Endocrine and metabolism disrupting chemicals in plastic food packaging: Addressing the unknowns

Sarah Stevens
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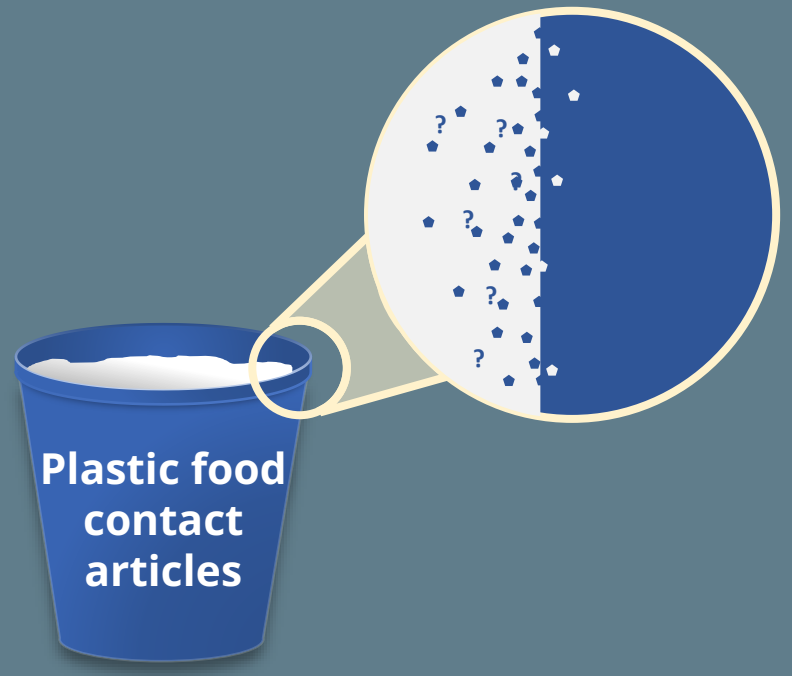
Zürich, 28.10.2024



This project has received funding from the European Union's Horizon 2020 research and
innovation programme under the Marie Skłodowska-Curie grant agreement No 860720

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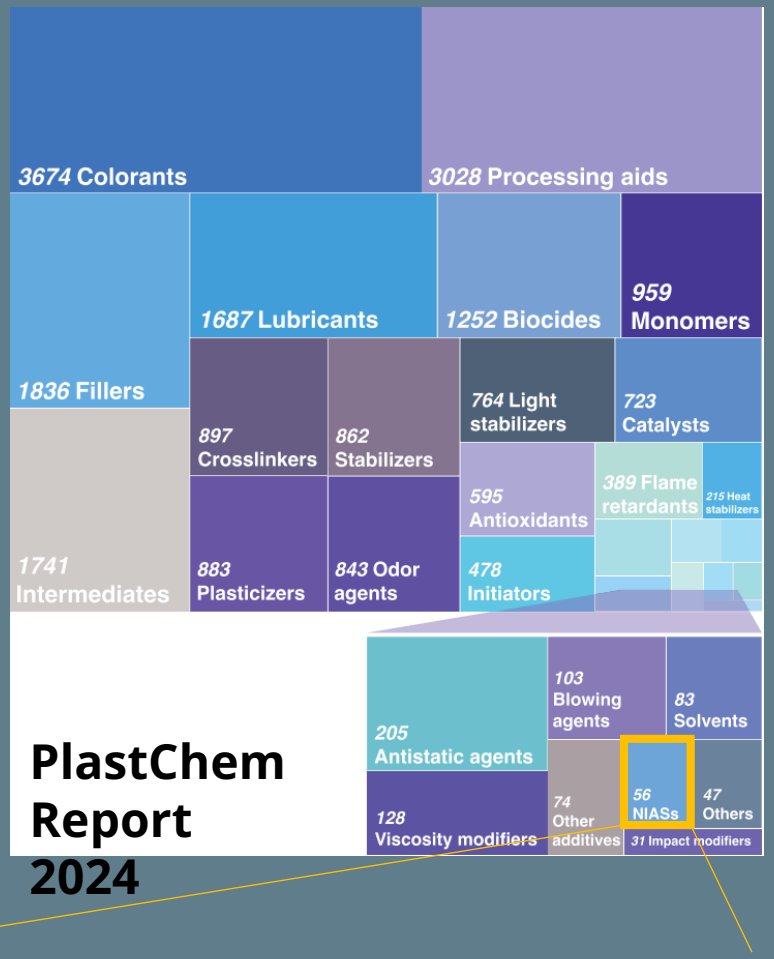
16 000 plastic chemicals

Intentionally added substances

- **Monomers**
- **Catalysts**
- **Solvents**
- **Additives: Plasticizer, UV stabilizer, Flame retardants, Colorants…**

- **No data for >10 000**
- > 4 200 are hazardous (PBMT)



Non-intentionally added substances (NIAS)

- **Impurities,** reaction by-products, breakdown products
- But: estimations ~ 100 000 (Grob 2019)

Wagner et al., 2024

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Migration of plastic chemicals

- **Human exposure via foods**

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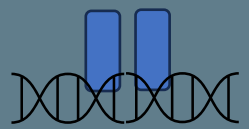
Endocrine Disrupting Compounds (EDC)

- Estrogen Receptor α (ERα)
- Androgen Receptor (AR)



Nuclear

Metabolism Disrupting Compounds (MDC)

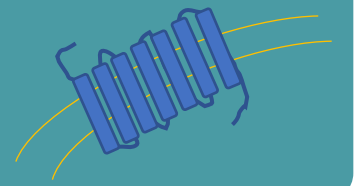
- Peroxisome Proliferator Receptor γ (PPARγ)
  Key receptor of adipogenesis
- Pregnane X Receptor (PXR)
  Xenobiotic sensor &
  energy homeostasis

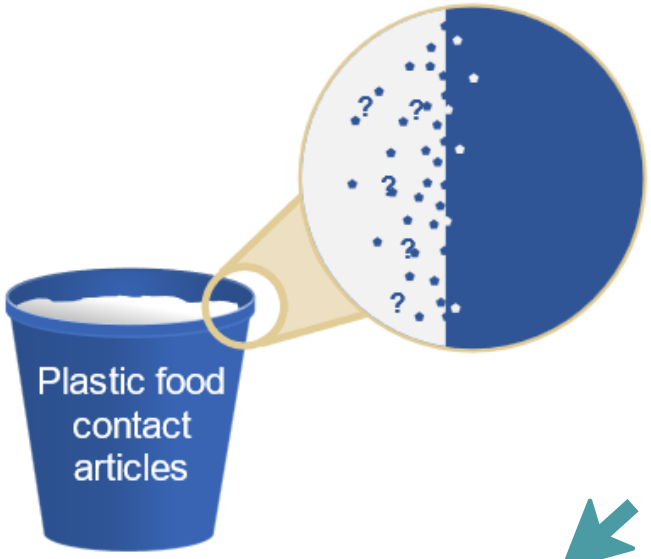
Nuclear

Additionally

G-Protein Coupled Receptors (GPCR)

- Cell-surface receptors
- 80% of transmembrane signaling
- Non-genomic signaling
- Important drug targets (35%)





Are humans exposed to EDCs and MDCs from plastic food contact articles (FCA)?

Effect-based tools & nontarget chemicals analysis

Cell-surface Receptors

GPCRs
Are other receptors disrupted by plastic chemicals?

Nuclear Receptors

Extraction
Are EDCs and MDCs present in plastic FCAs?

Migration
Do EDCs and MDCs leach into foods?

Identification
What are the active chemicals?

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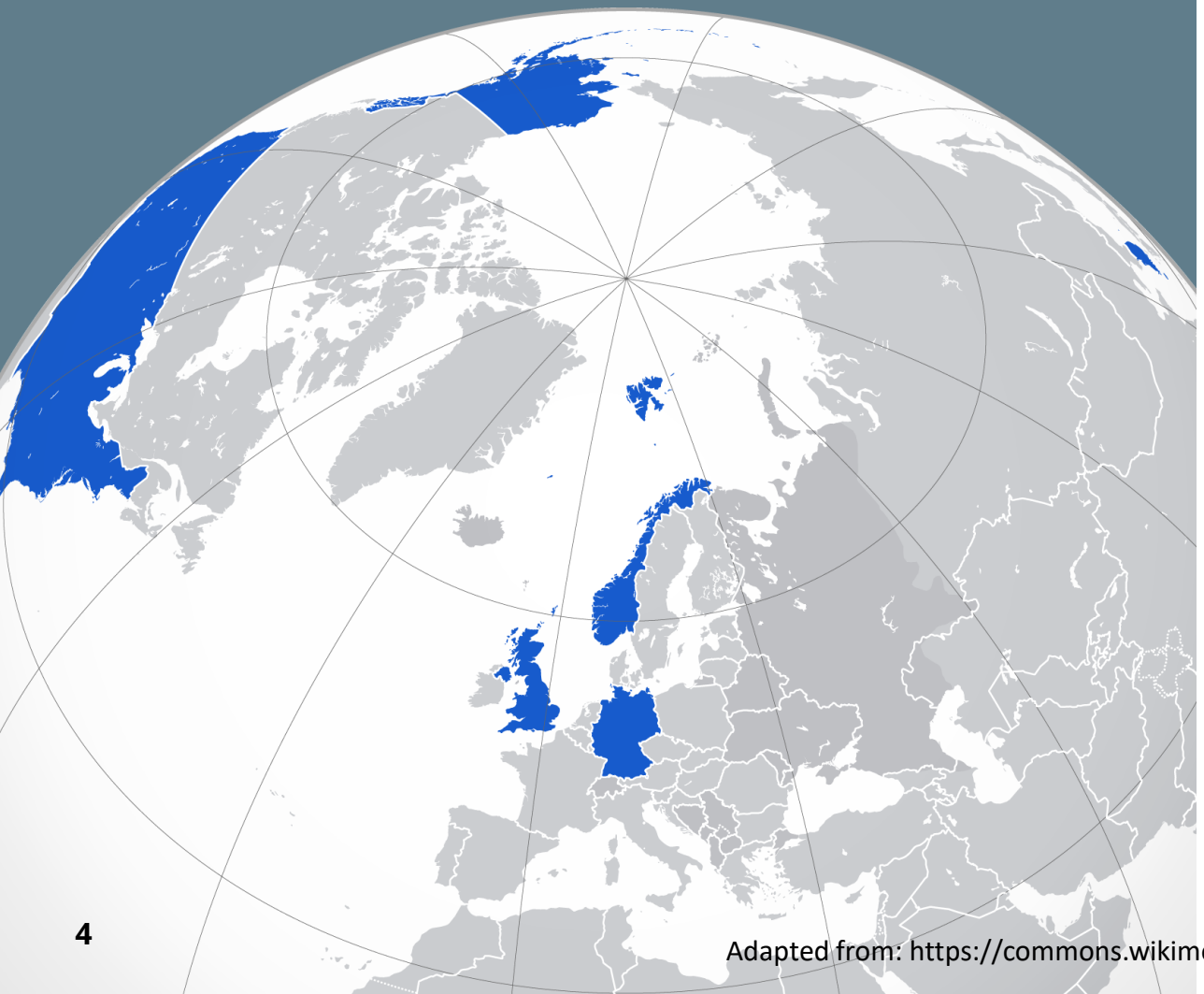
Plastic samples



- 36 food contact articles
- Made of the seven polymers with highest market / waste share

PUR

- From countries with a high plastic waste generation per capita USA, UK, South Korea, Germany, and Norway

Adapted from: https://commons.wikimedia.org/wiki/File:EU-Germany_(orthographic_projection).svg

