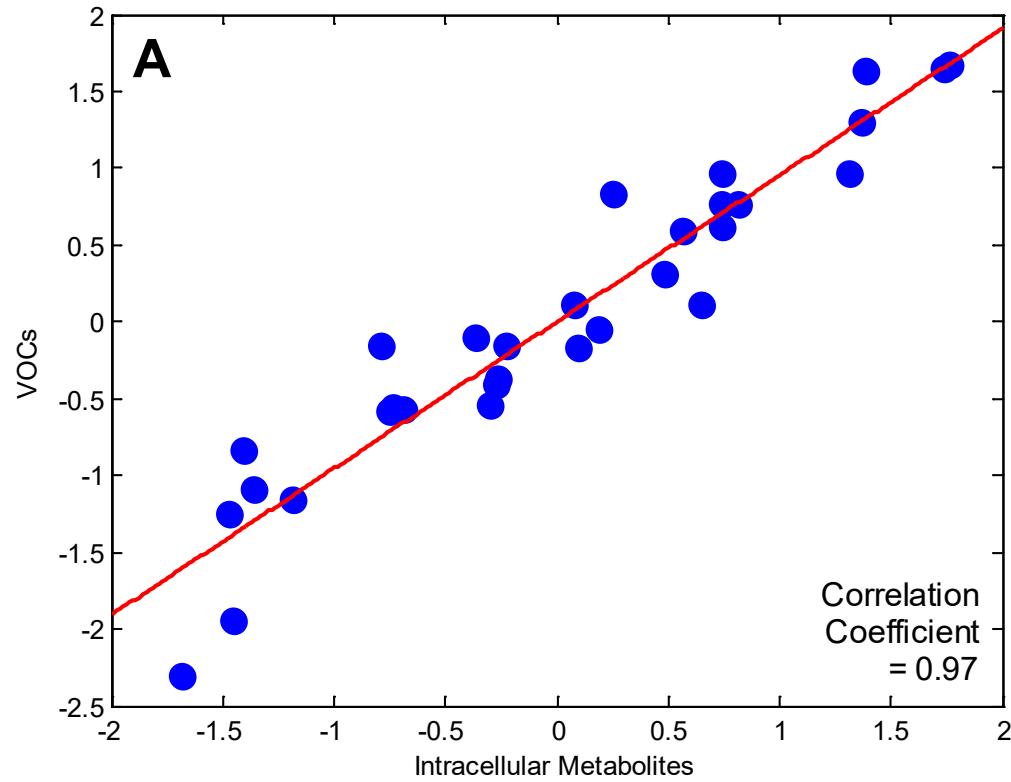


Gene set analysis to convert gene expression to pathway expression

