3rd NORMAN Workshop, Amsterdam, 29-30 October 2007

Toxicity profiling in European river sediments with emphasis on the identification of thyroid hormone disrupting compounds

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Modelkey SSPI-CT-2003-511237-2

Background

(http://www.modelkey.ufz.de/)

- Selection of samples
- Bioassays performed
- Effect directed analysis (EDA)

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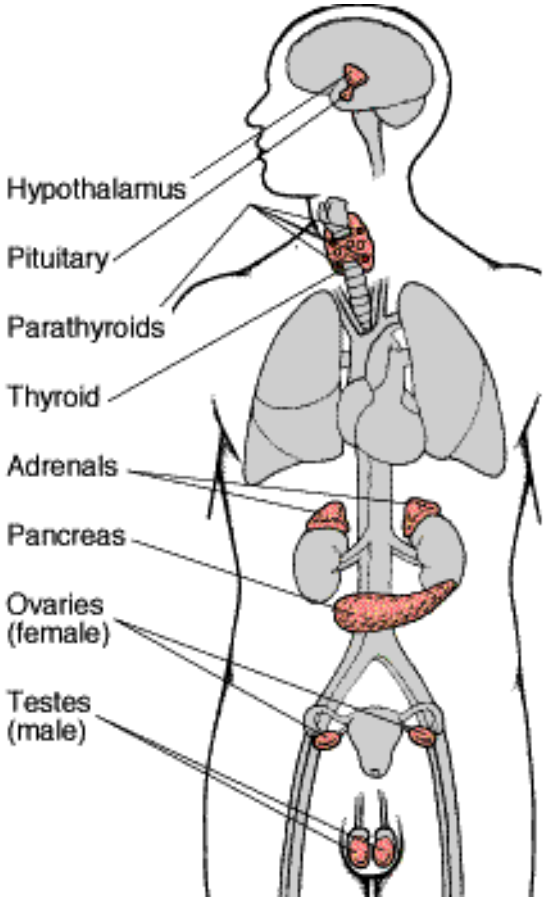
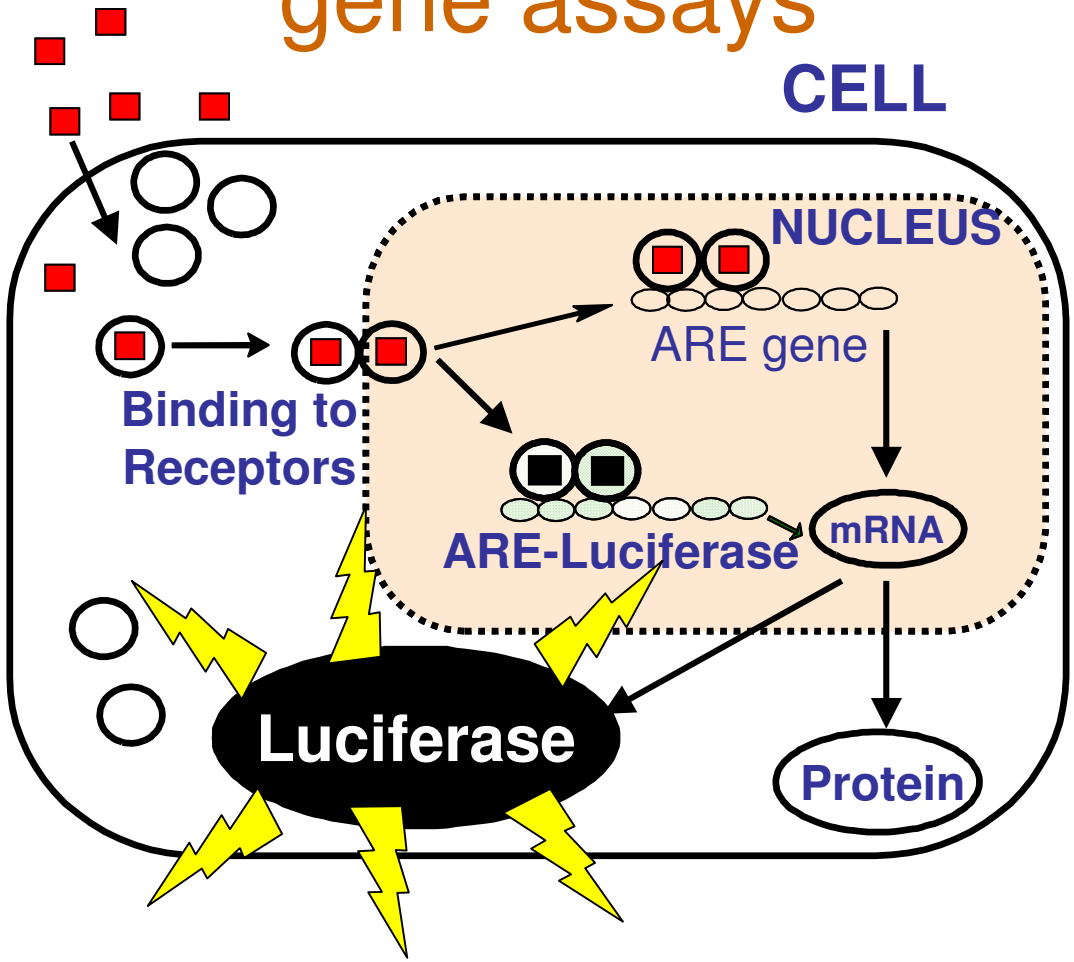
Endocrine disruption

- ABC
- Ames II
- Anti-YAS
- Anti-YES
- AR Calux (antagonistic)
- AR-CAlux (agonistic)
- DR Calux
- Green screen
- Narcosis SPME
- T4-TTR
- ToxAlert
- UmuC
- YES