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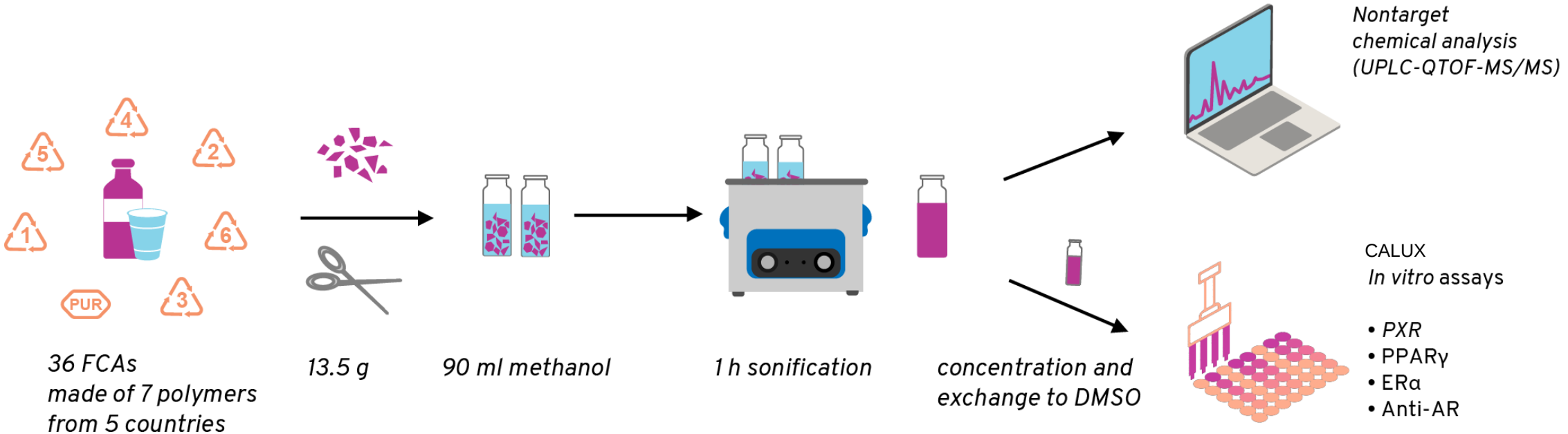
Methods



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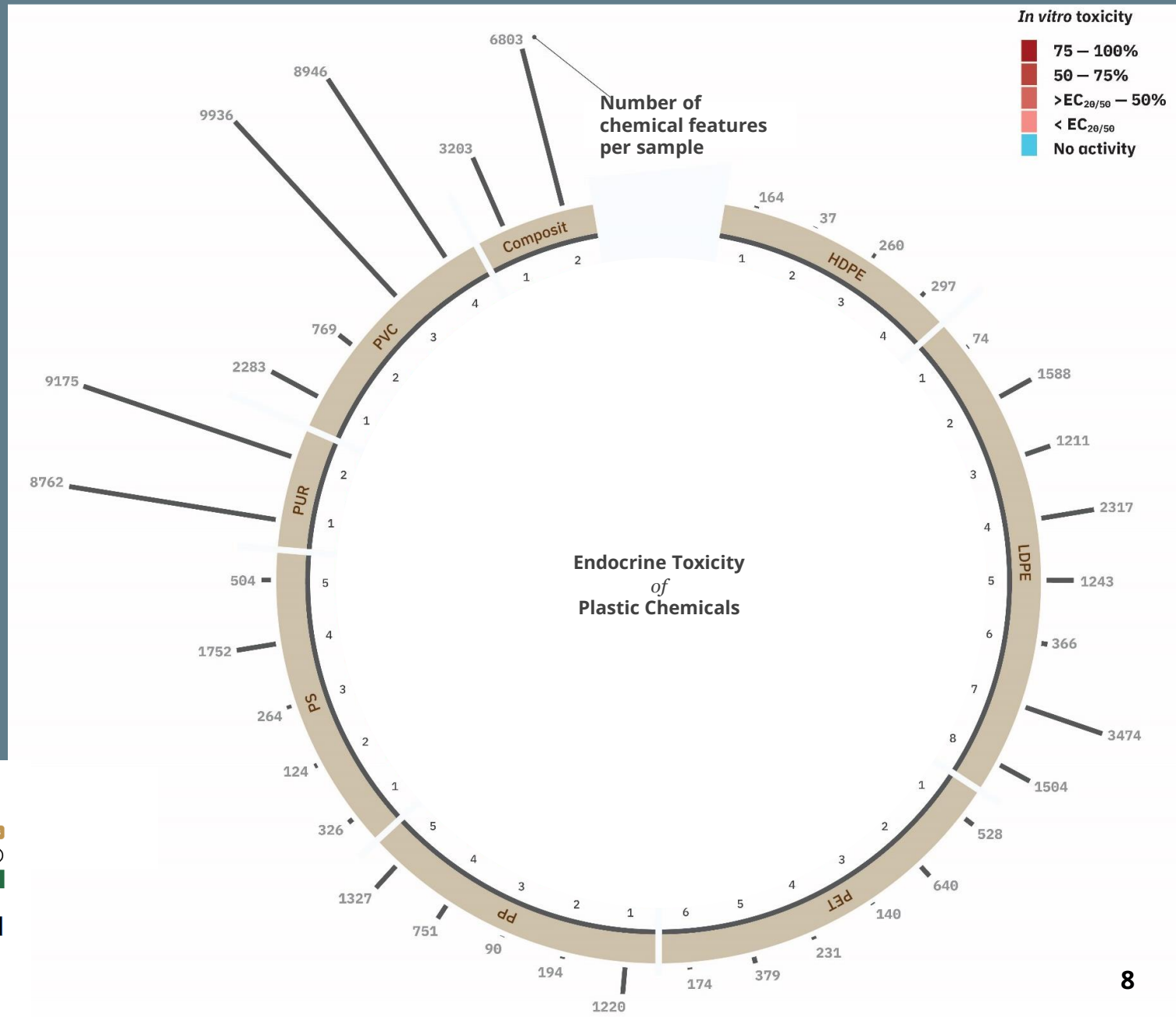
Extracts – Results

- Large chemical complexity
- Most extracts containing EDCs &MDCs
- A global issue
- Samples of all polymers inducing effects *in vitro*



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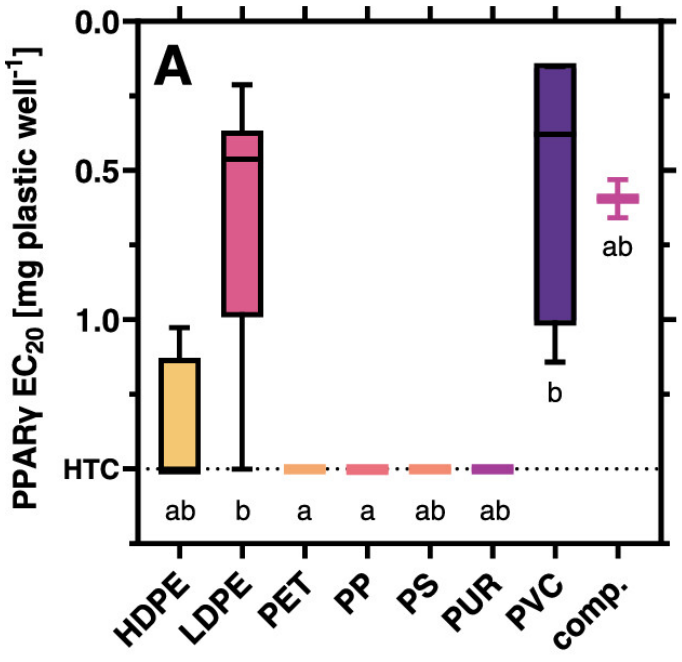
Article

Plastic Food Packaging from Five Countries Contains Endocrine- and Metabolism-Disrupting Chemicals

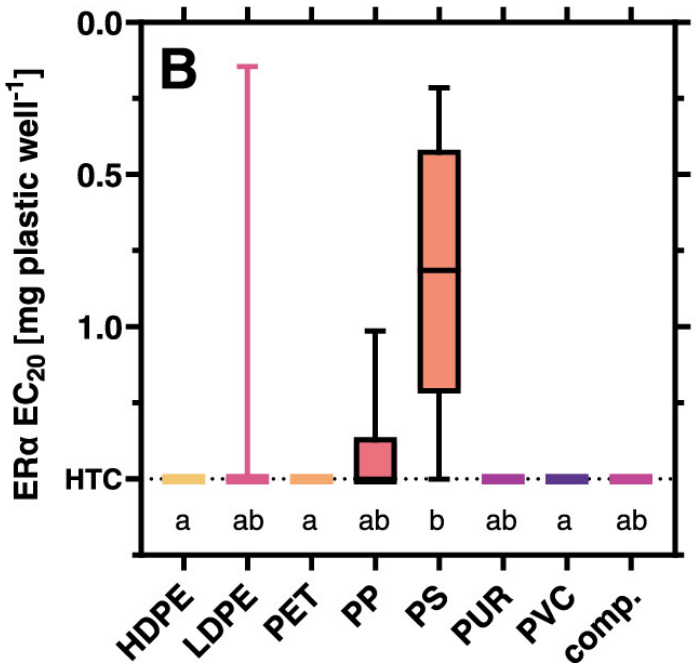
Sarah Stevens,* Molly McPartland, Zdenka Bartosova, Hanna Sofie Skåland, Johannes Völker, and Martin Wagner*

Differences across polymers

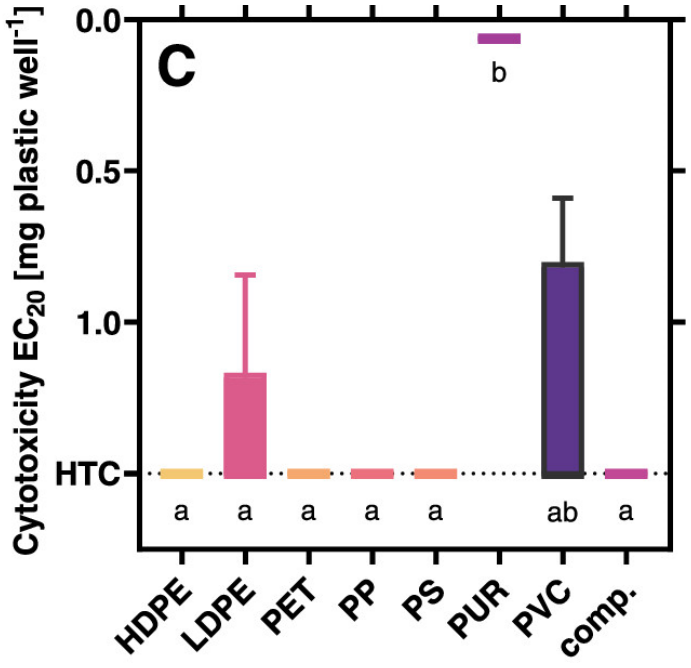
PPARγ



ERα



Cytotoxicity



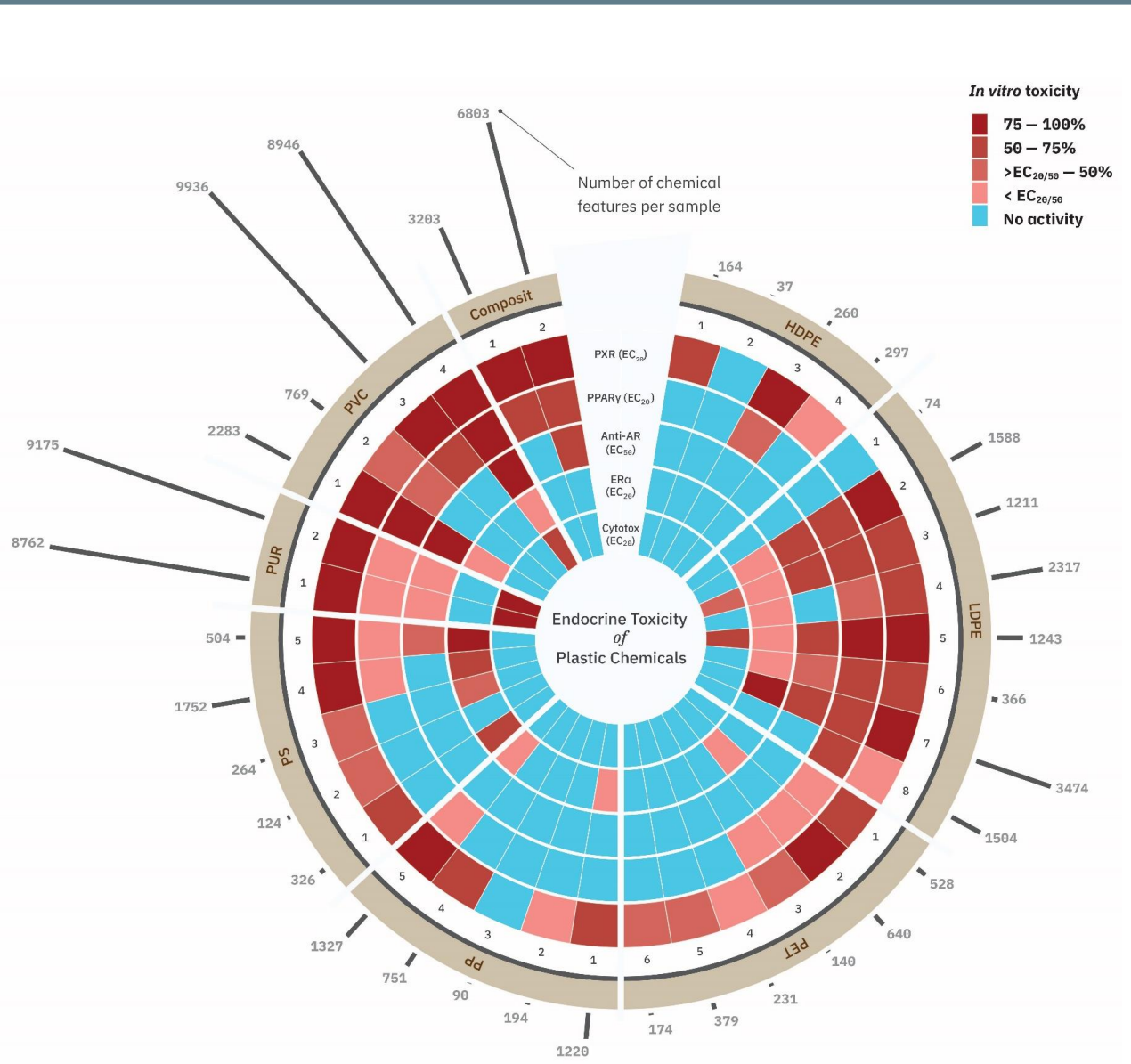
Polymers:

High- and Low-Density Polyethylene (HDPE, LDPE), Polyethylene terephthalate (PET), Polypropylene (PP), Polystyrene (PS), Polyurethane (PUR), Polyvinylchloride (PVC), Composite sample > 1 polymer (comp).