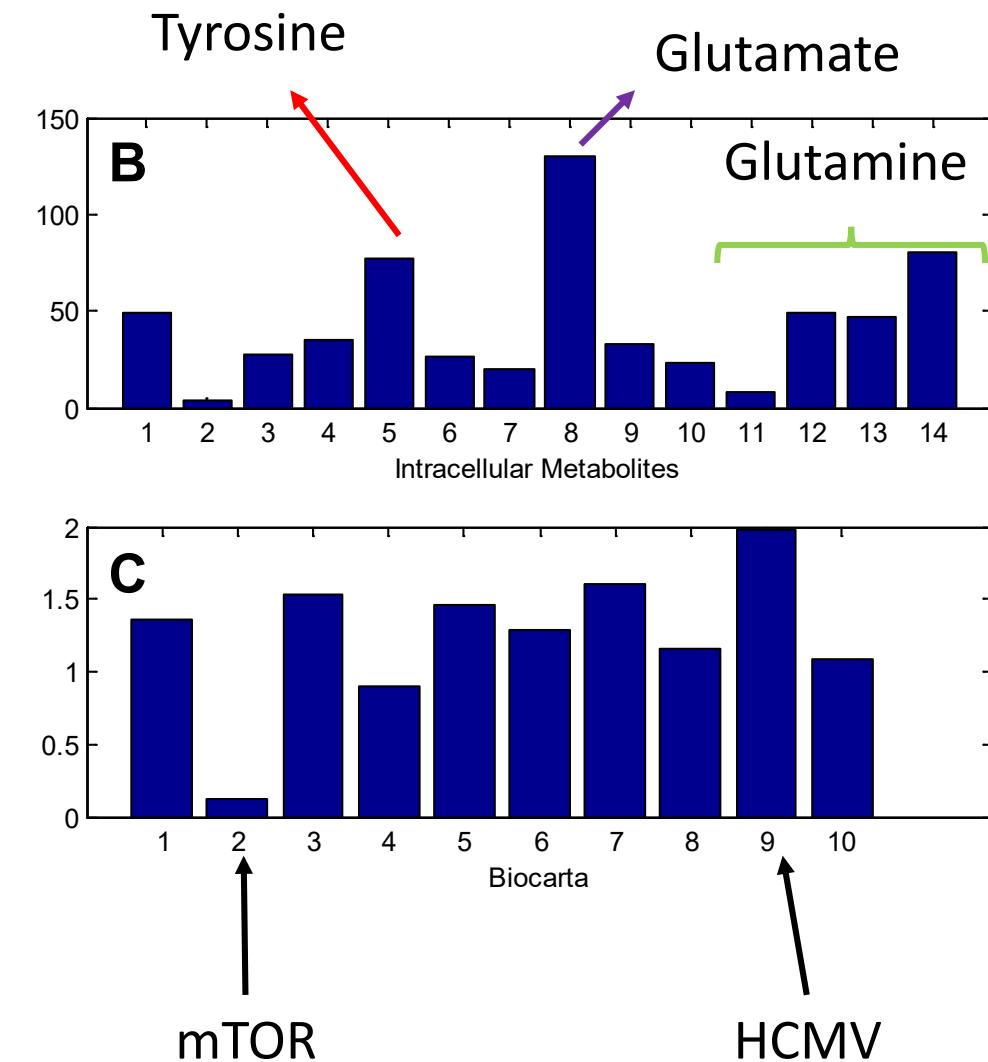
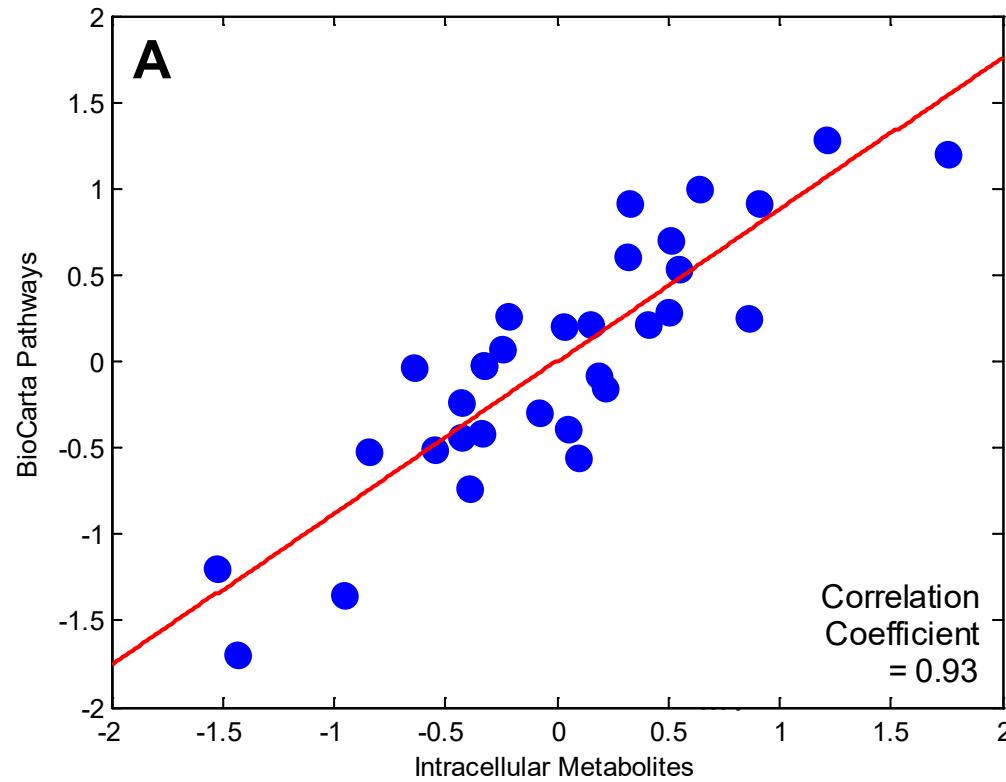
Selection of discriminatory pathways