Principle of (anti-) AR-CALUX® reporter gene assays

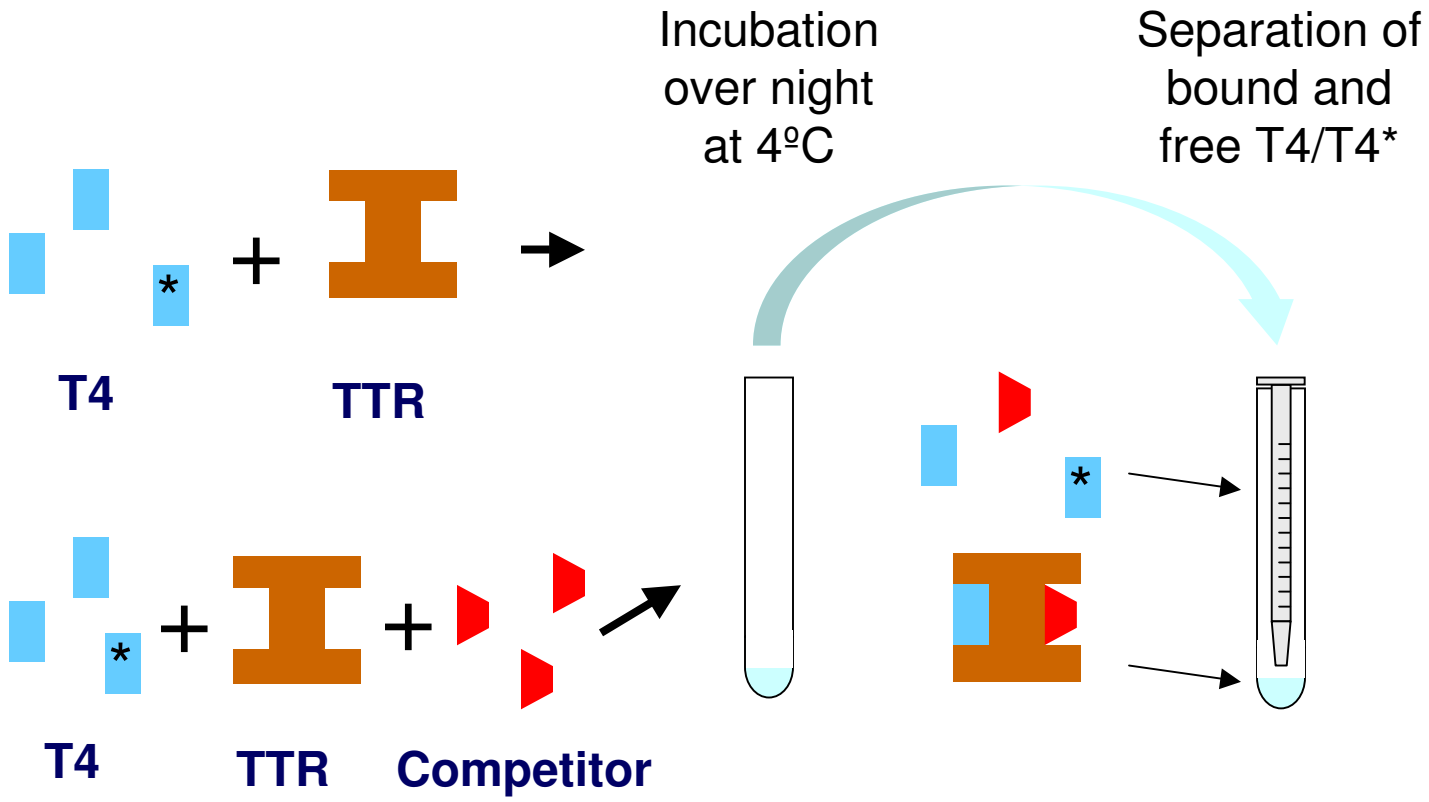
Endocrine Disrupting Compounds



Stable transfected cell lines

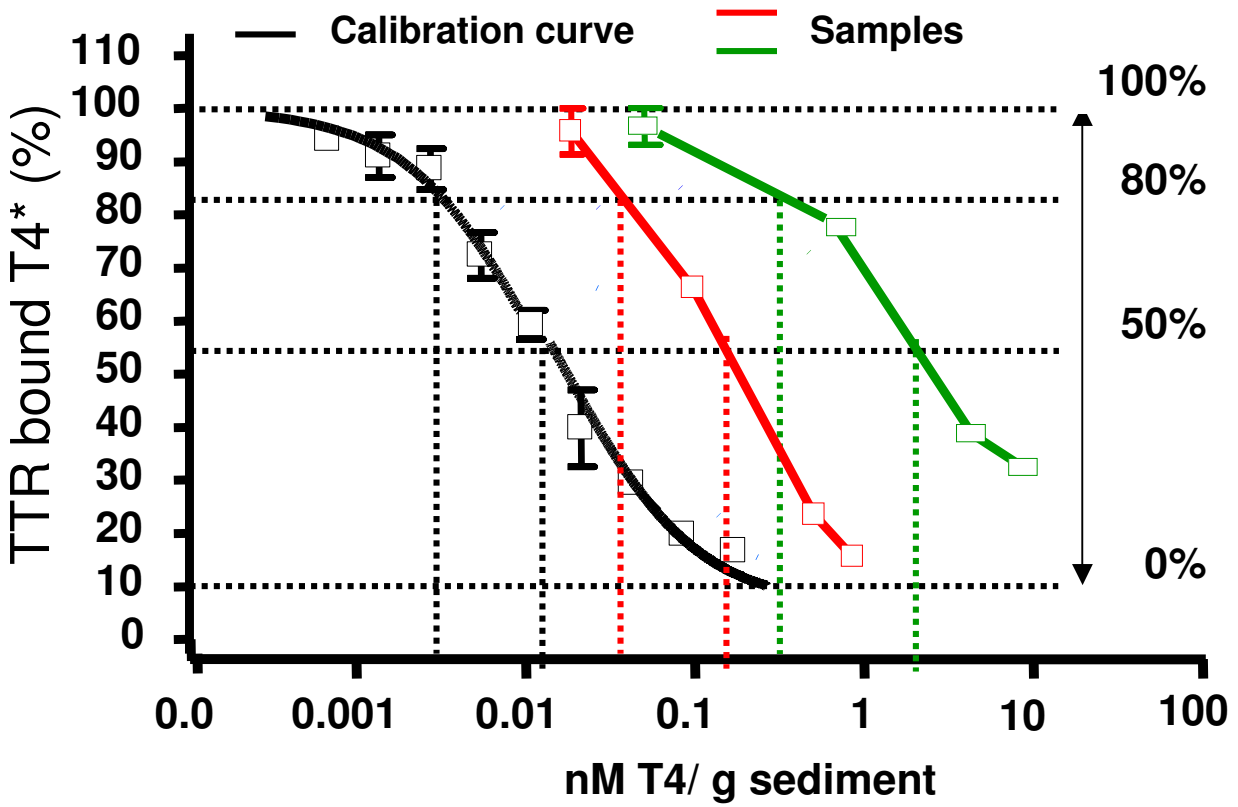
Sonneveld *et al.* 2005

Principle of Radio Ligand T4-TTR binding assays (RLBA)