Stevens et al., 2024, ES&T

Receptor-mediated toxicity

- Most plastic extracts activated nuclear receptors
- Many (bioactive) compounds
  - ➢ Additional targets of plastic chemicals?
- G-Protein Coupled Receptors (GPCR)
- **Cell-surface receptors**
- Important drug targets



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Methods

14 FCA

MeOH Extraction

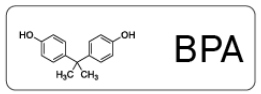
Non-target chemical analysis (UPLC-QTOF-MS/MS)

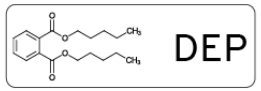
PET

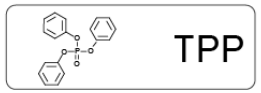
PVC

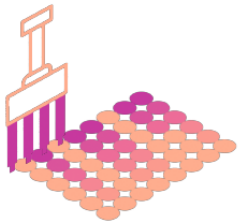
Assorted

Mix









PRESTO - TANGO 126 non-olfactory GPCRs

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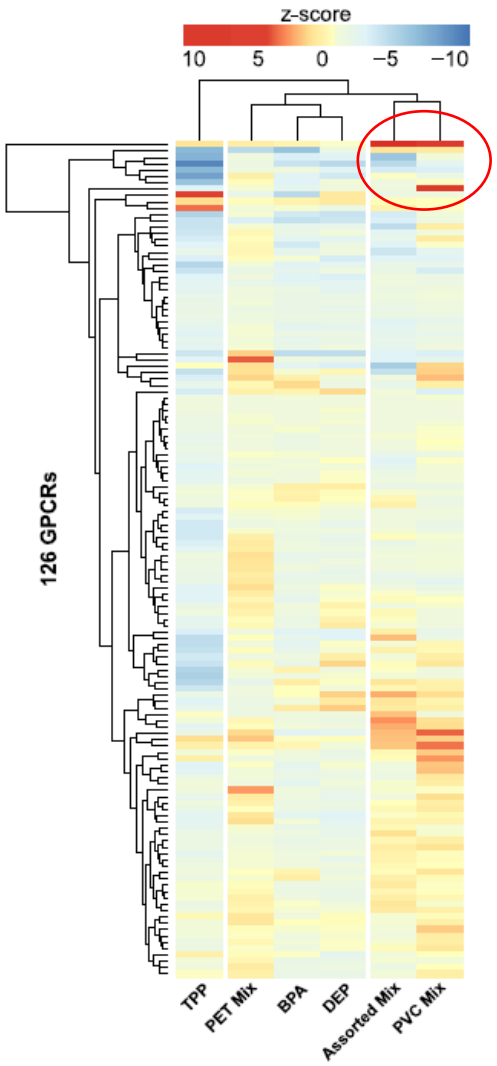
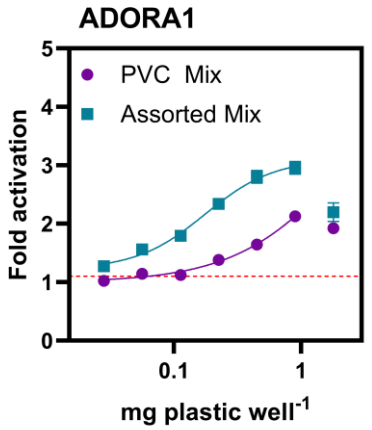
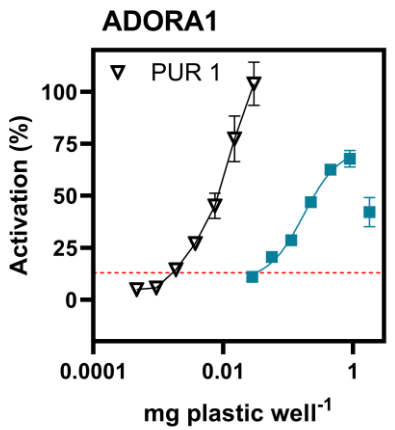
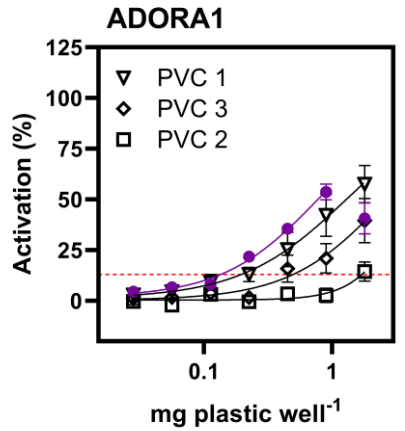


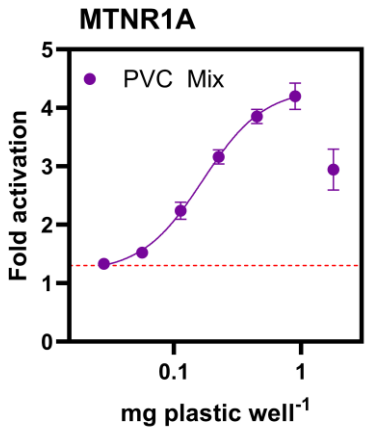
Adenosine 1 Receptor

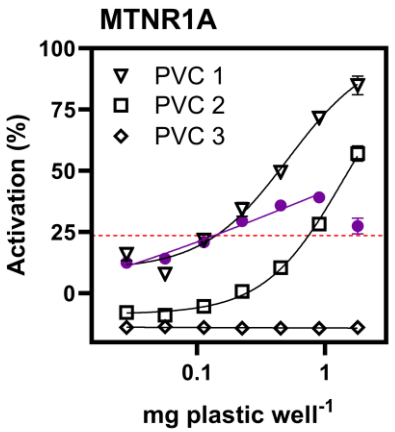






Melatonin 1A Receptor





McPartland et al., 2024, ES&T

Extracts – Conclusion

- Large chemical complexity
- Most plastics contain EDCs & MDCs
- GPCR agonists in PUR and PVC extracts

Migration

- Do chemicals and toxicity also migrate into food simulants?
  - ➢ Migration study with water and water-ethanol mixture (1:1, v:v)

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Full length article

Migration of endocrine and metabolism disrupting chemicals from plastic food packaging

Sarah Stevens [a,*], Zdenka Bartosova [a], Johannes Völker [a,b], Martin Wagner [a,*]

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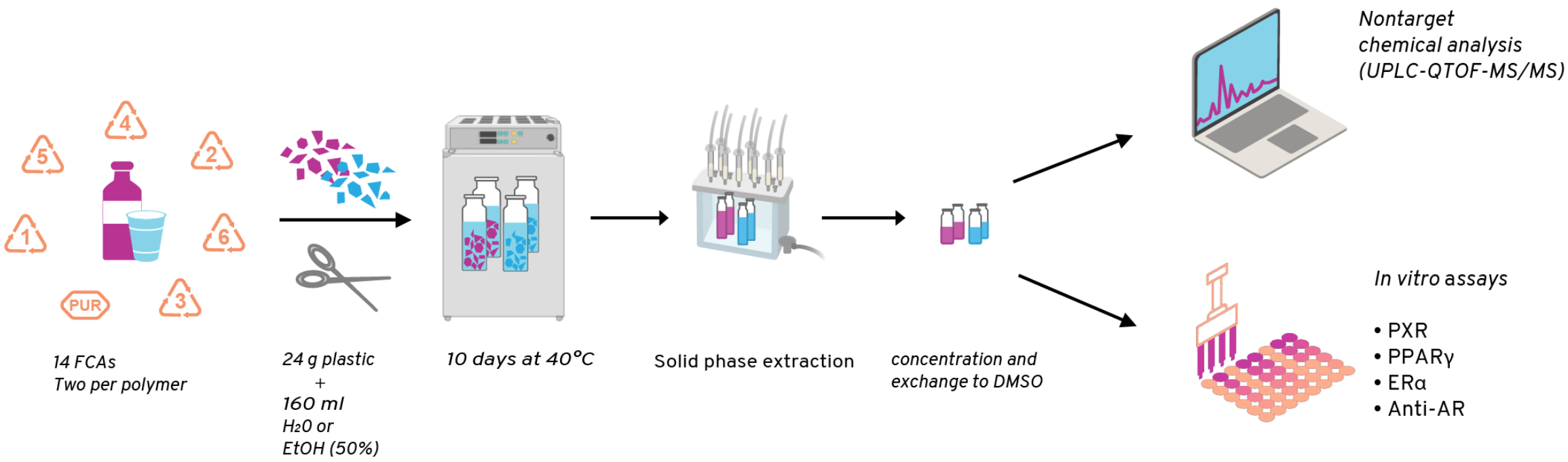
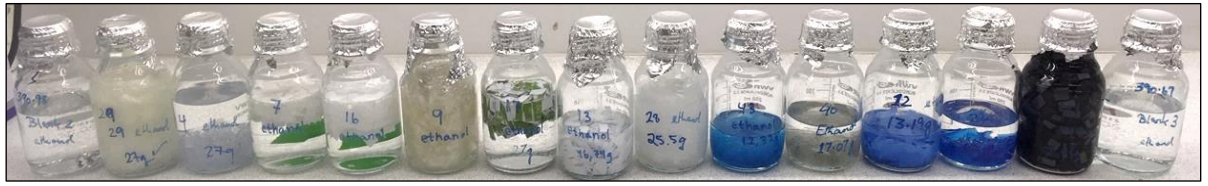
Methods