1. Canonical Correlation Analysis (CCA)
2. Individual Pearson correlations

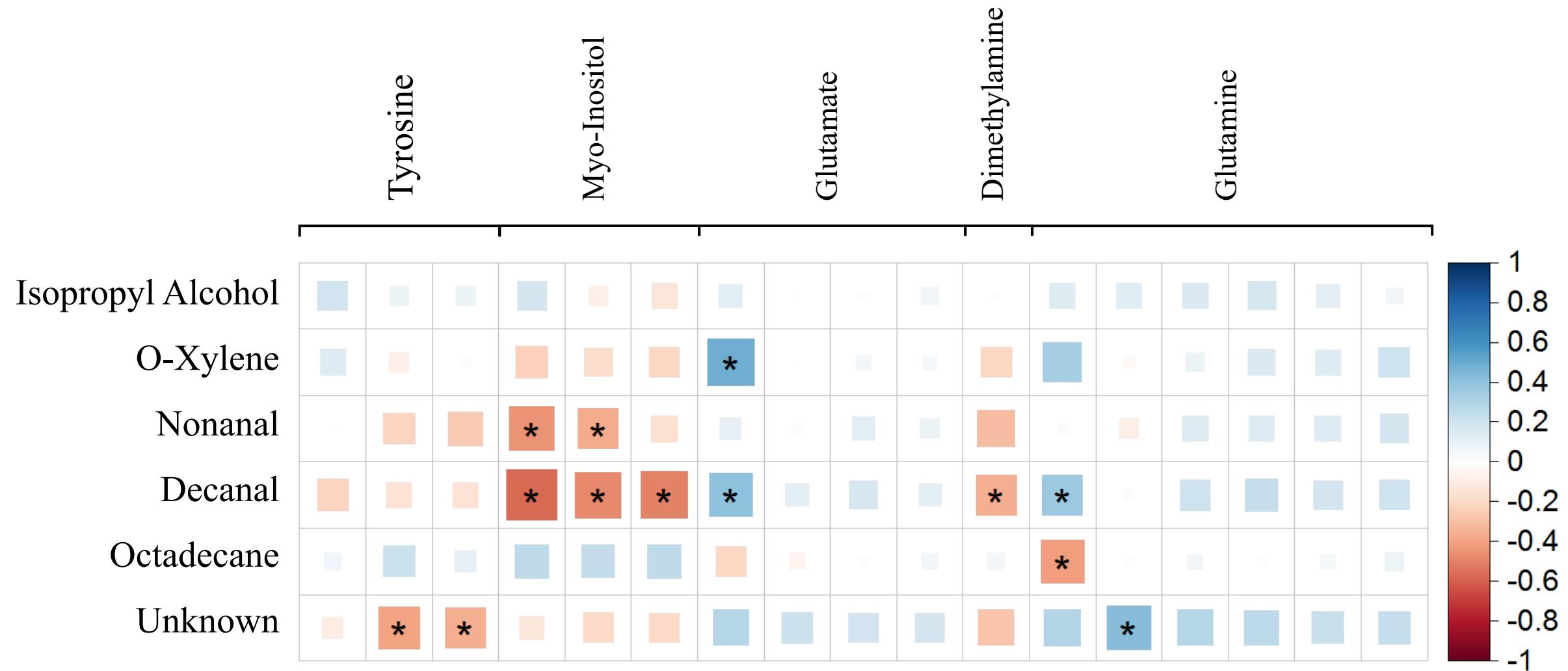
VOCs & metabolites



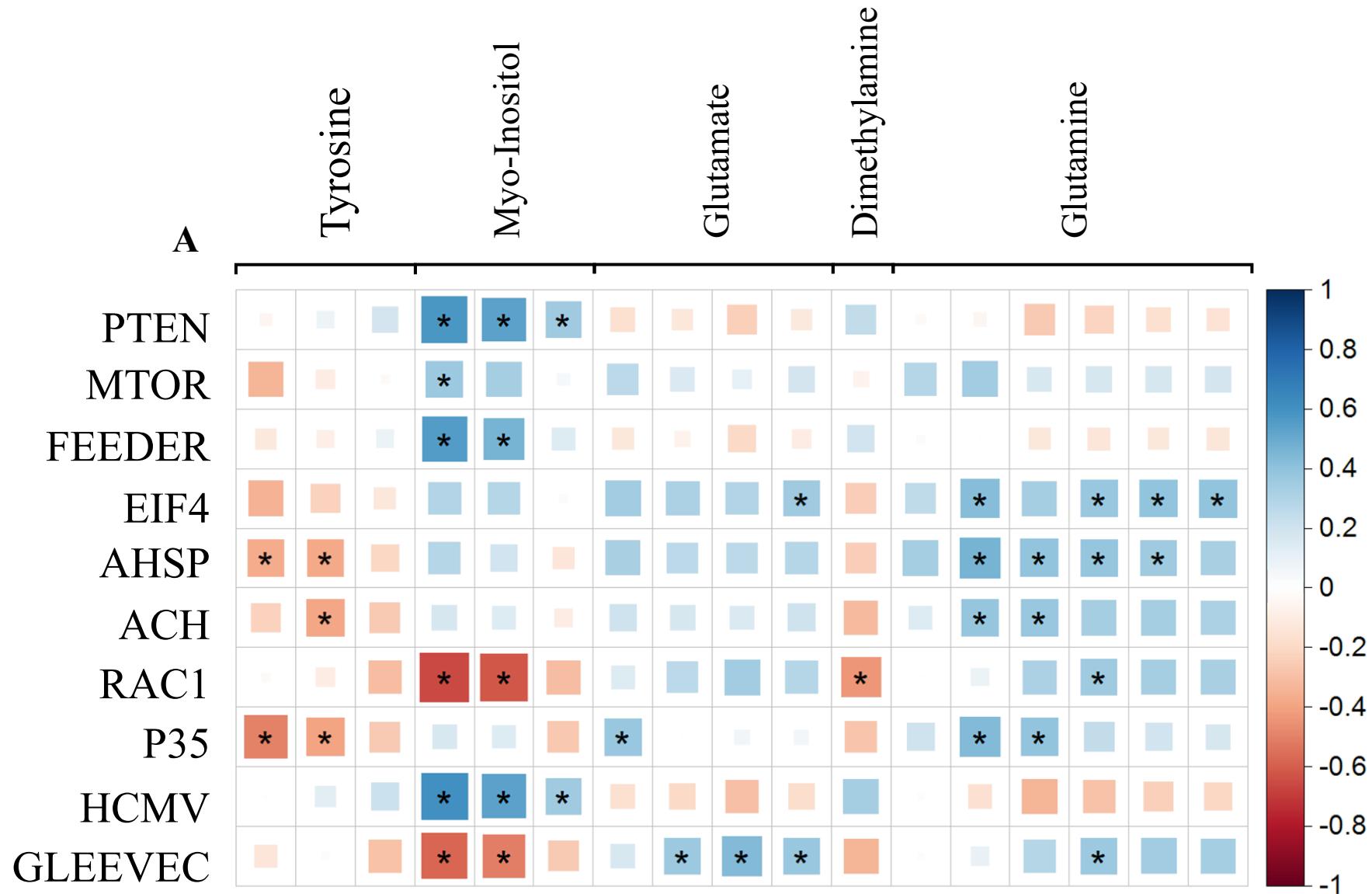
Metabolites vs. Pathways