Lans *et al.* 1993

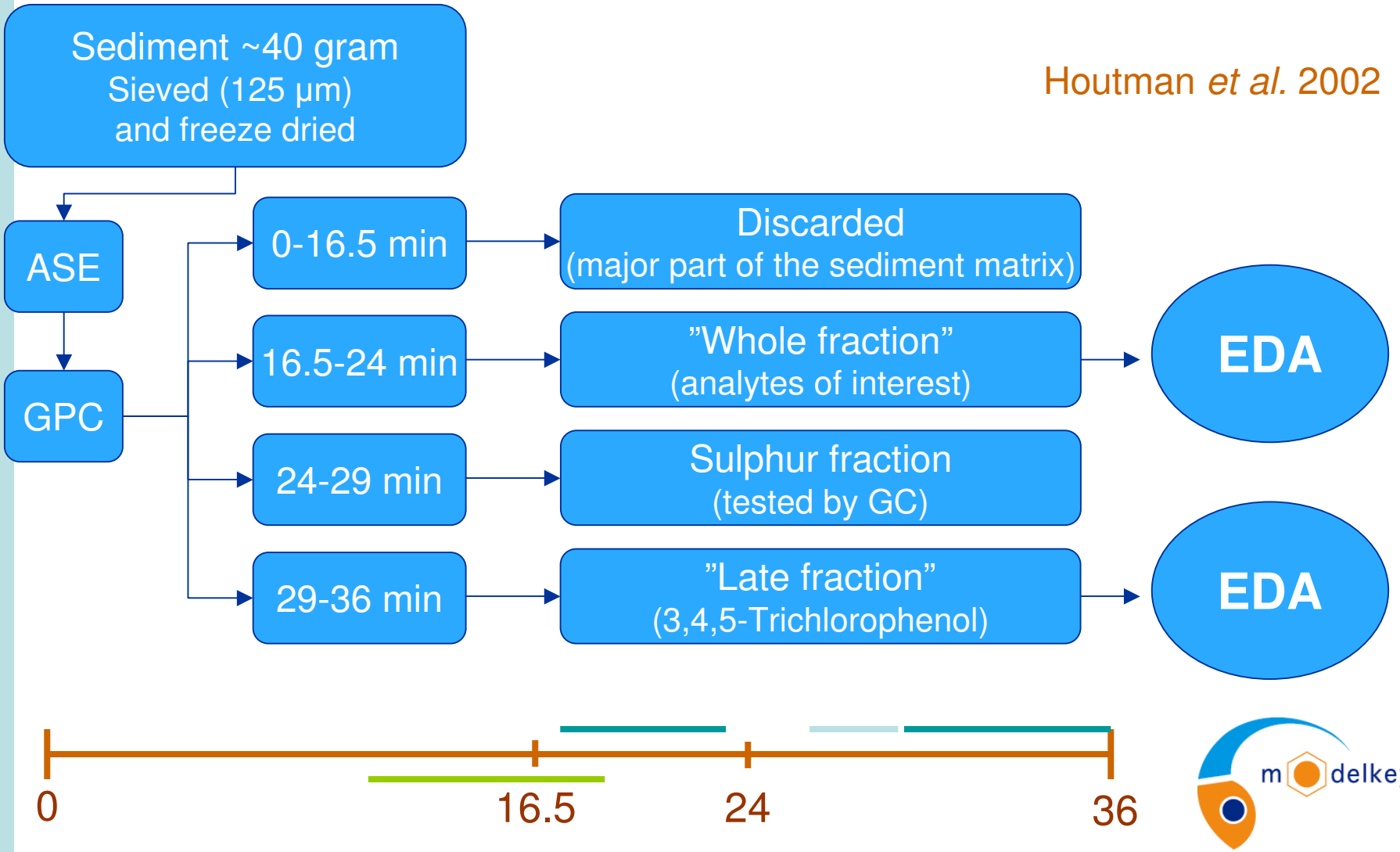
Principle of T4-TTR binding assays



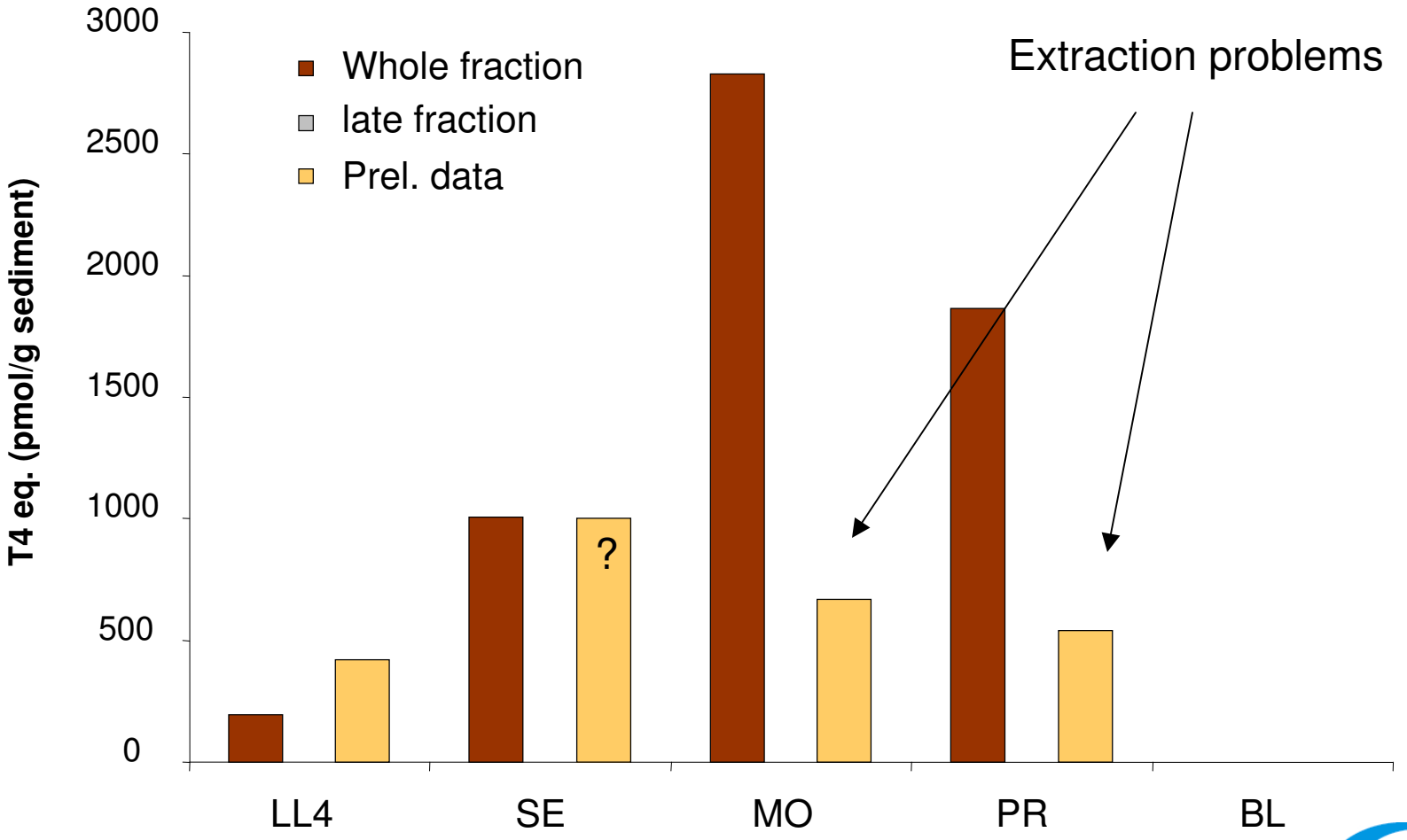
Preliminary results

		RLBA	CALUX	
		TTR-binding	AR-agonist	AR-antagonist
Llobregat	A1	x		
Llobregat	A2	x	x	
Llobregat	4	x	x	
Bilina	Jirkov			
Bilina	Most	x		x
Elbe	Pardubile	x		
Elbe	Prelouce	x		x
Scheldt	Schijn	?		x
Scheldt	SRV	x	x	
Scheldt	TRN	x		
Scheldt	HW	x		