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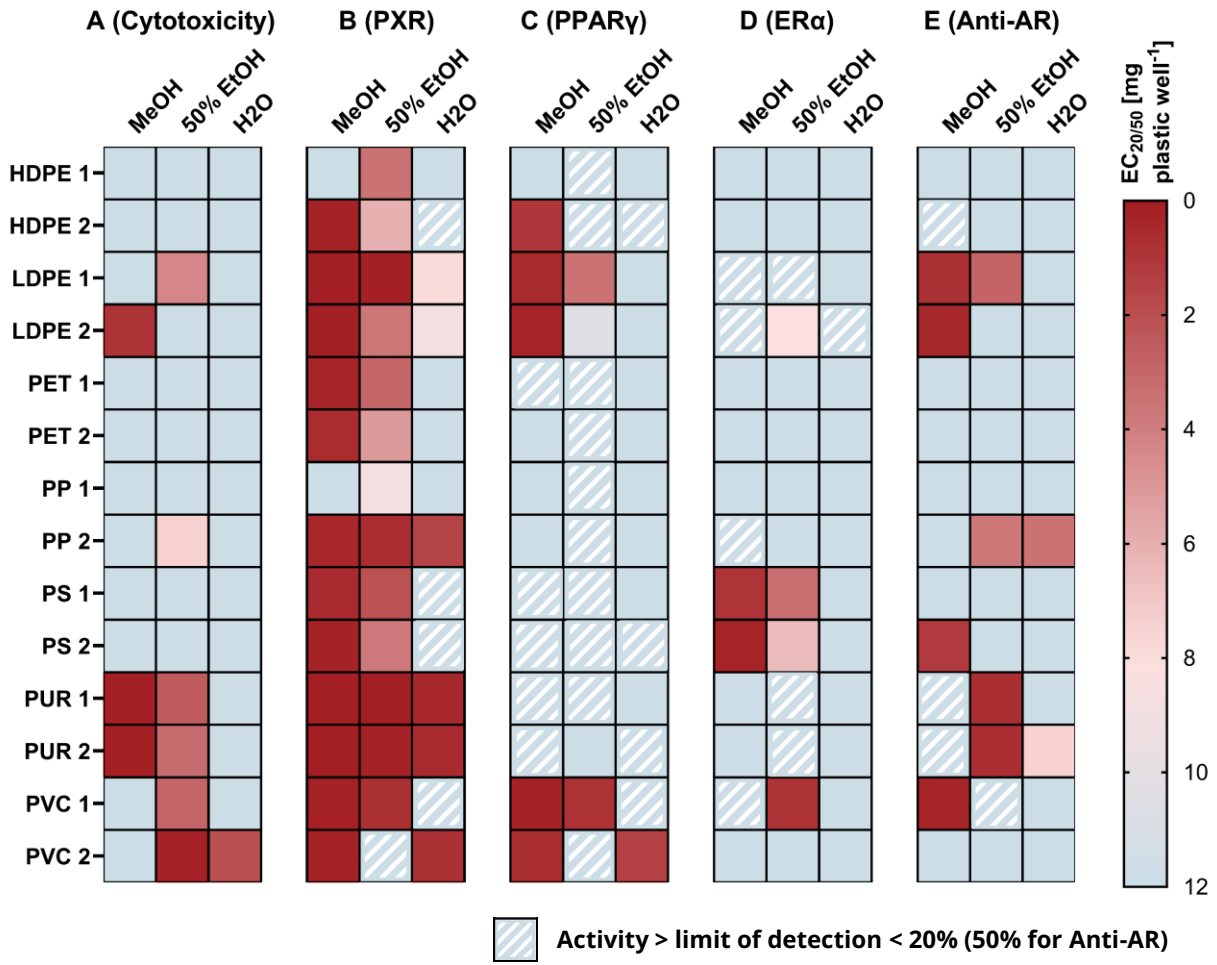
Migration into food simulants

- Most plastics leach EDCs & MDCs into food simulants
- LDPE, PUR & PVC induced most effects
- HDPE & PET migrates were less toxic
- Toxicity lower in water than in water-ethanol leachates



Stevens et al., 2024, Env. Int.

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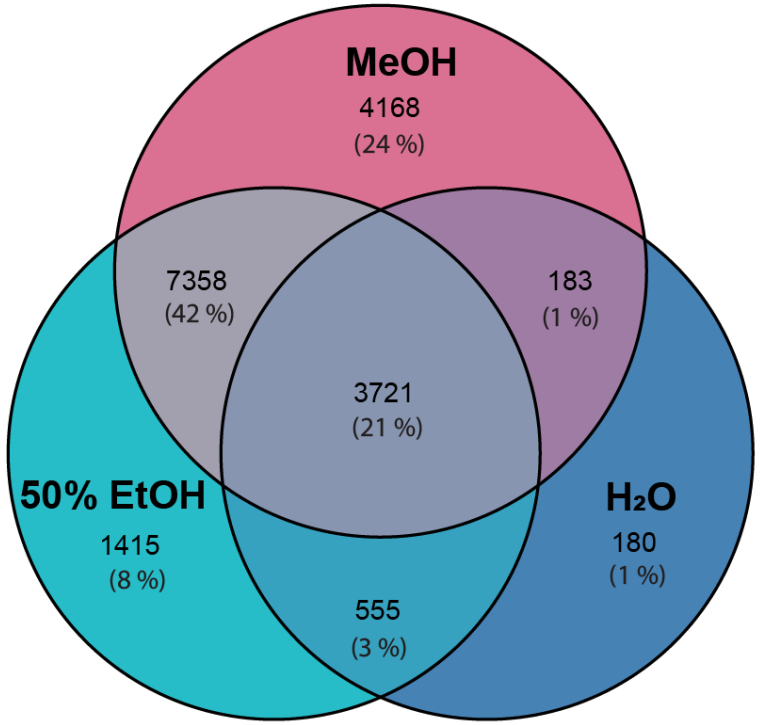
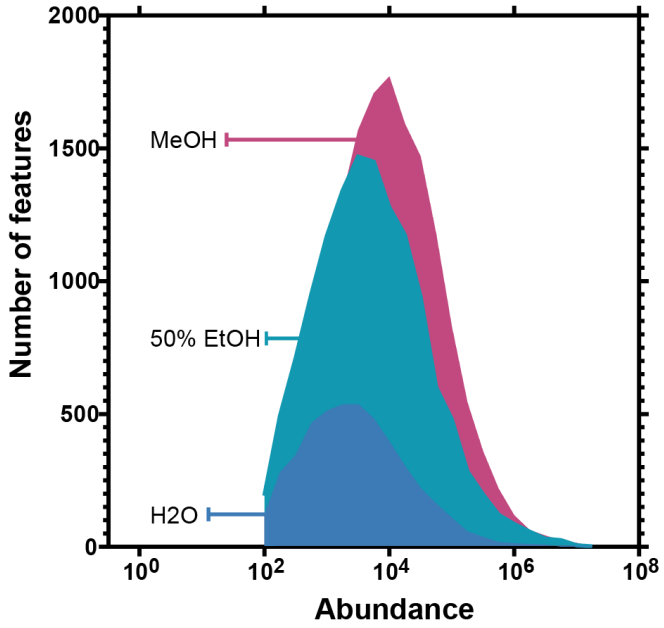
Chemical Landscape





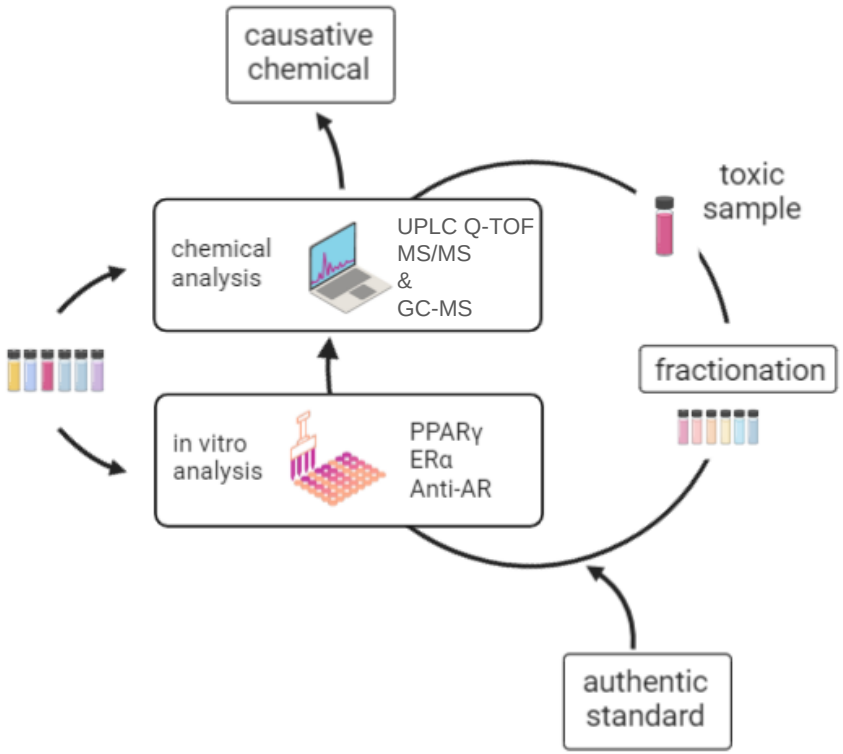
Toxicity-driving compounds?

17 000 chemical features

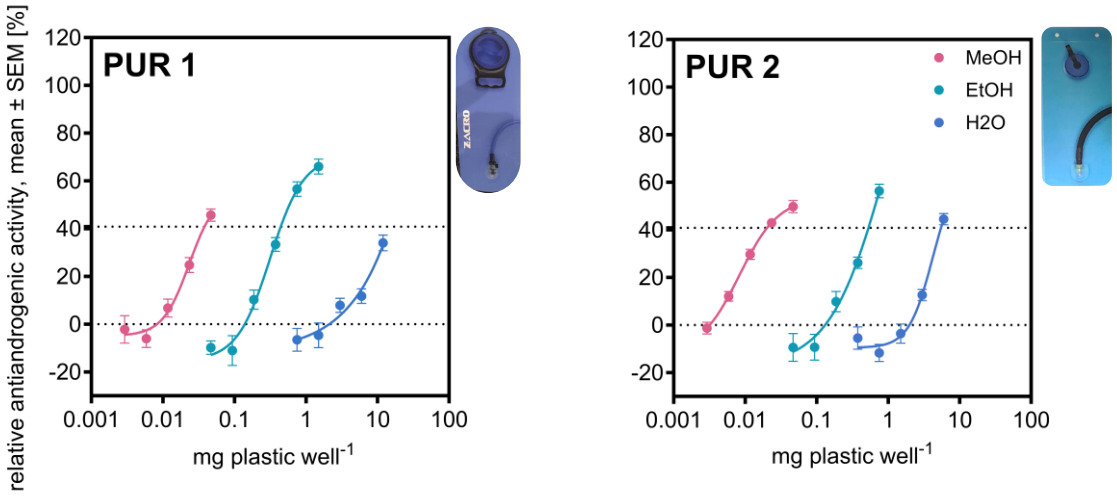
Stevens et al., 2024, Env. Int.

Effect-Directed Analysis– EDA

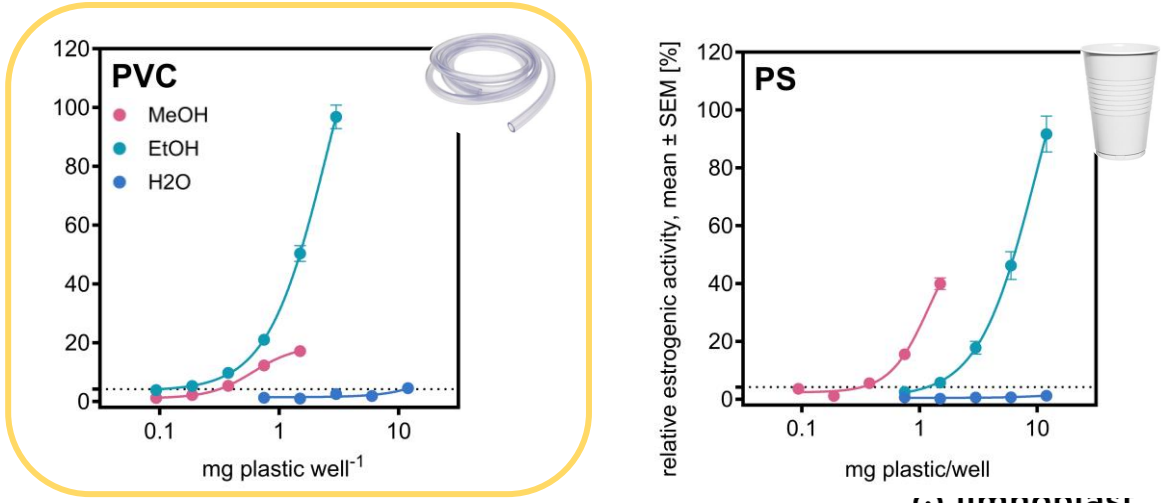
Identification of toxic chemicals in plastic food contact articles guided by effect-directed analysis (EDA).