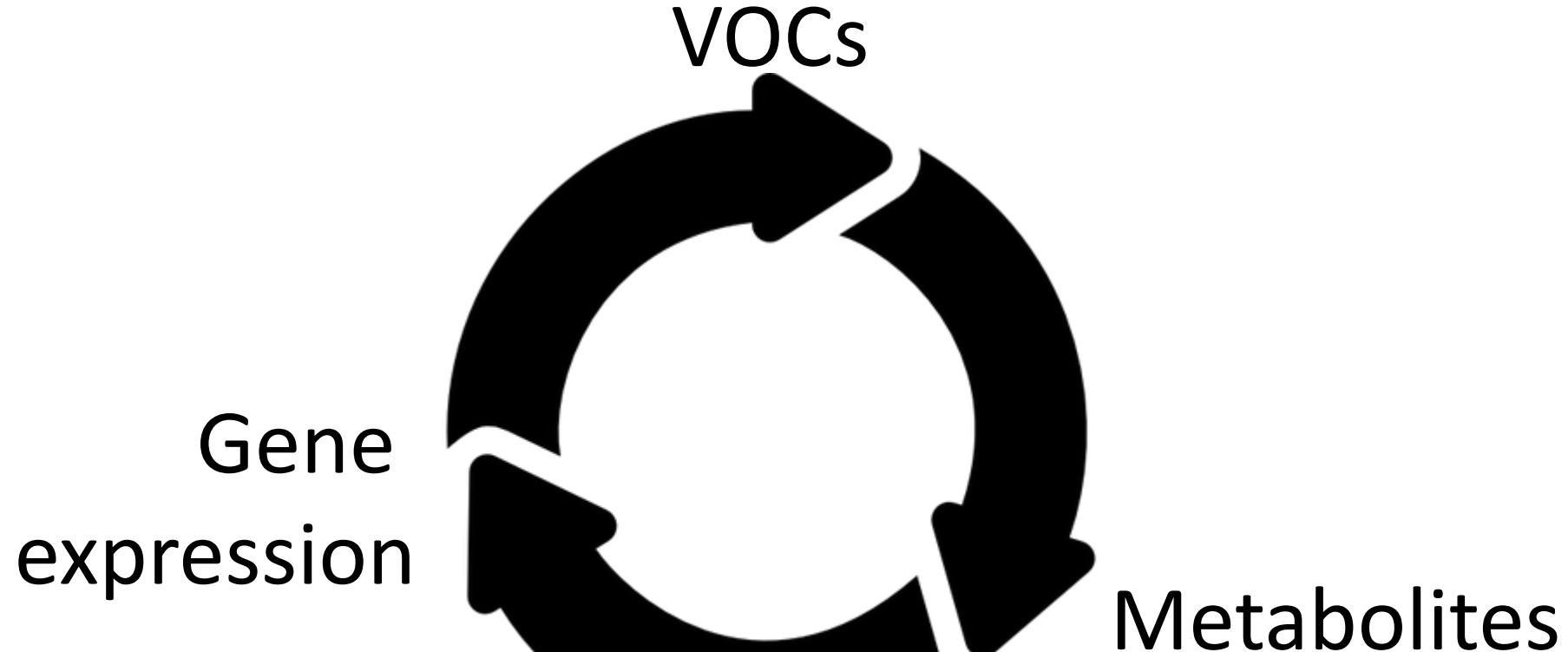


Individual correlations: VOCs vs. Metabolites



Individual correlations: Metabolites vs. Pathways



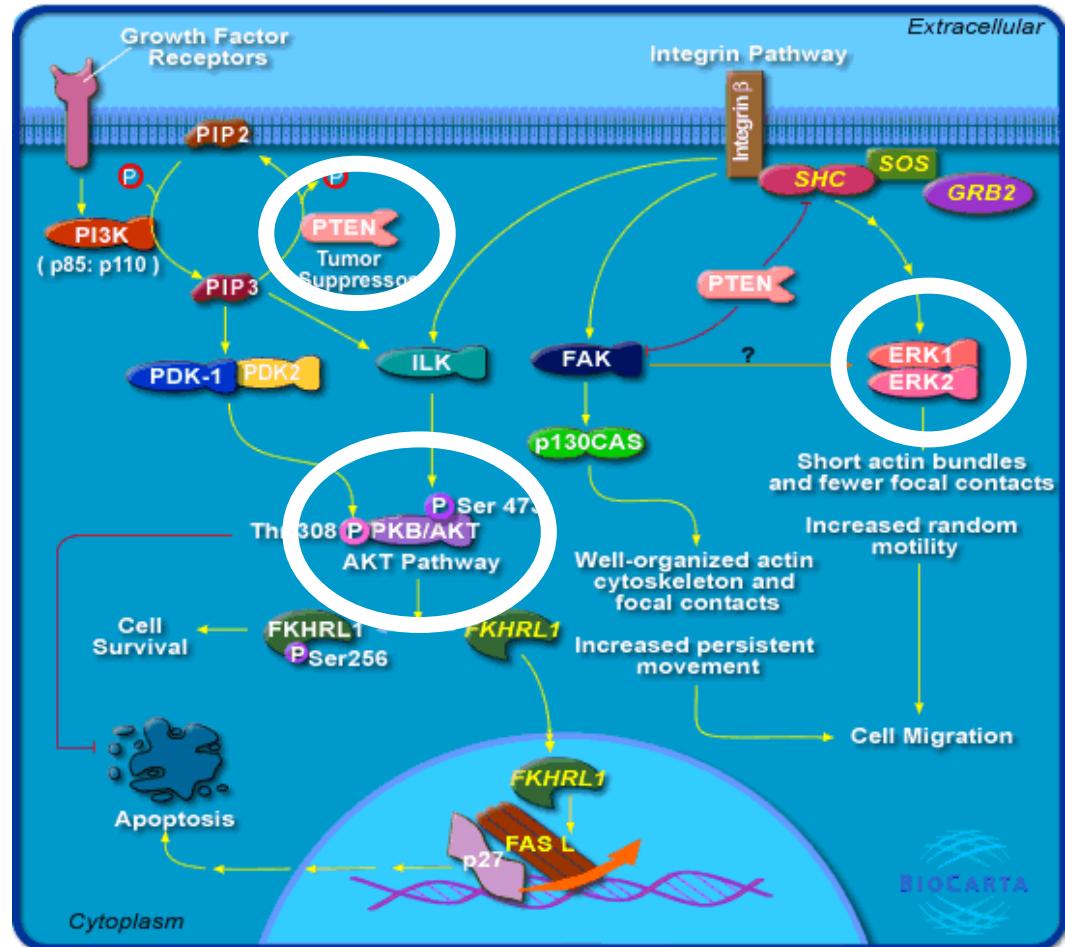