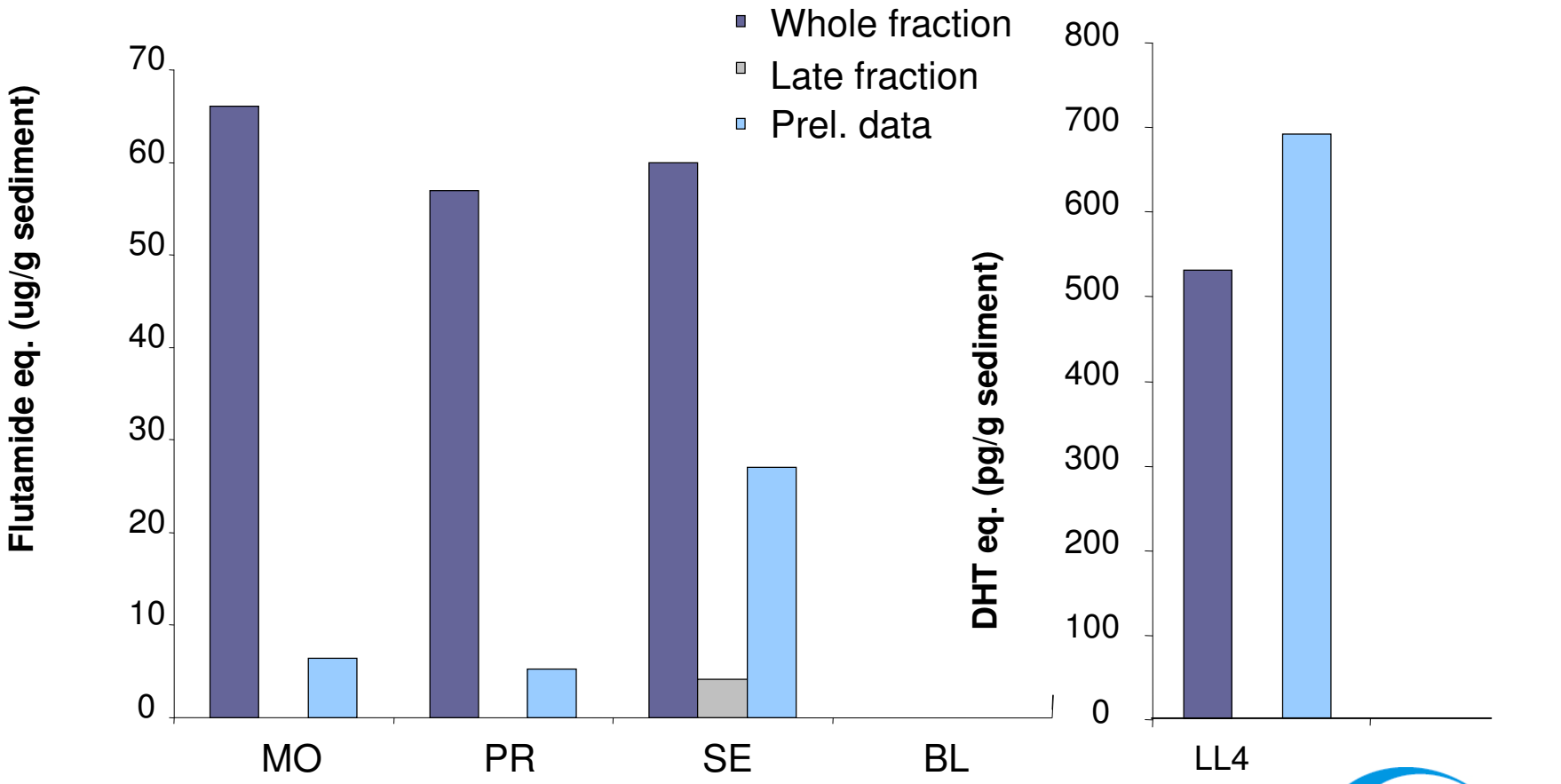
Effect Directed Analysis/ GPC



EDA results/ TTR Binding assay



EDA results/ (anti-) AR-CALUX



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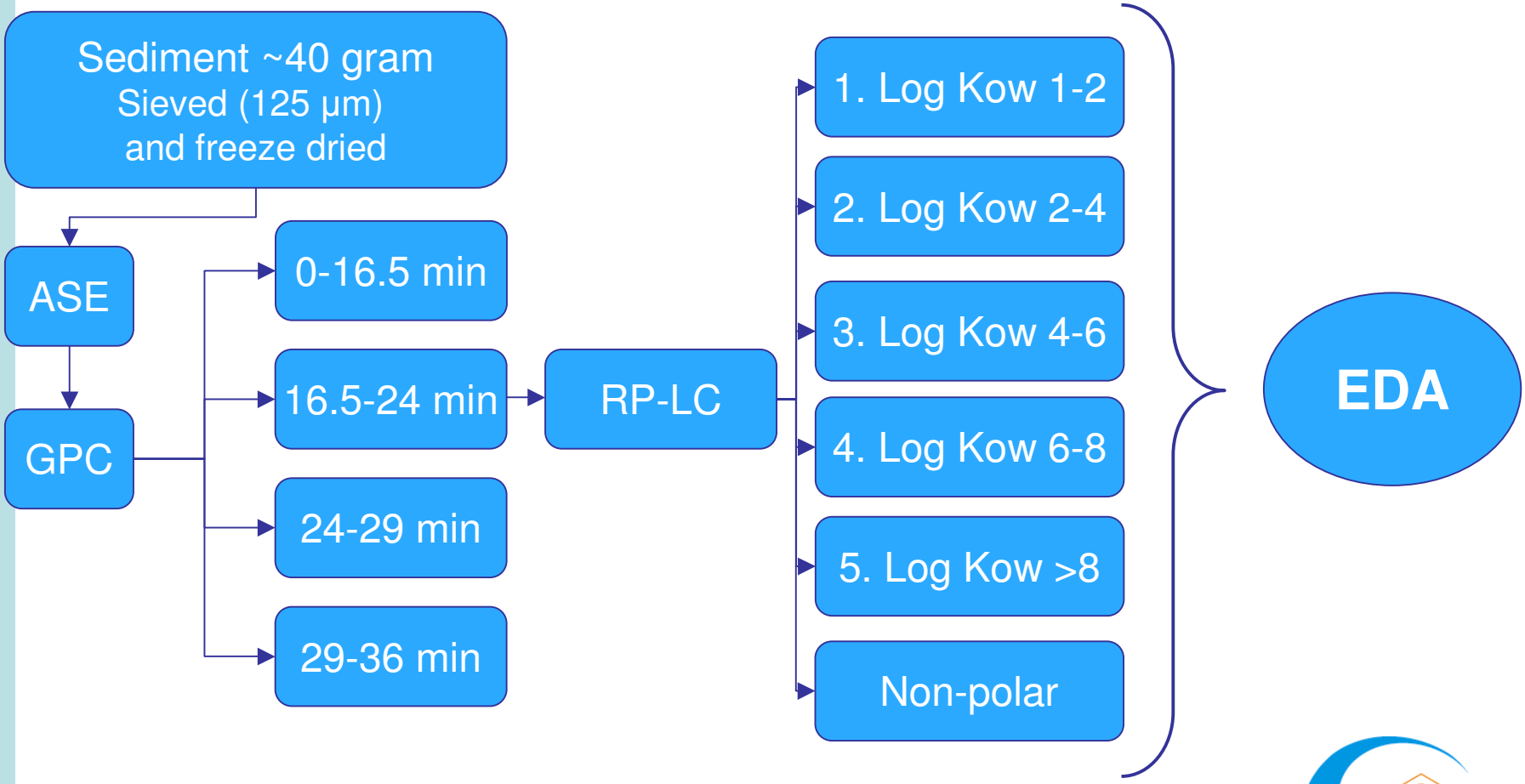
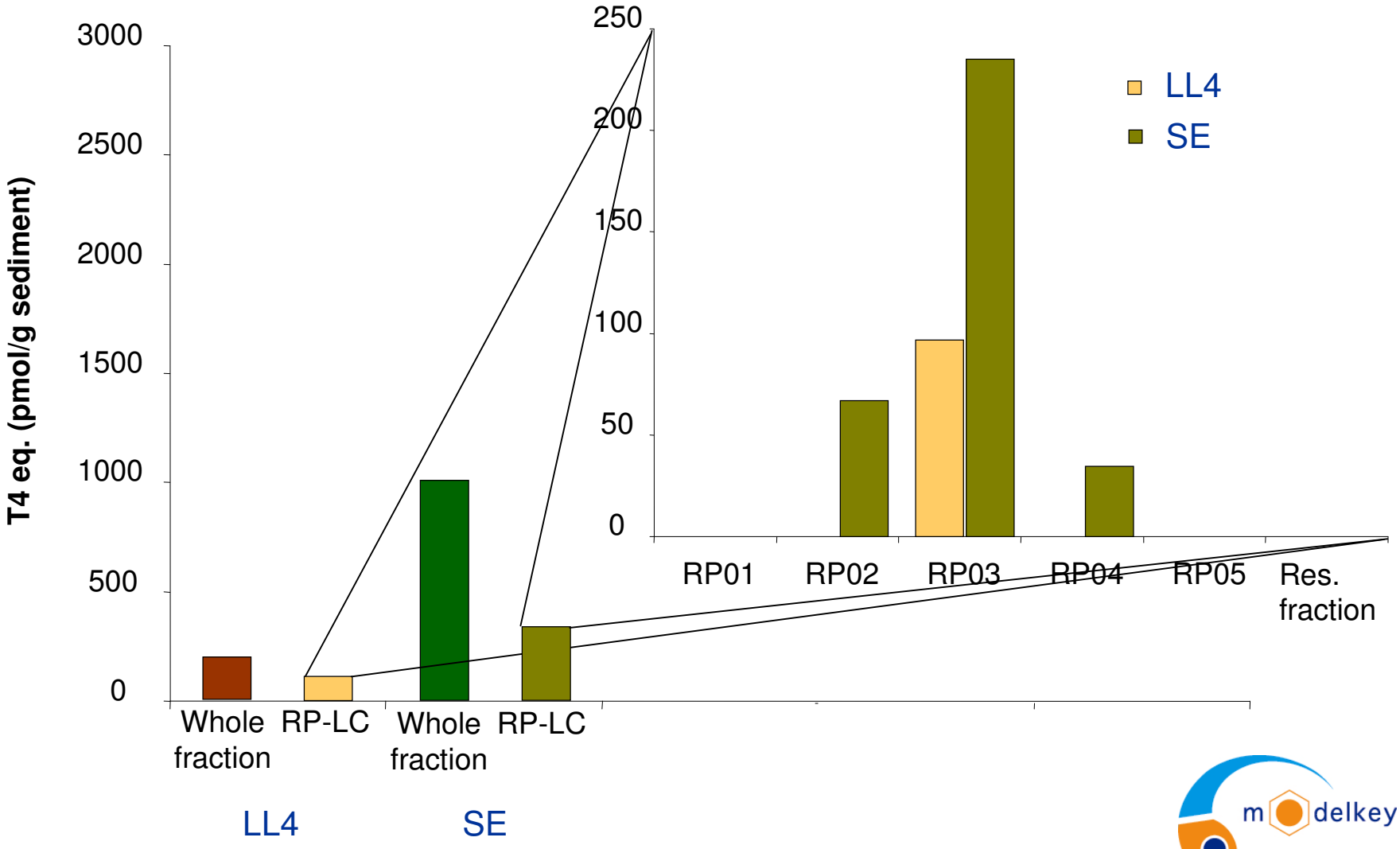
Effect Directed Analysis / RP-LC