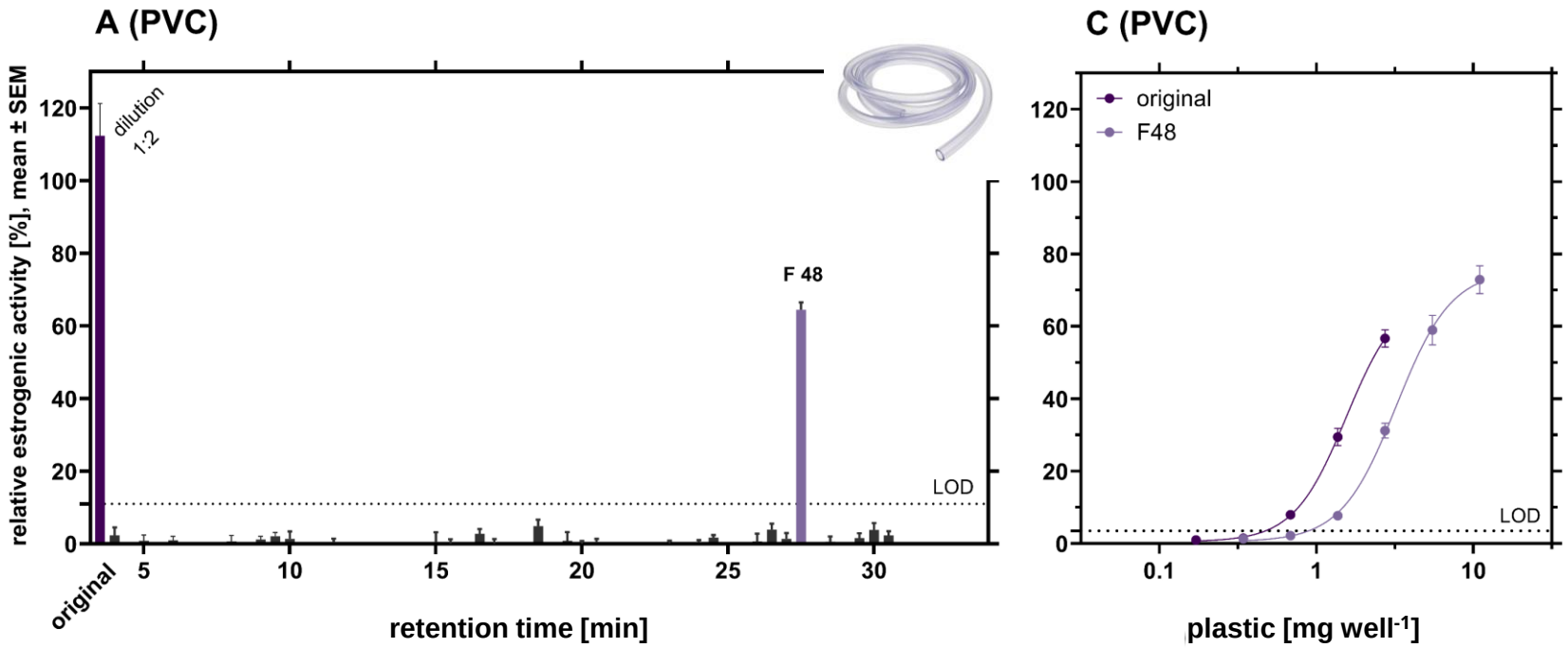
Anti-AR



ERα



Estrogenic activity



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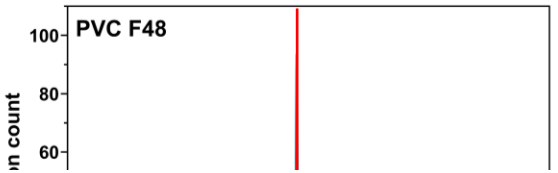
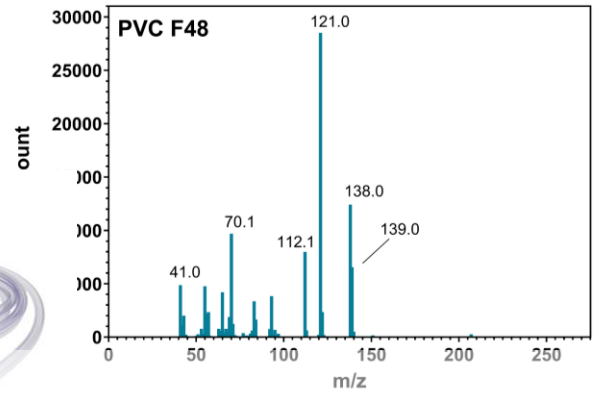
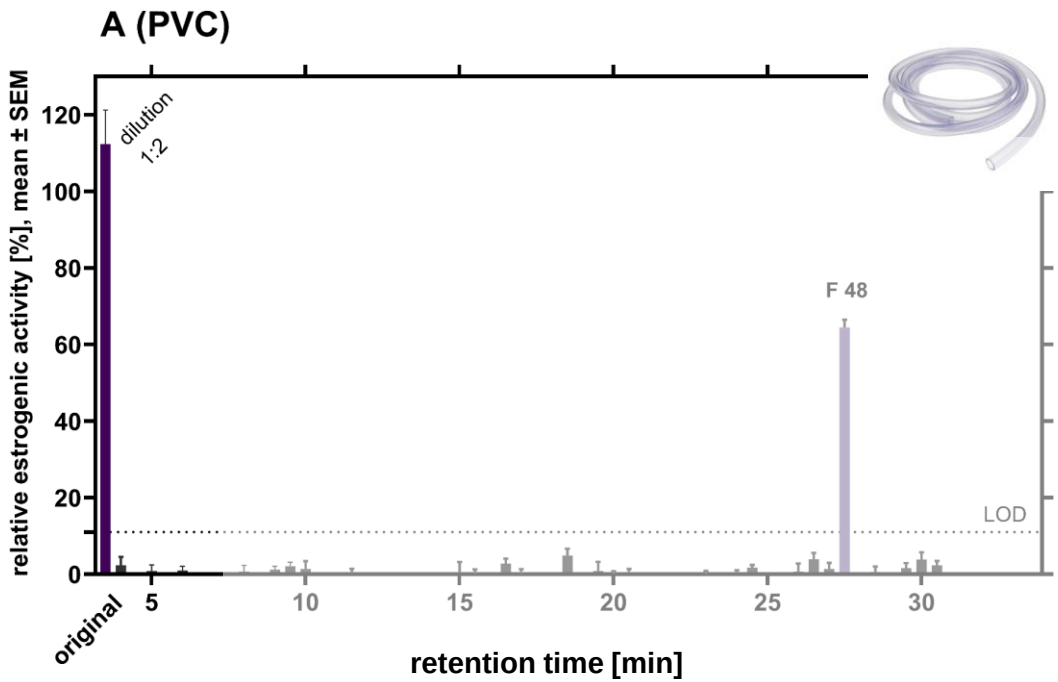
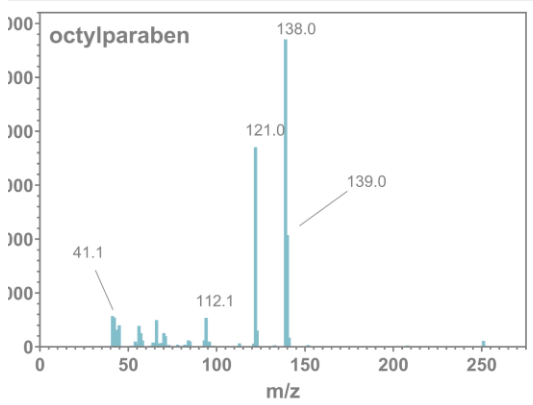
Estrogenic activity





?





octylparaben

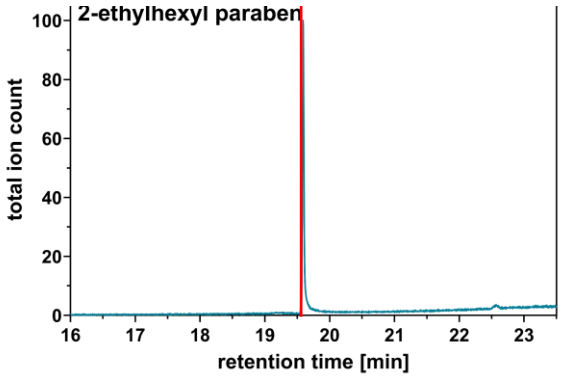
GC-I

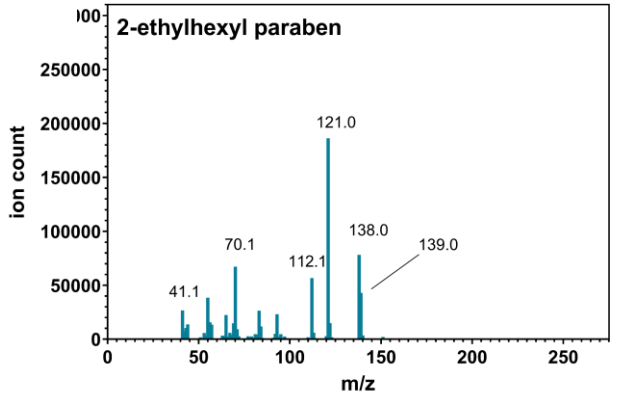
2-et

250.15 g/mol

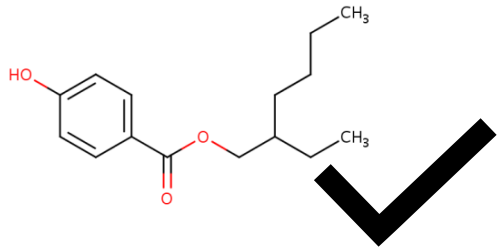
$C_{15}H_{22}O_3$

CAS 5153-25-3





2-ethylhexylparaben



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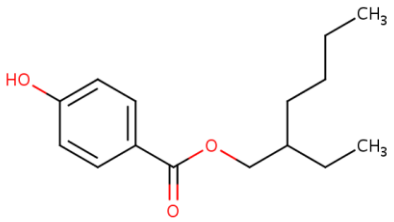
Estrogenic activity



2-ethylhexylparaben

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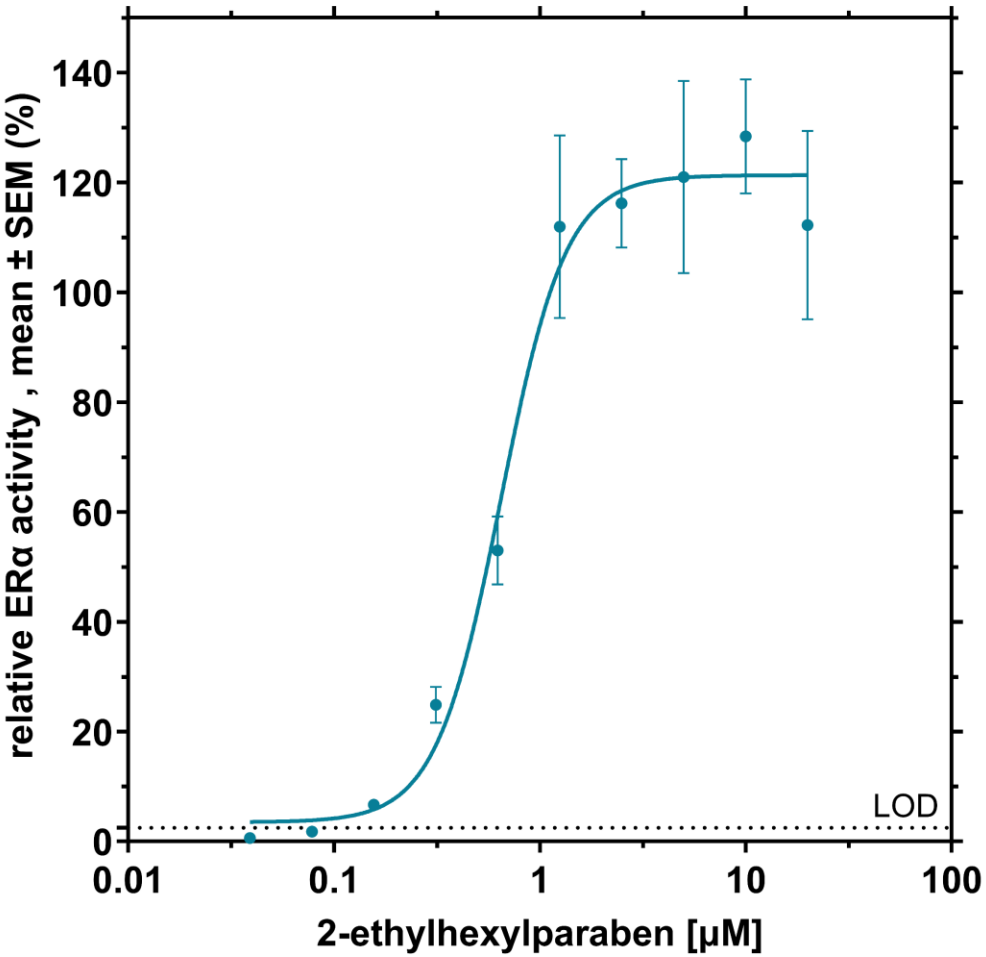