1. Decanal & Nonanal
2. Octadecane

PTEN dependent cell cycle arrest and apoptosis



Myo-Inositol ↑



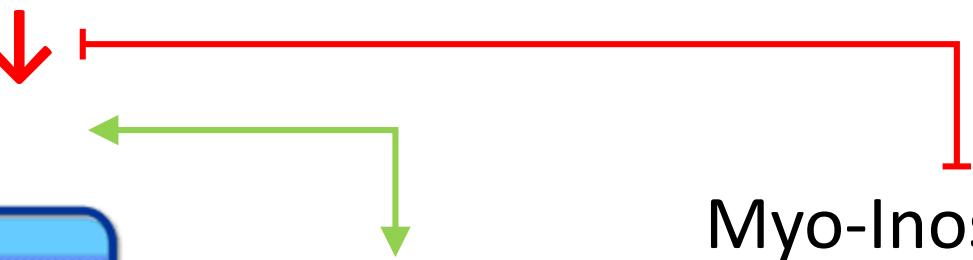
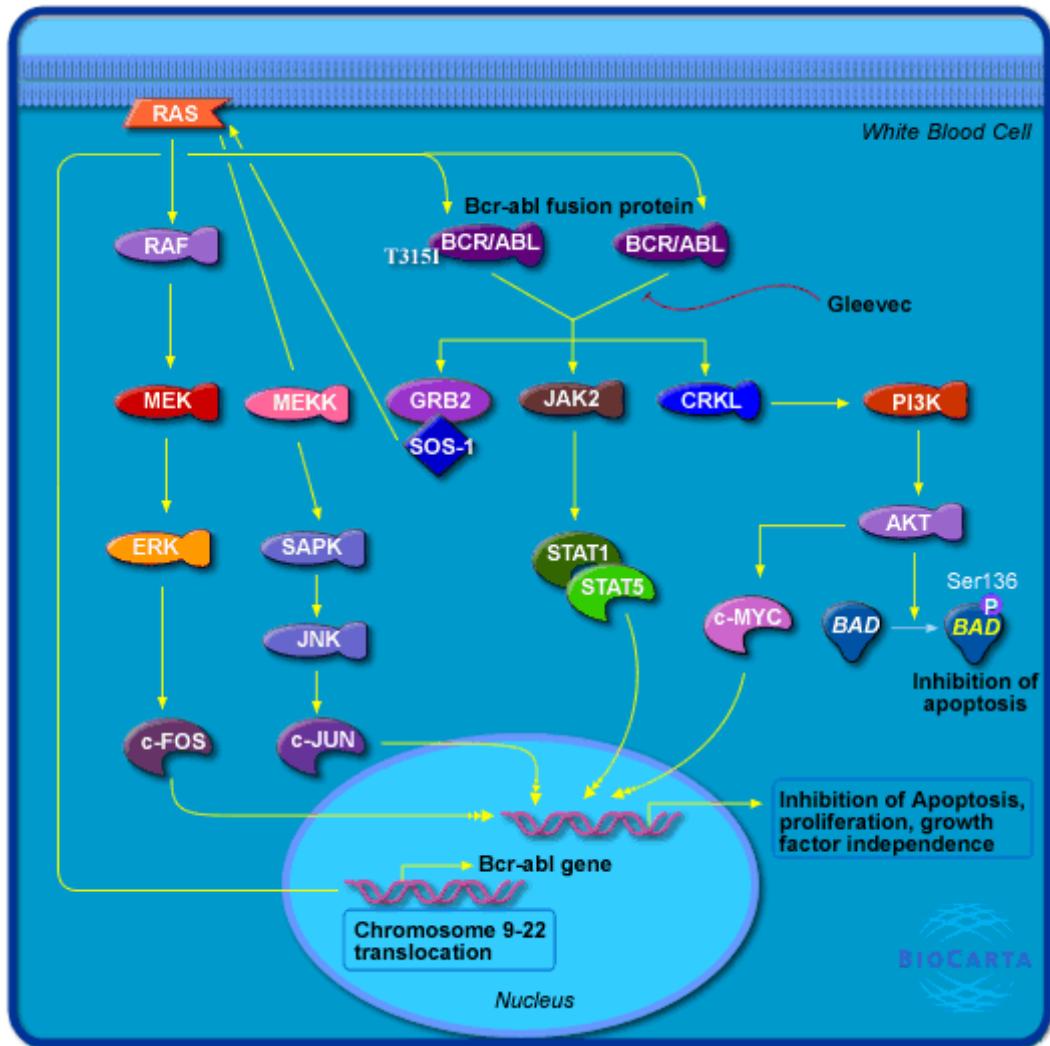
- Glucose isomer
- Involved in cell signaling, proliferation, etc.
- Can inhibit AKT/Pi3K pathway

Compensation mechanism

Decanal & Nonanal

- Aldehydes
- By-products of:
- Normal physiological processes
 - Biotransformation pathways

Inhibition of Cellular Proliferation by Gleevec



Glutamine ↓

- Amino acid
- Present in cell medium
- Involved in: biosynthesis of proteins & lipids
- Energy & carbon source

