

Application of Metabolomics - Introduction

Metabolomics / Metabolic Profiling in vivo

Mostly unknown



Mostly known

DNA

40,000 genes

RNA

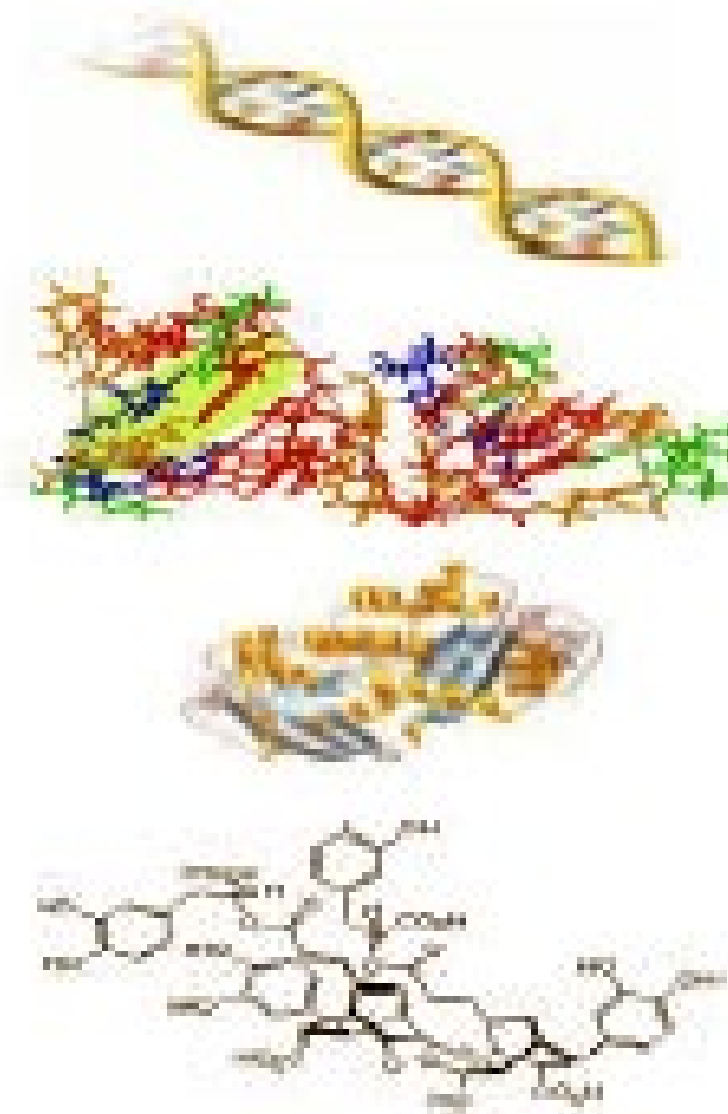
150,000 transcripts