EC_{50} 0.65 µM

ToxCast: Luc VM7
AC_{50} 1.41 µM

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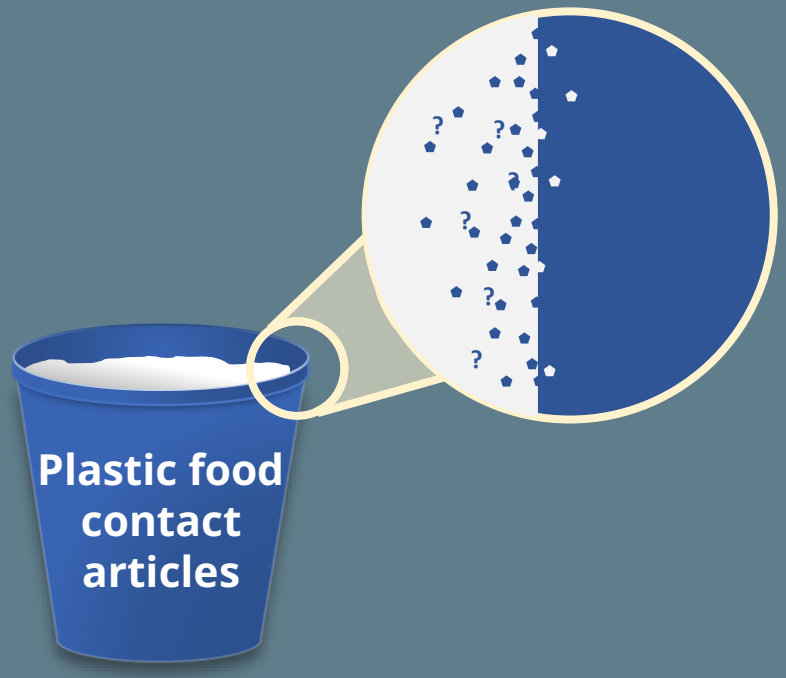
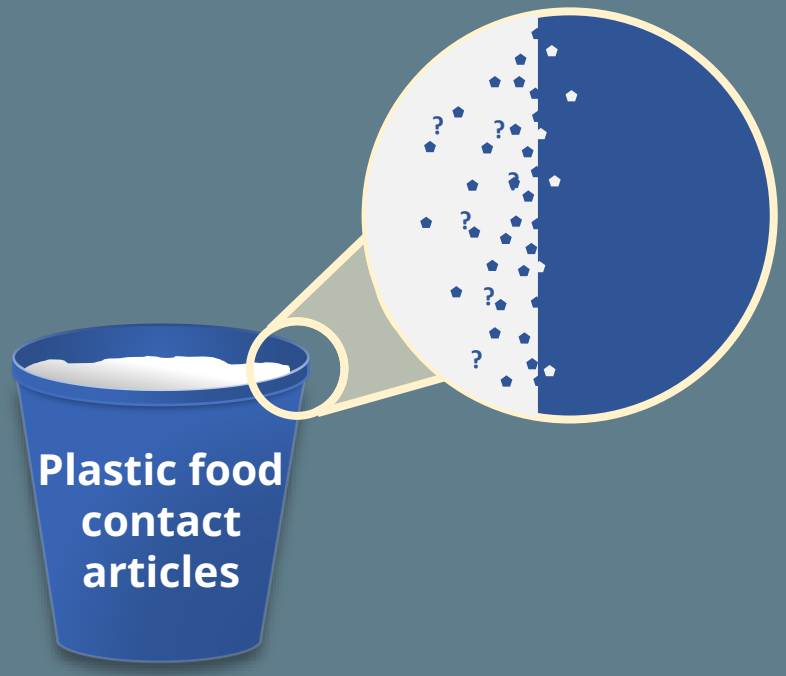
Conclusion

- Large chemical complexity
- Most plastics leach EDCs & MDCs into food simulants
- A global issue
- GPCRs targeted by chemicals in PVC and PUR
- Products of all polymers induced receptor activity
- 2-ethylhexylparaben in estrogenic PVC fraction



Implications

- Information on use, identity, and toxicity of plastic chemicals
- Chemical simplicity is key for safer plastics
- Prioritization of LDPE, PUR & PVC for regulation / redesign
- Toxicity-driving compounds belong to priority groups
- International efforts required



Thank you for listening!

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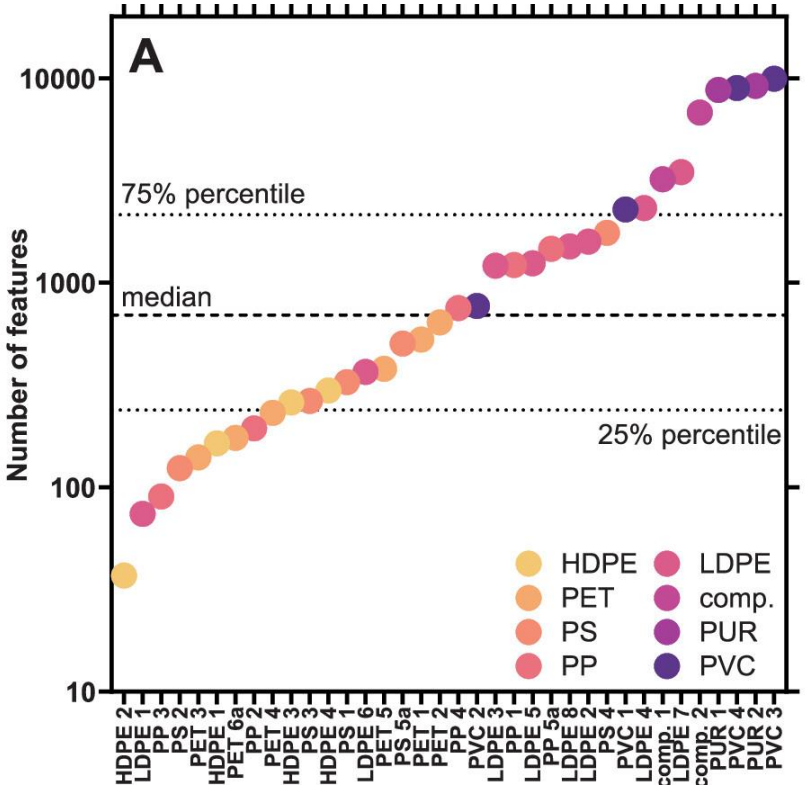
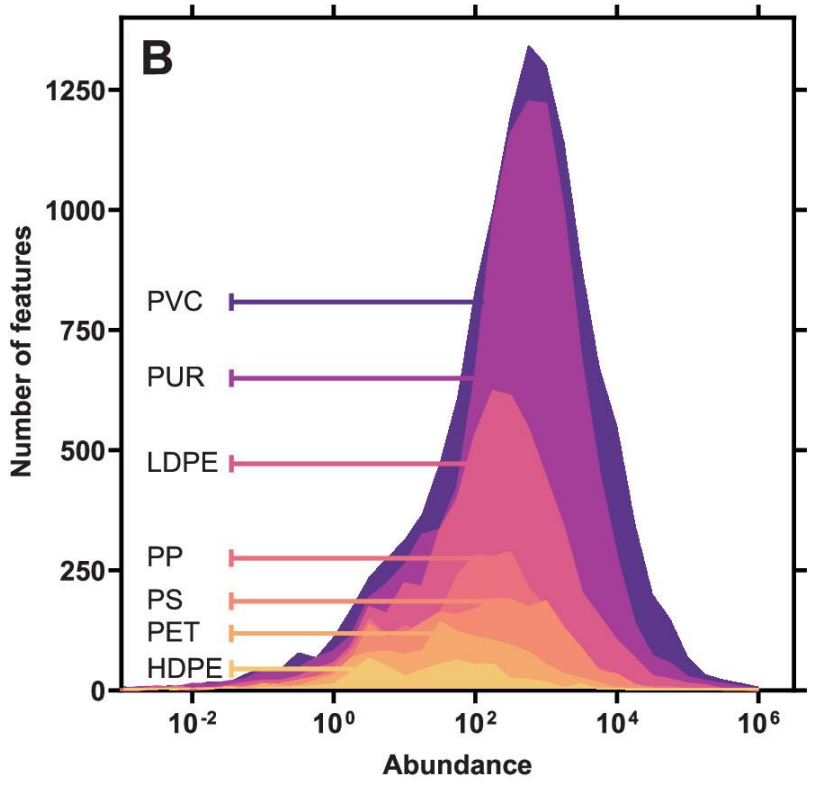
Chemical Landscape

Number of chemical features per sample



Abundance of features per polymer type



- **> 16 000 chemical features**
- **16 % tentatively identified**

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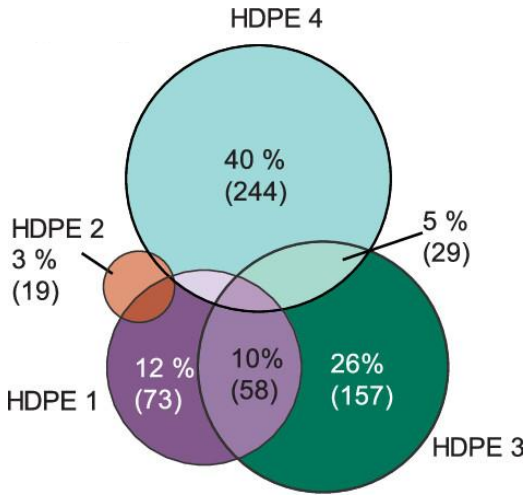
Chemical similarity across samples