Reduced uptake due to DNA damage

Myo-Inositol ↑

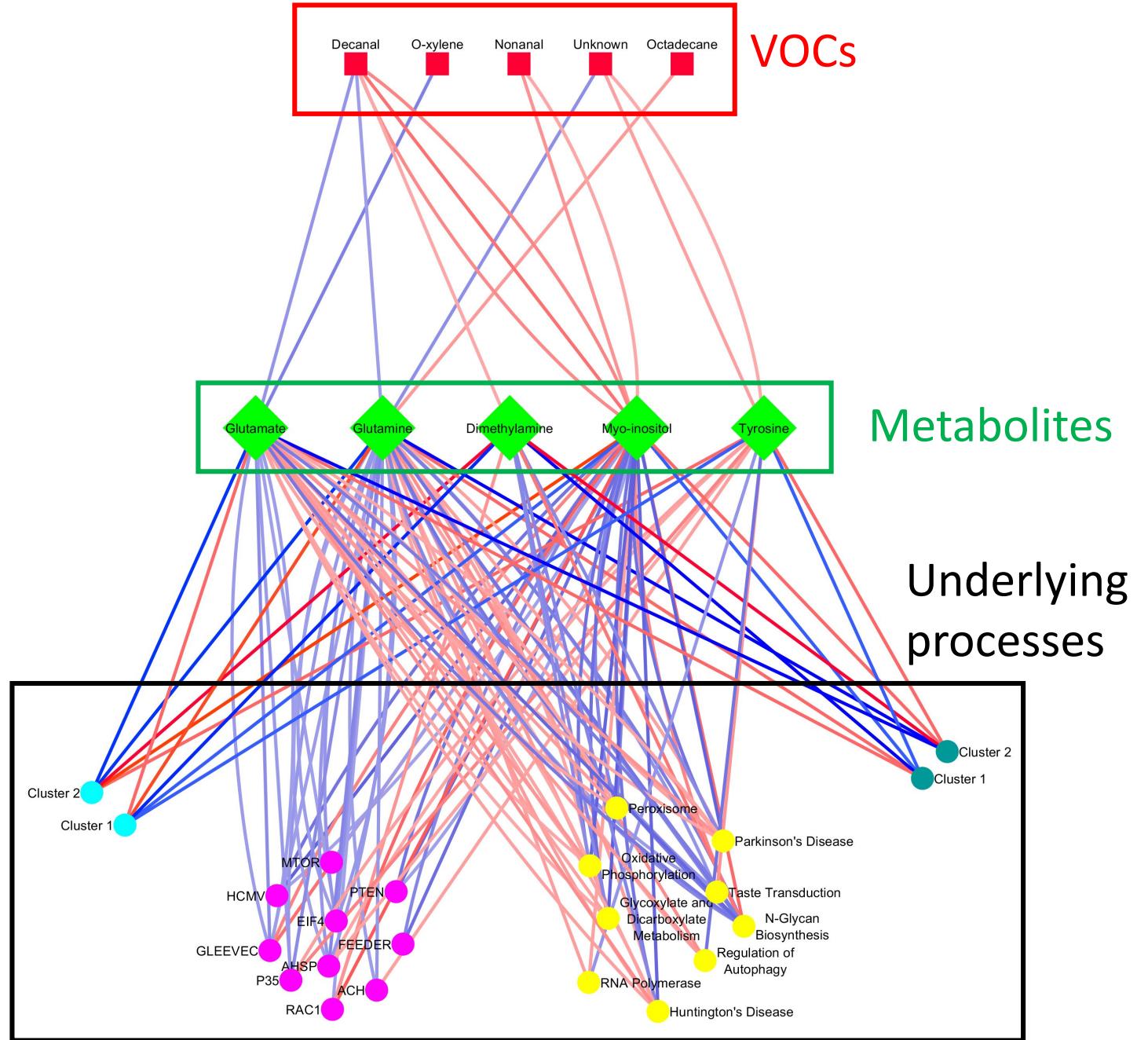
- Stimulates cell growth and survival

Again a compensation mechanism

Octadecane ↑

By-product of :

- Oxidative stress
- Dna damage
- Lipid peroxidation



VOCs

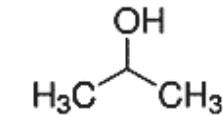
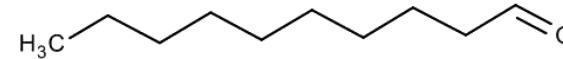
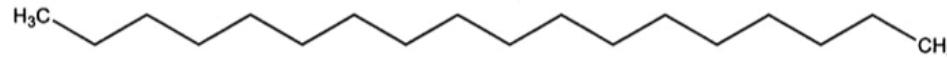
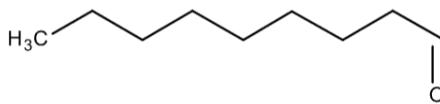
Metabolites

Underlying
processes



Conclusions

- Association ≠ Causation, but...
- Several VOCs identified as **viable targets** for further research



- Next step: Prove causation; **narrow down** potential predictors of disease/exposure

Acknowledgements



F. Van Schooten



A. Smolinkska



A. Boots

And...

- Quan Shi
- Danielle Pachen
- Jan Dallinga