Houtman *et al.* 2004



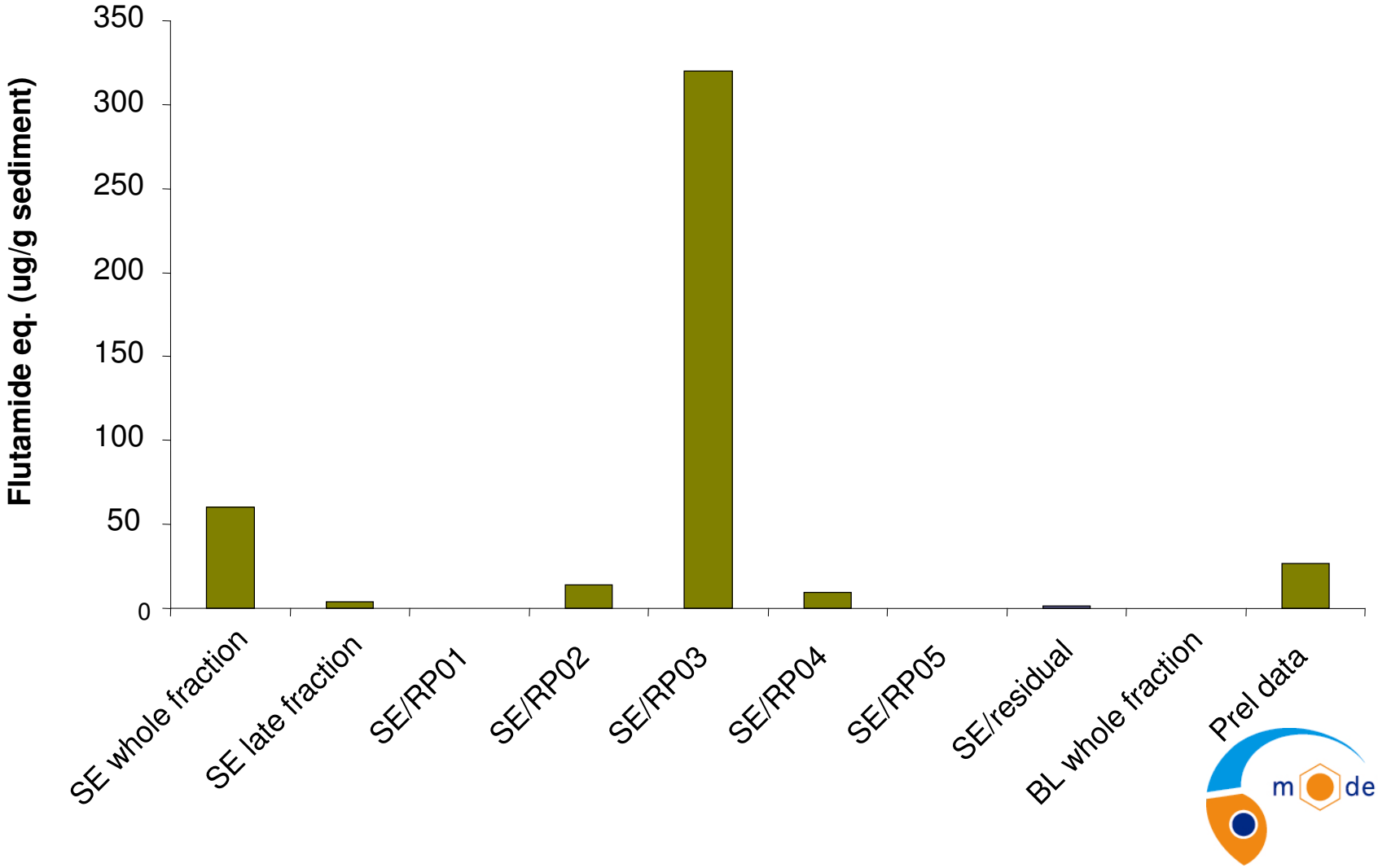
modelkey

EDA results/ TTR Binding assay

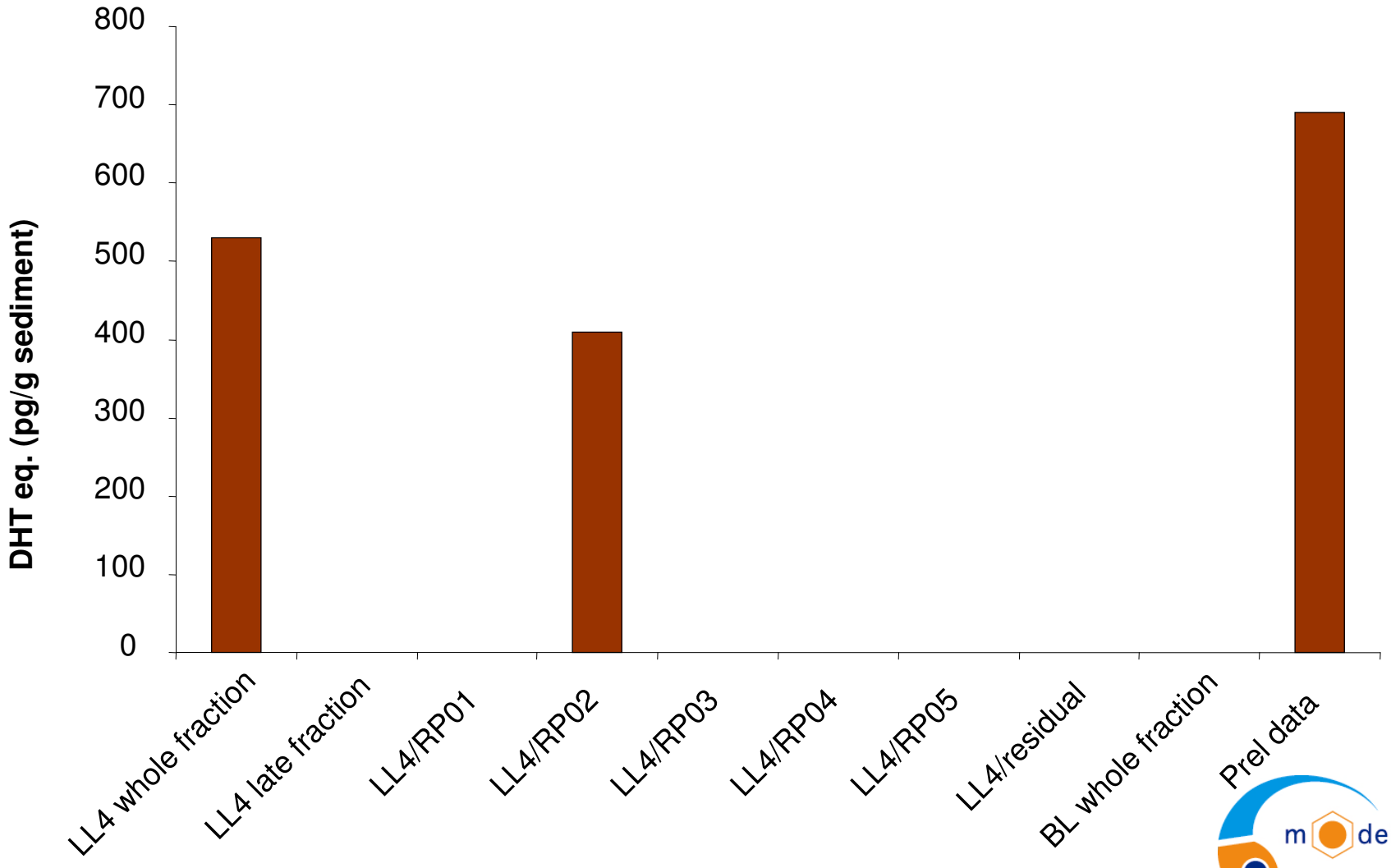


modelkey

EDA results/ anti AR-CALUX

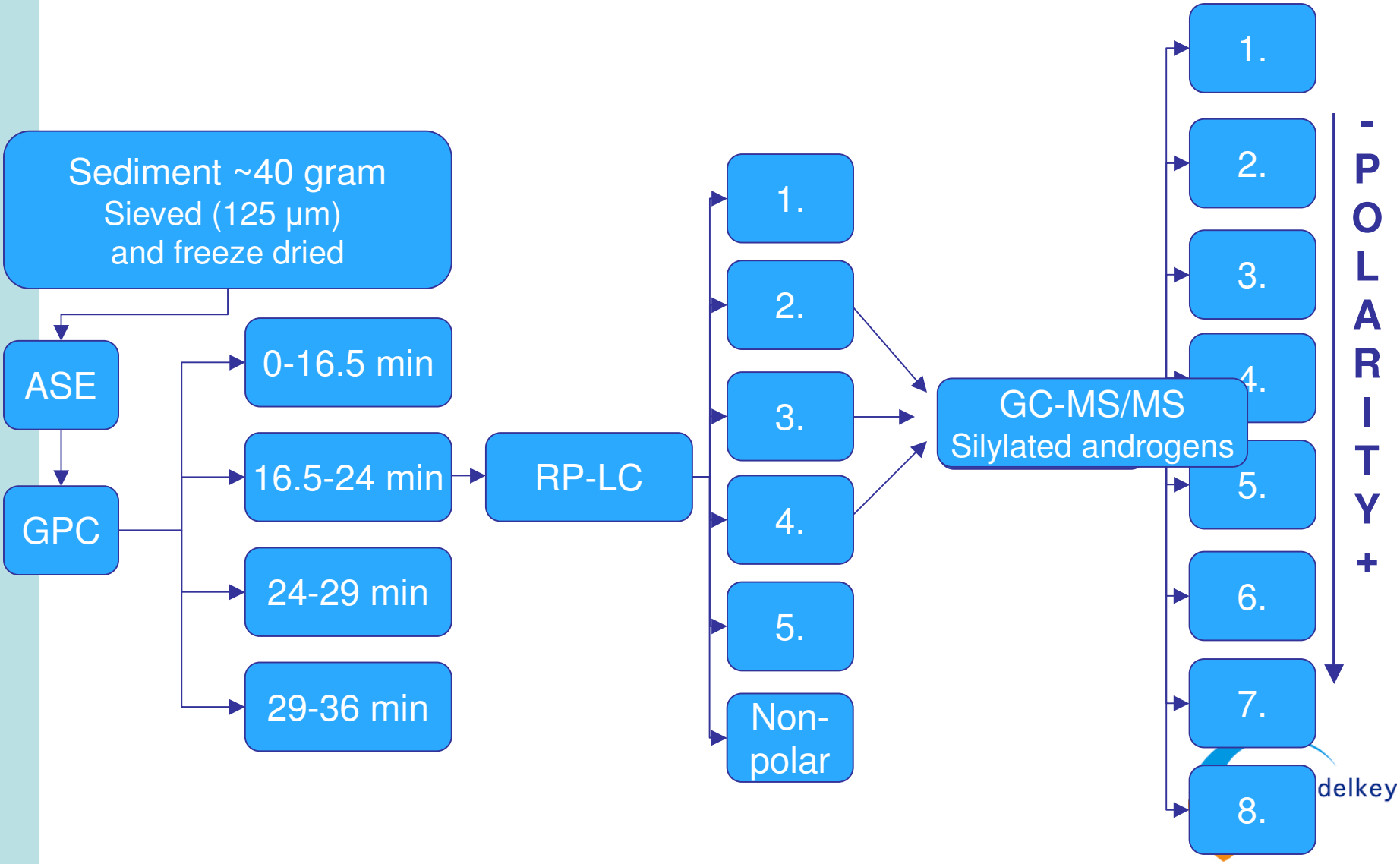