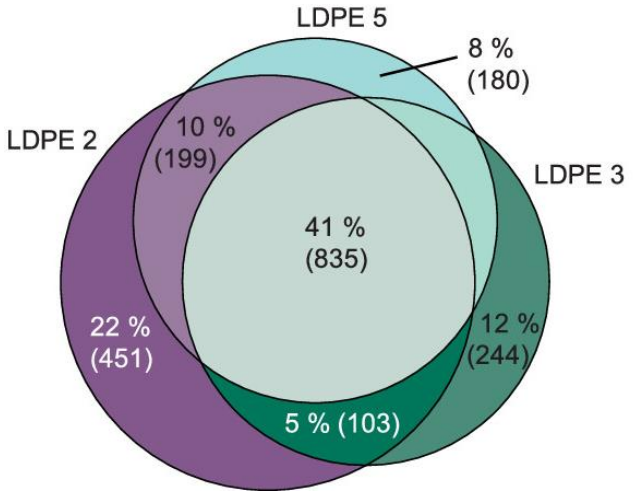
Polymer

HDPE

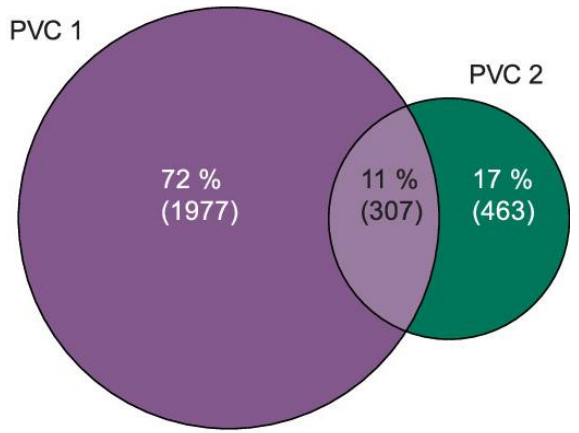


Polymer + Product

Freezer Bag



Drinking Tube



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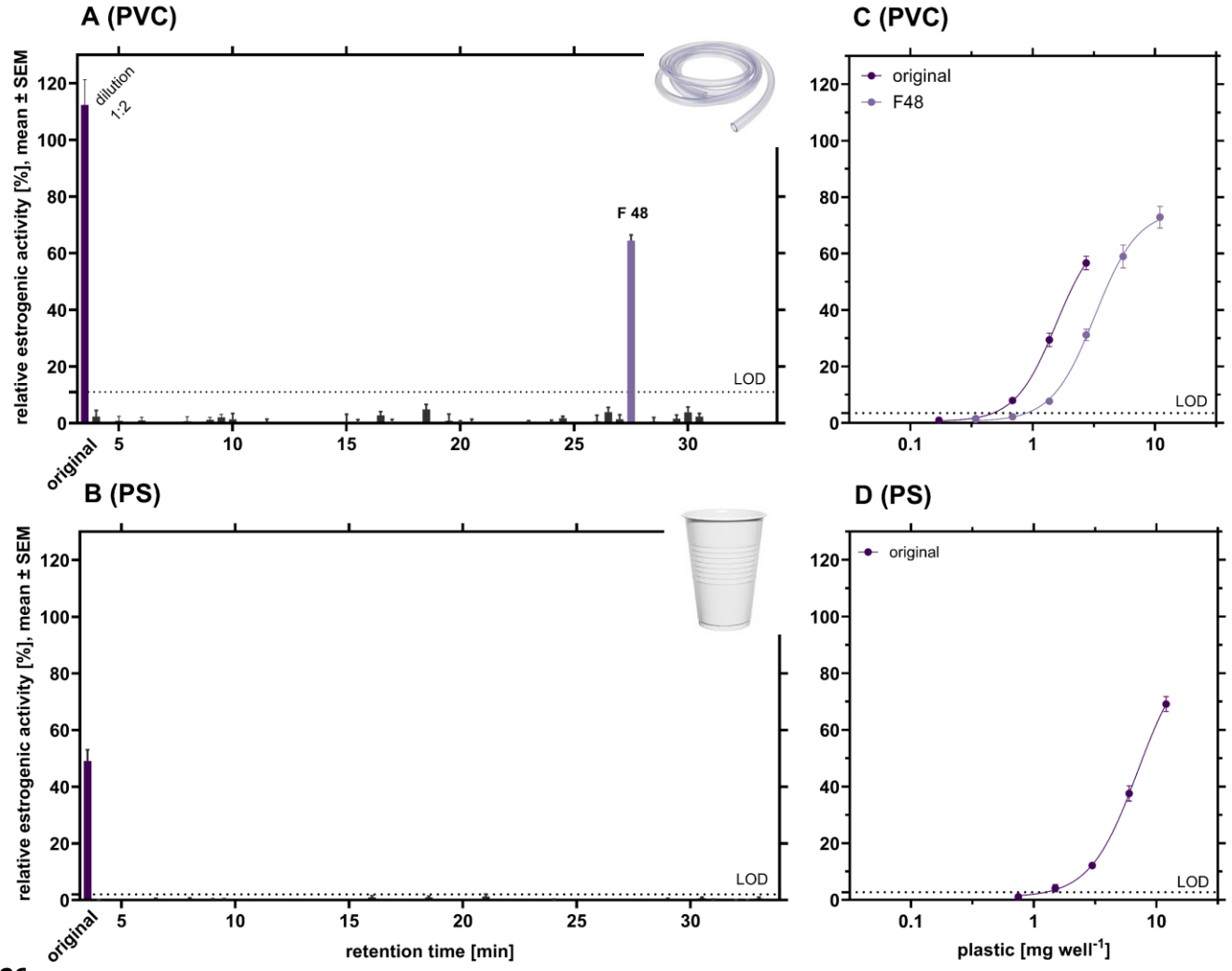
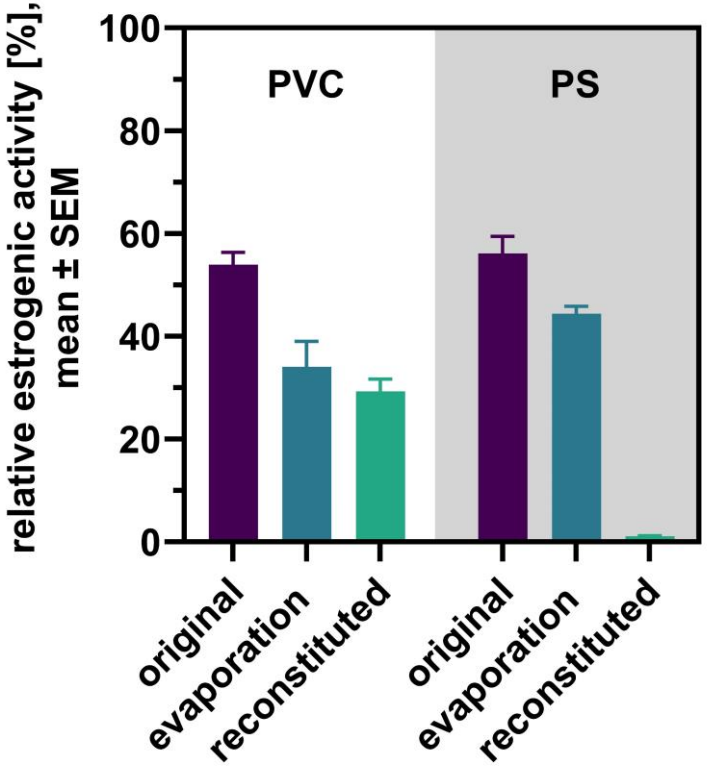
Estrogenic activity





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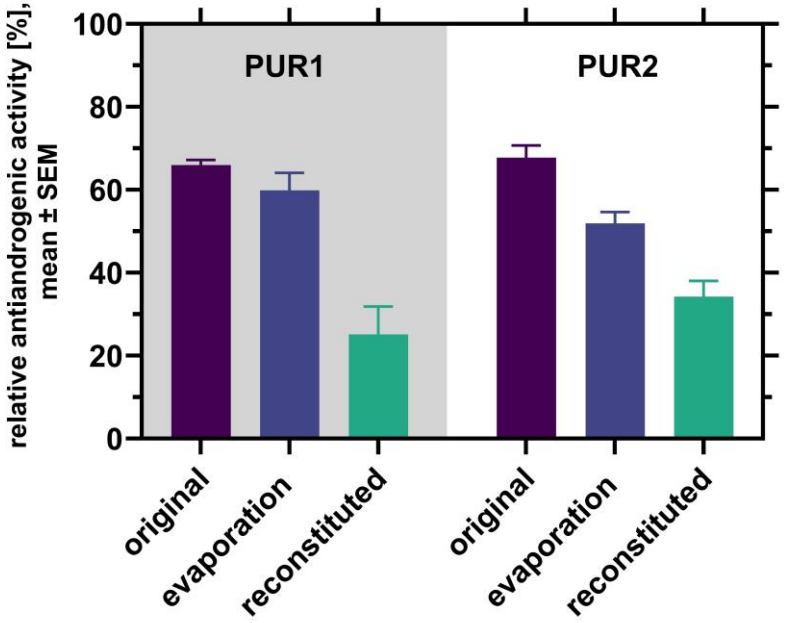
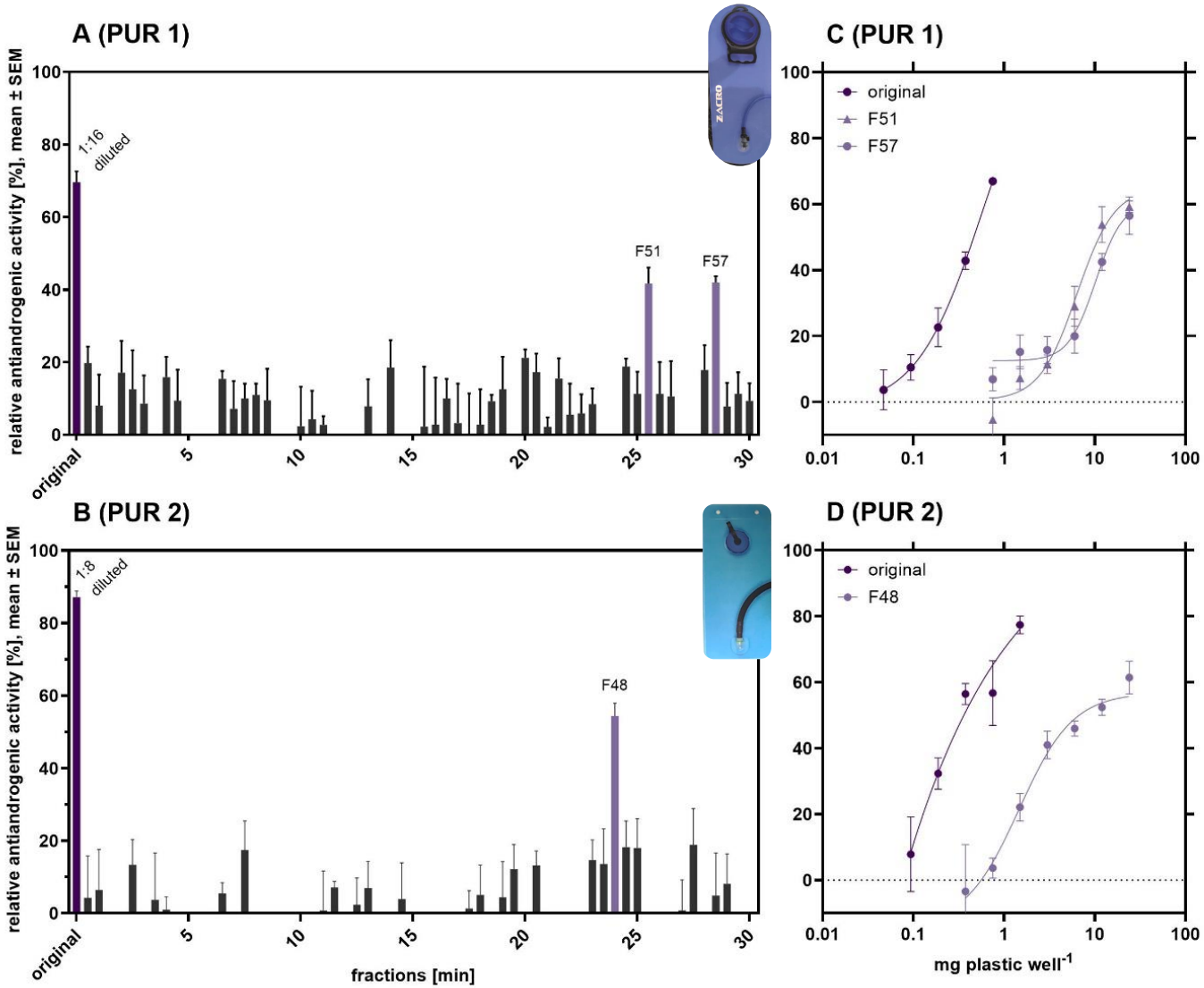
Anti-Androgenic Activity





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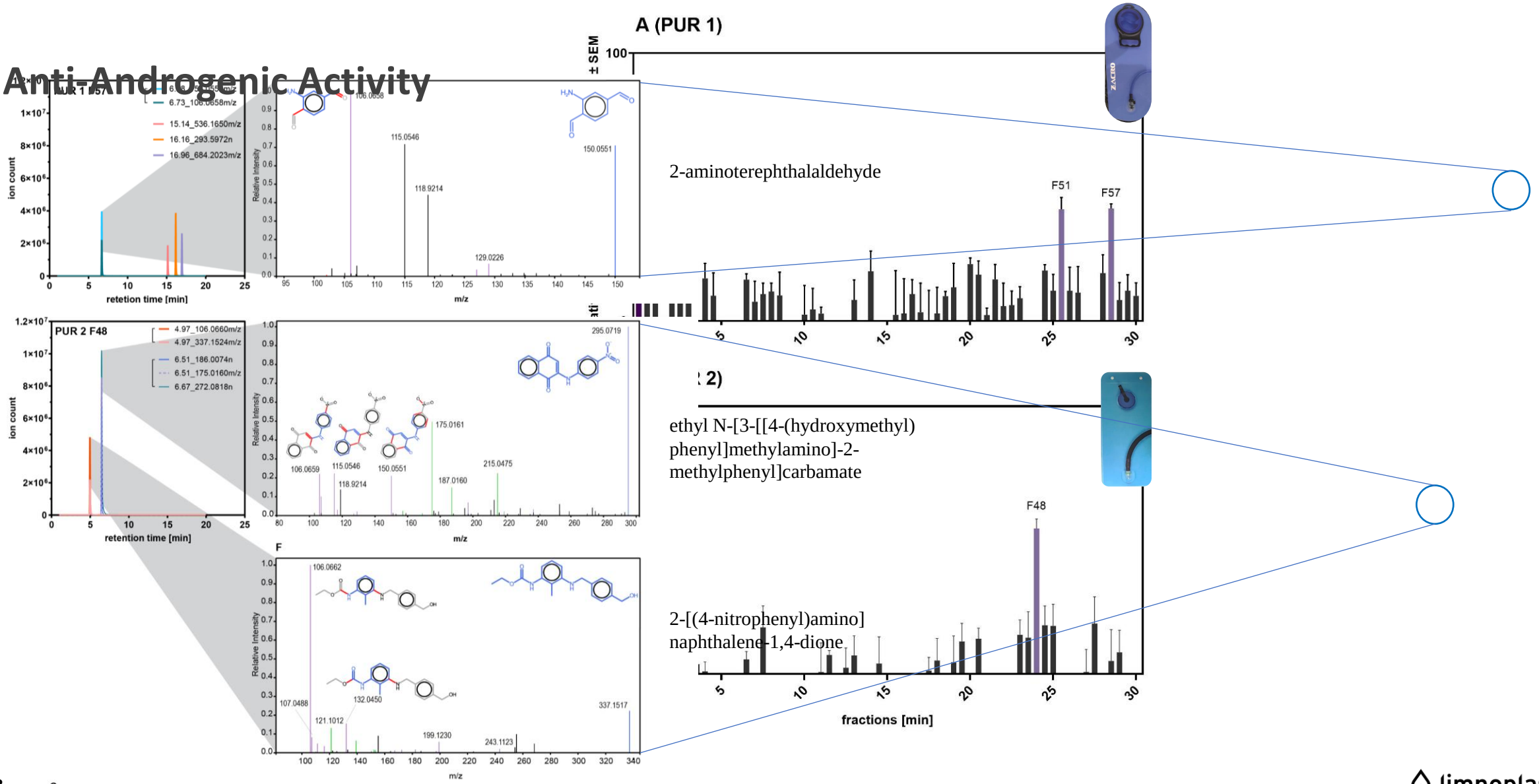
Anti-Androgenic Activity