Proteins

1,000,000 proteins

Metabolites

2,500 metabolites



Genomics

Transcriptomics

Proteomics

Metabolomics

Advantage

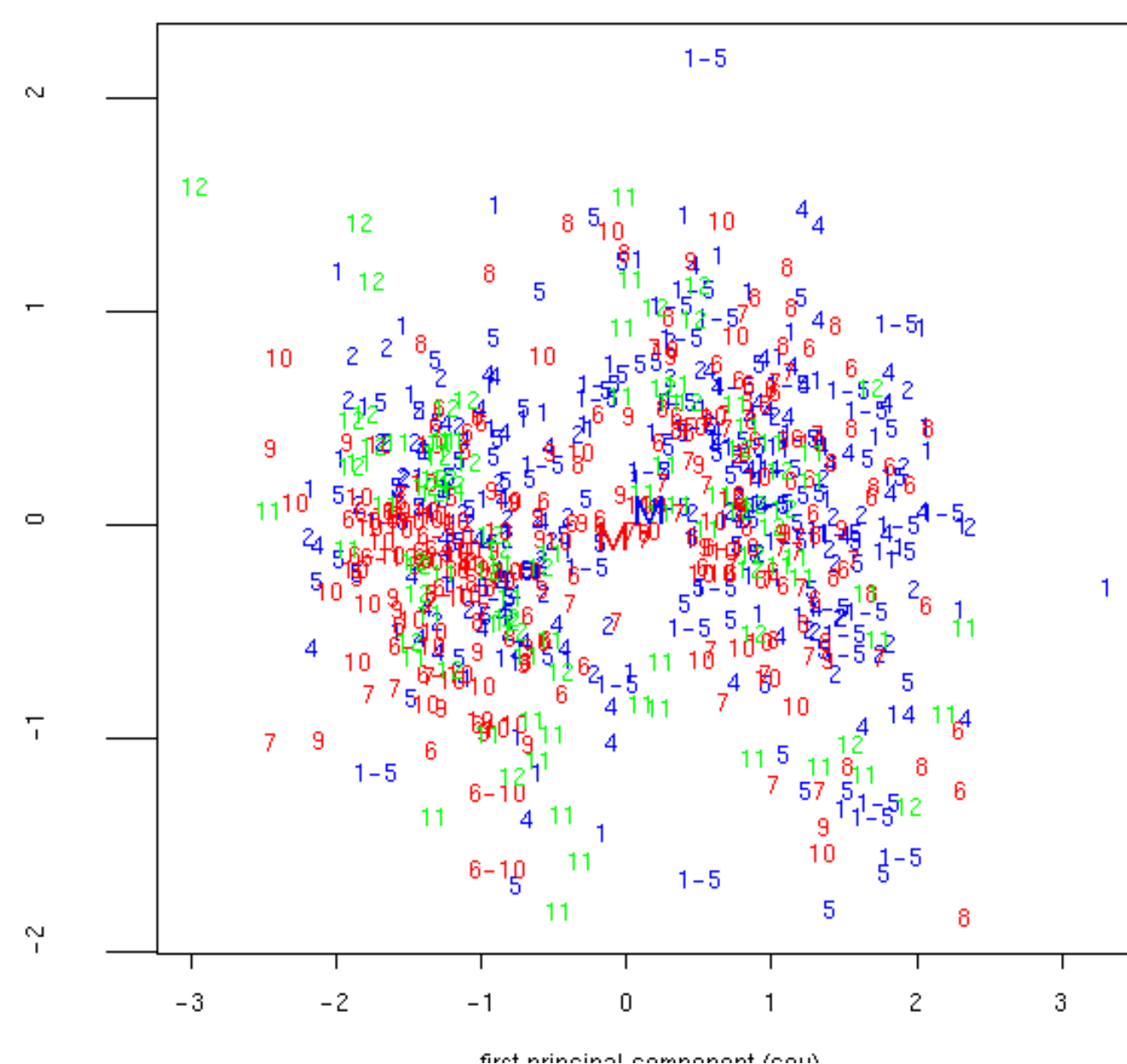
Single matrix (blood)