EDA results/ AR-CALUX

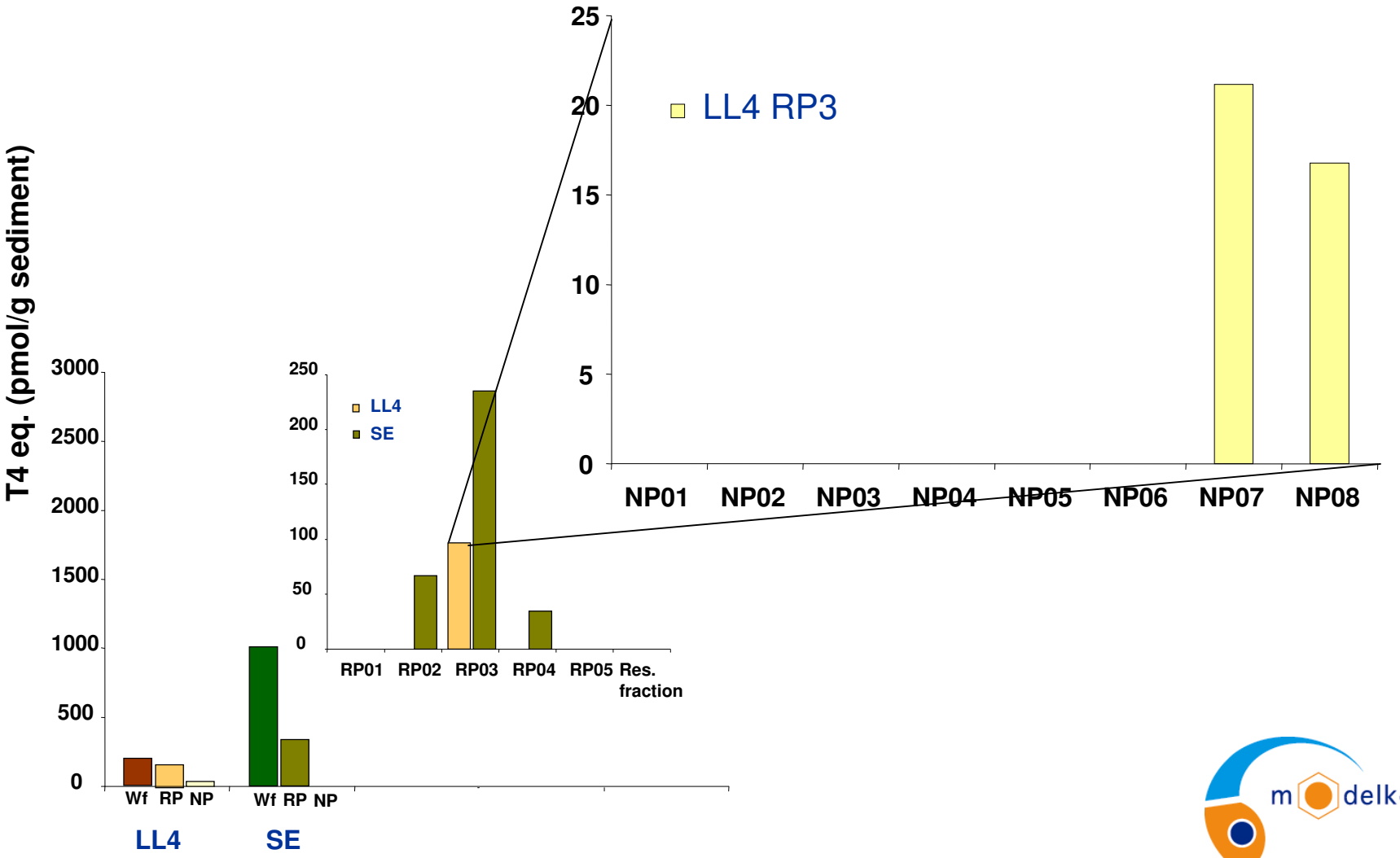


modelkey

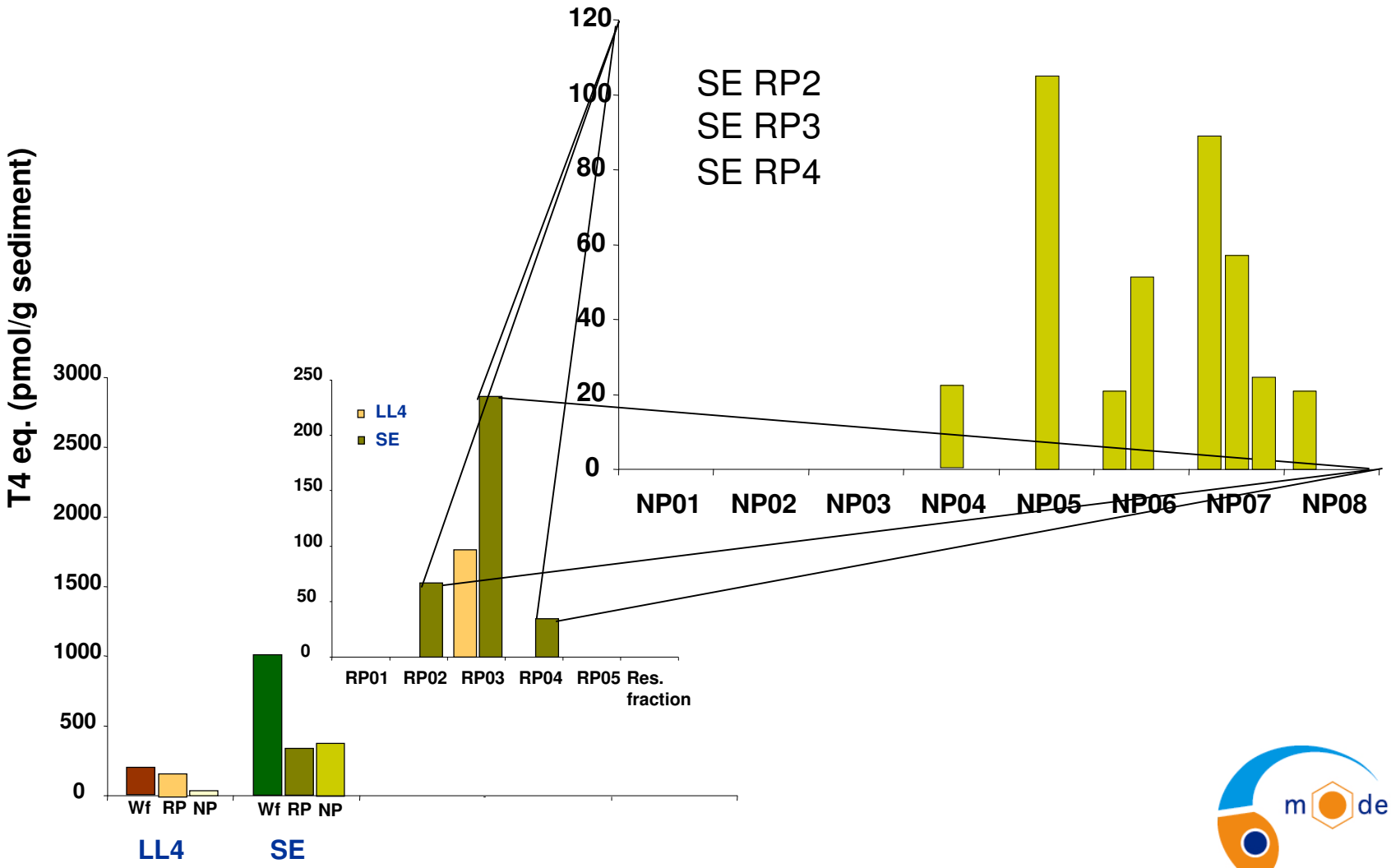
Effect Directed Analysis/ NP-LC



EDA results/ TTR Binding assay

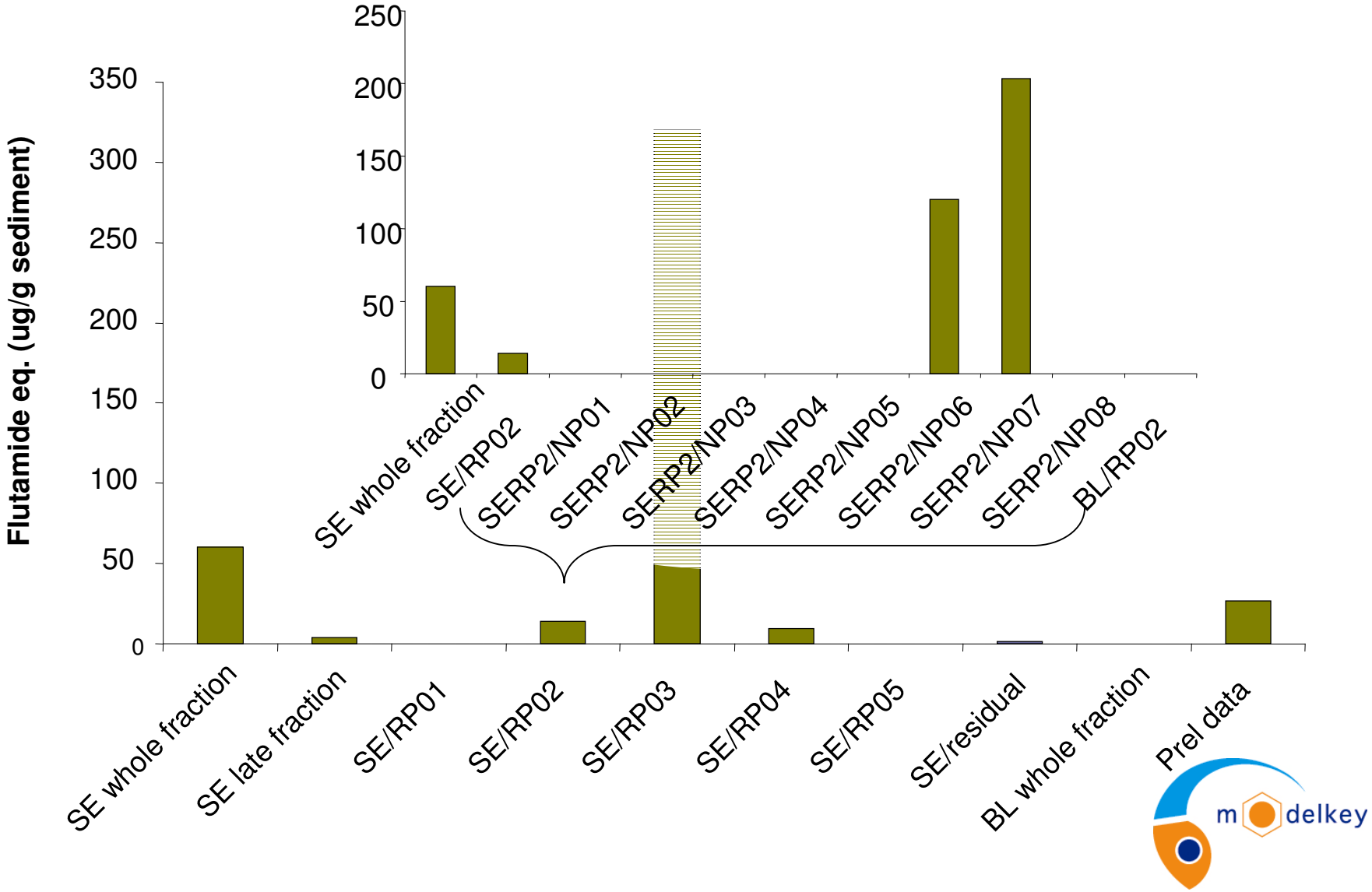