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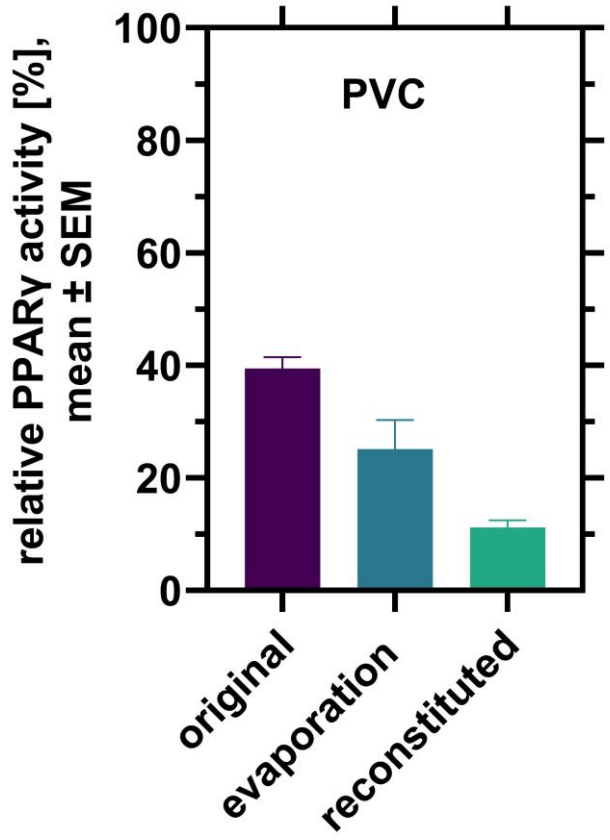
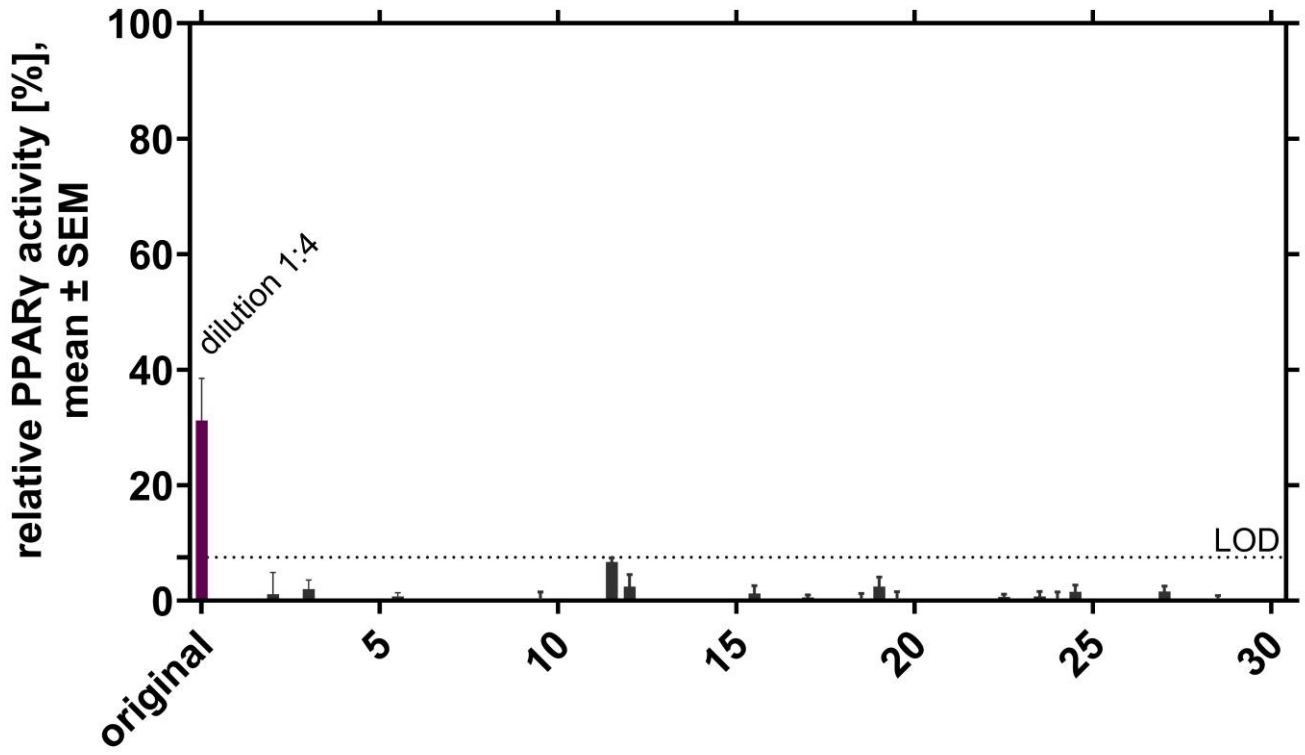
PPARγ activity of PVC drinking tube





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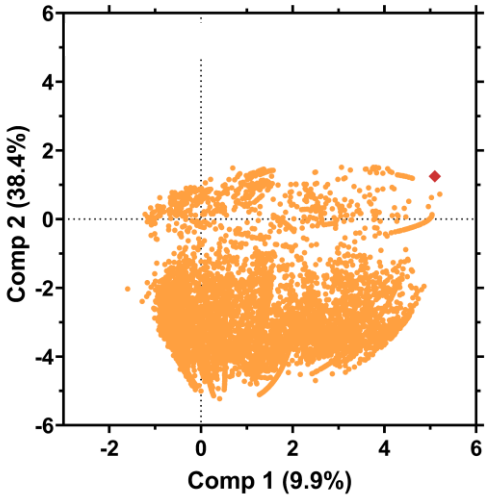
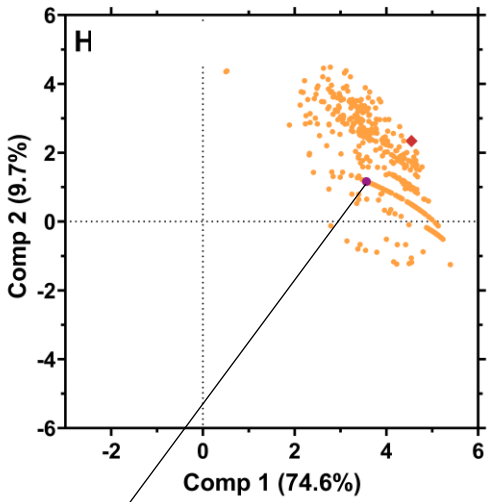
Partial Least Squares (PLS) Regression

Anti-AR

14379 chemical features



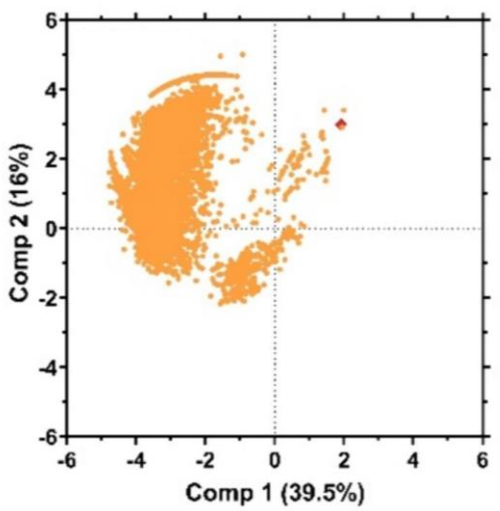
909 chemical features



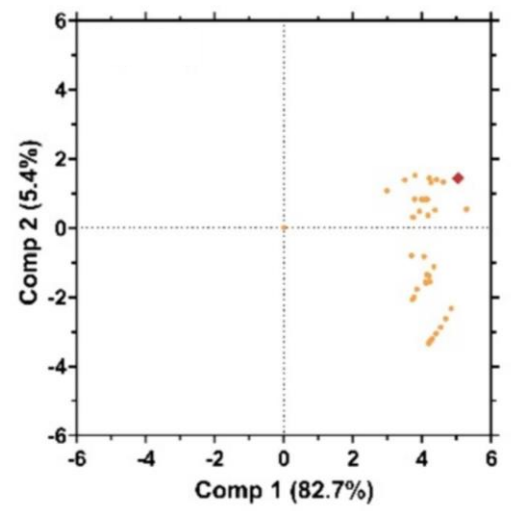
triphenyl phosphate

ERα

13468 chemical features

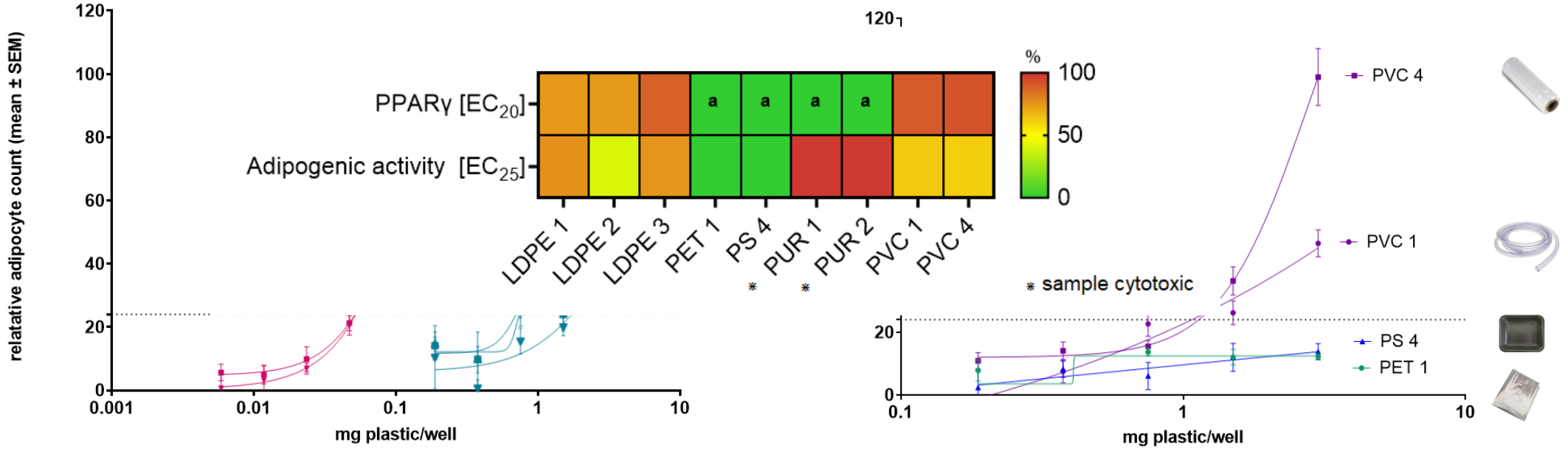


115 chemical features



Stevens et al., 2024, Env. Int.

Adipogenesis in 3T3 L1



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