Closer to classical toxicology

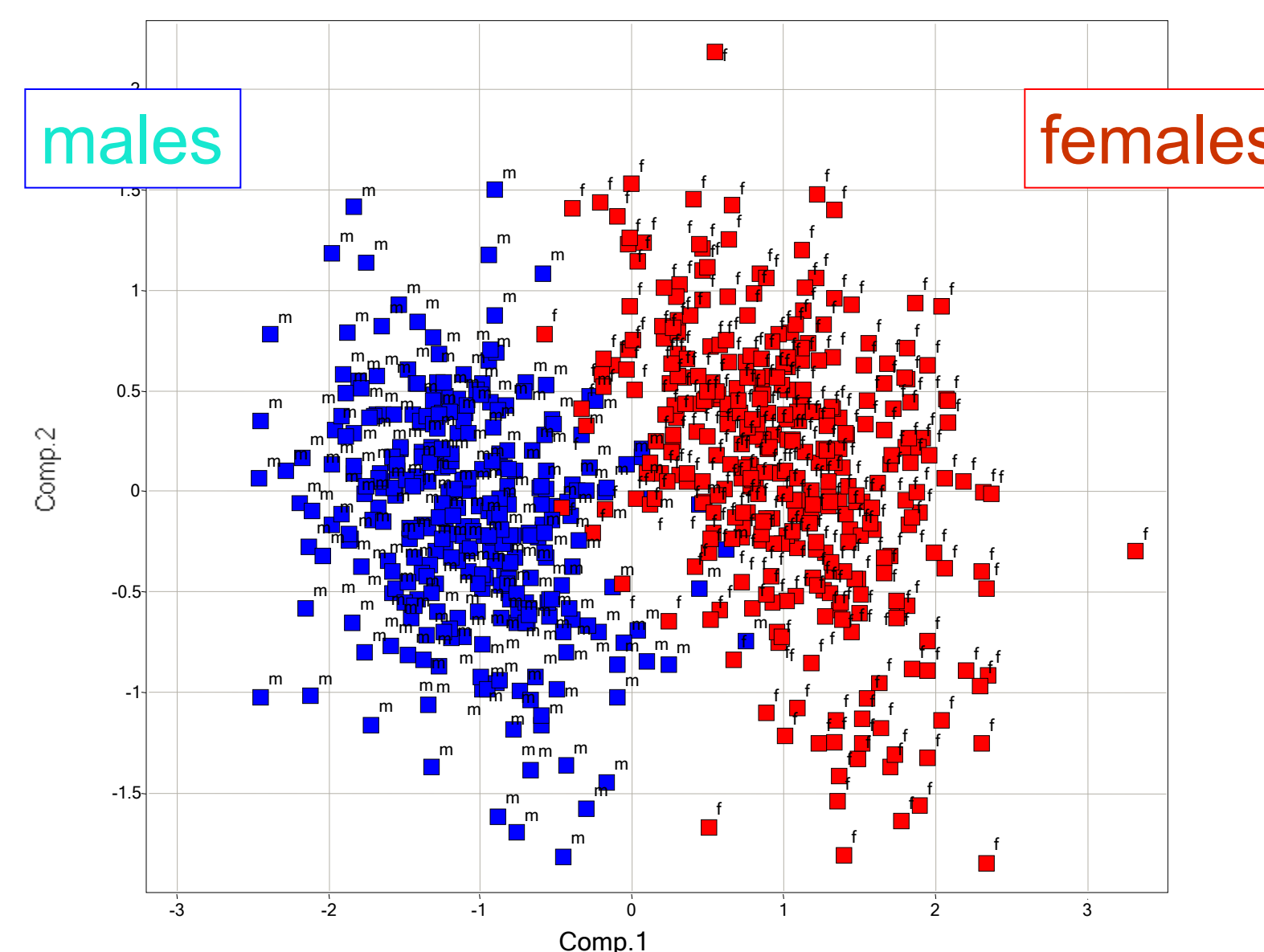
The Basis for Assessment is Reproducibility & Reliability

Metabolome plasma profiles from

- Subset of about 700 control male & female rats
- Controls of different experiments spanning about 5 months
- Data represent biological, handling and profiling variability



Colors indicate different experiments over 5 months



→ main differentiator in control animals and experiments is gender only

Application: Identification of MoA peroxisome proliferation

Compound Ranking: Clofibrate

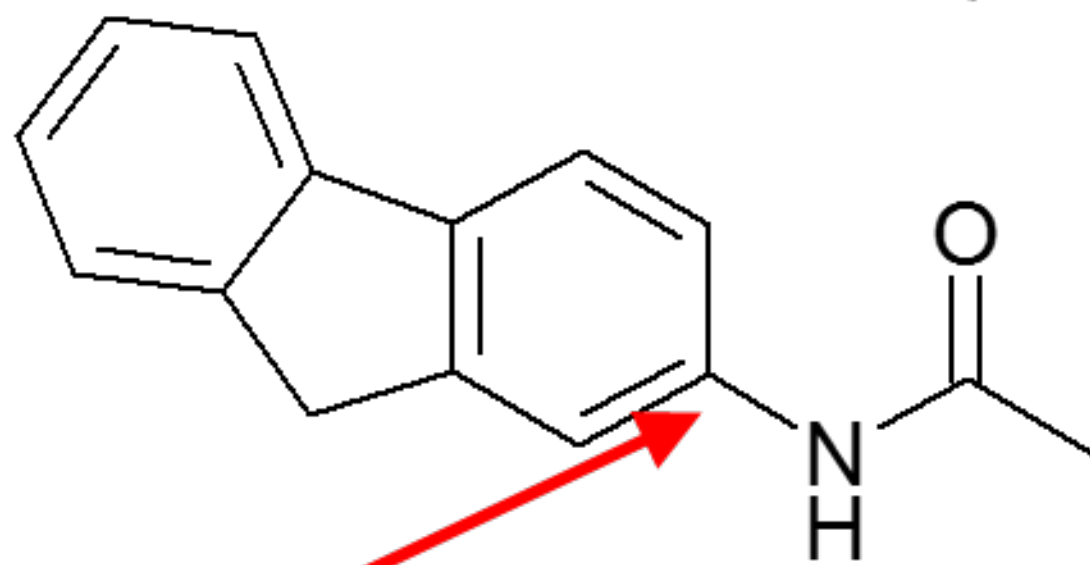
The individual and combined metabolite profiles (metabolomics) of dibutylphthalate and di(2-ethylhexyl)phthalate following a 28-day dietary exposure in rats

B. van Ravenzwaay ^a, G. Coelho-Palermo Cunha ^a, V. Strauss ^a, J. Wiemer ^b, E. Leibold ^a, H. Kamp ^a, T. Walk ^b, W. Mellert ^a, R. Looser ^b, A. Prokoudine ^b, E. Fabian ^a, G. Krennrich ^a, M. Herold ^b

Clofibrate (MOA50)	Pearson			Spearman			norm. vector product		
Treatment	rp	p	rank	rs	p	rank	nvp	p	rank
Clofibrate (MOA50)	1,00	0,00	1	1,00	0,00	1	1,00	0,00	1
Fenofibrate (MOA48)	0,79	0,00	2	0,70	0,00	3	0,80	0,00	2
Mecoprop-p (MOA58)	0,78	0,00	3	0,66	0,00	5	0,76	0,00	4
Pravastatin + Fenofibrat (MOAFW05)	0,73	0,00	4	0,63	0,00	11	0,73	0,00	7
Bezafibrate (MOA49)	0,72	0,00	5	0					

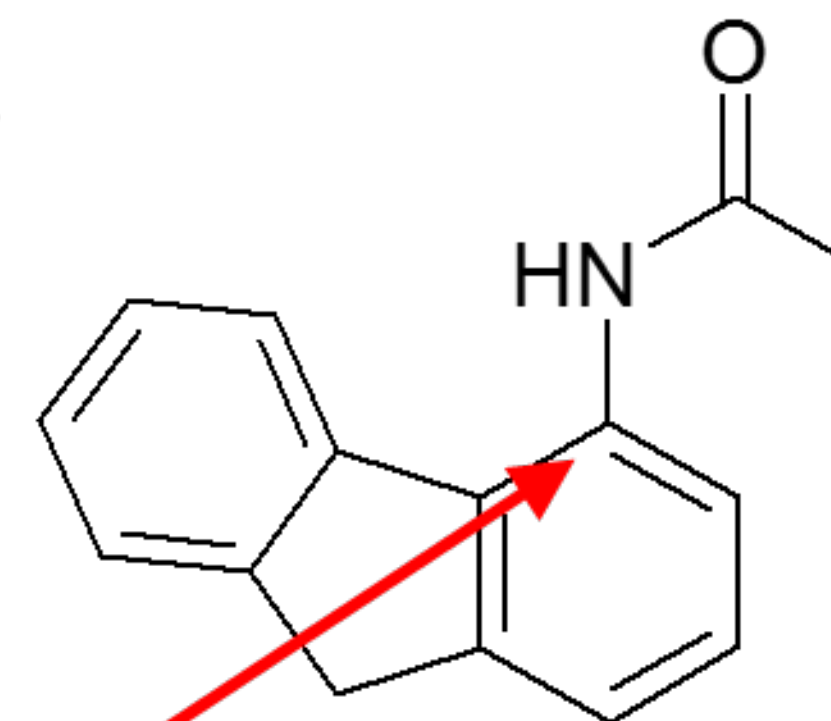
2- and 4-Acetylaminofluorene: structural similarity does not always indicate similar toxicity

Tanimoto score: 63%



2-Acetylaminofluorene

- strong liver enzyme inducer
- liver carcinogen
- immune suppressant
- bladder carcinogen



4-Acetylaminofluorene

- **slight** liver enzyme inducer
- **no** liver carcinogen
- lipid accumulation in liver
- immune suppressant