EDA results/ TTR Binding assay

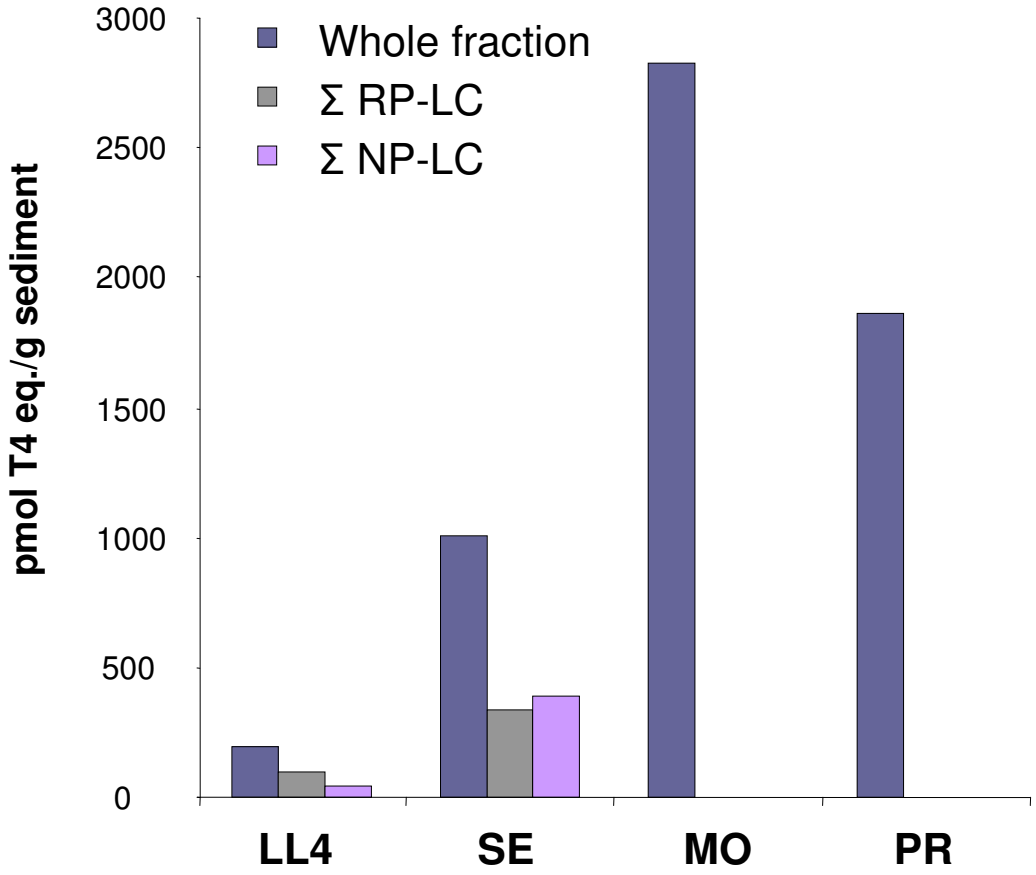


modelkey

EDA results/ anti AR-CALUX



Summary and comparison/ T4 equivalency

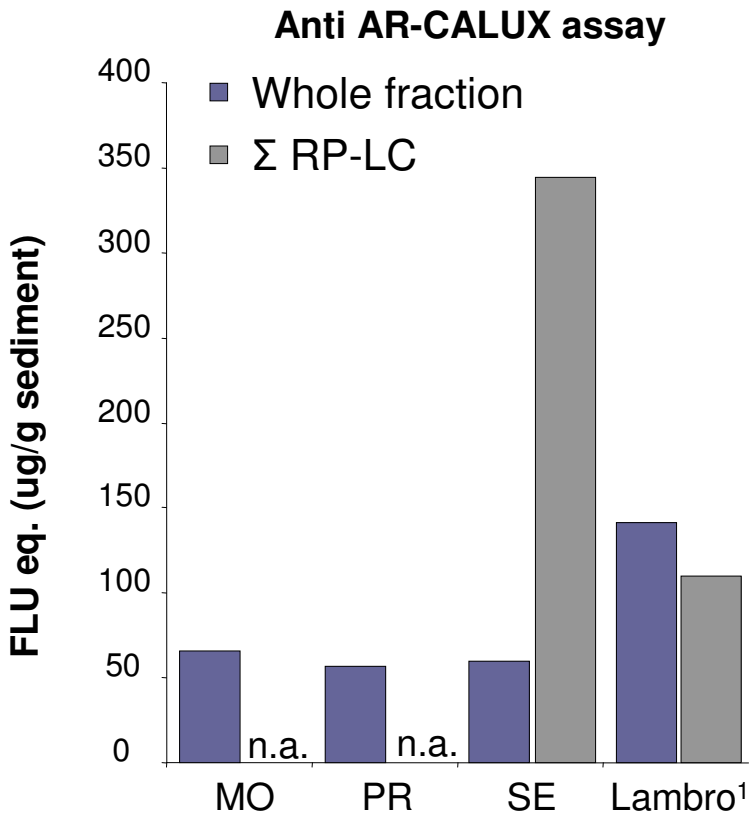


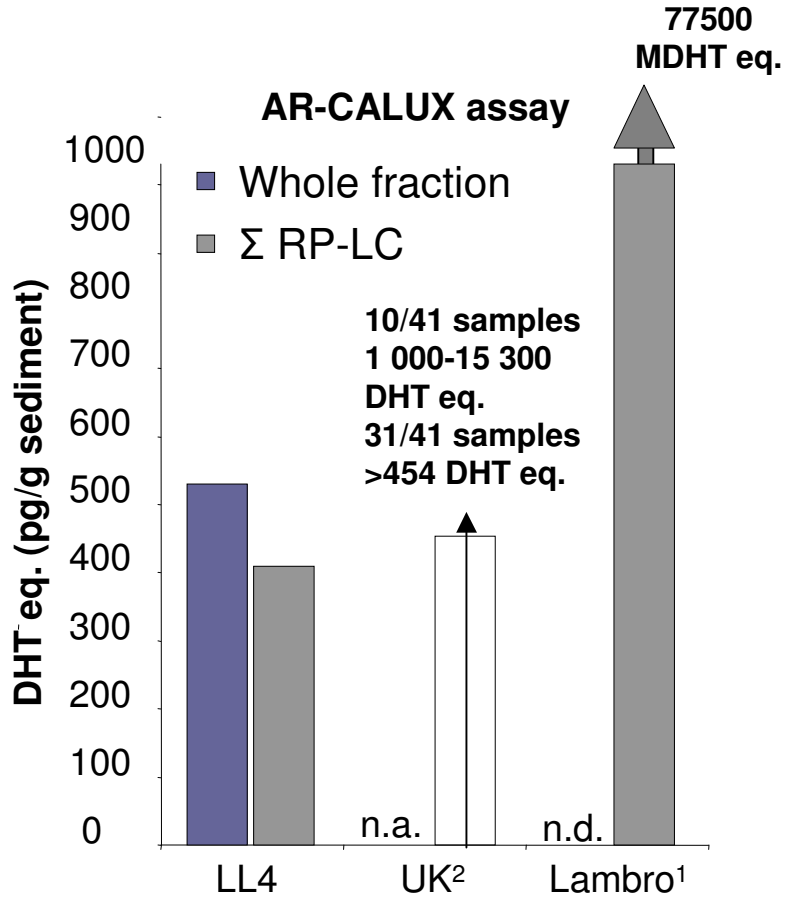
6-16 pmol T4 eq./g sediment (Zierikzee, NL)

Houtman *et al.* 2004

modelkey

Summary and comparison/ (anti-)andrenogenicity





[1] Urbatzka *et al.* 2007, [2] Thomas *et al.* 2002

Effect Directed Analysis / Identification

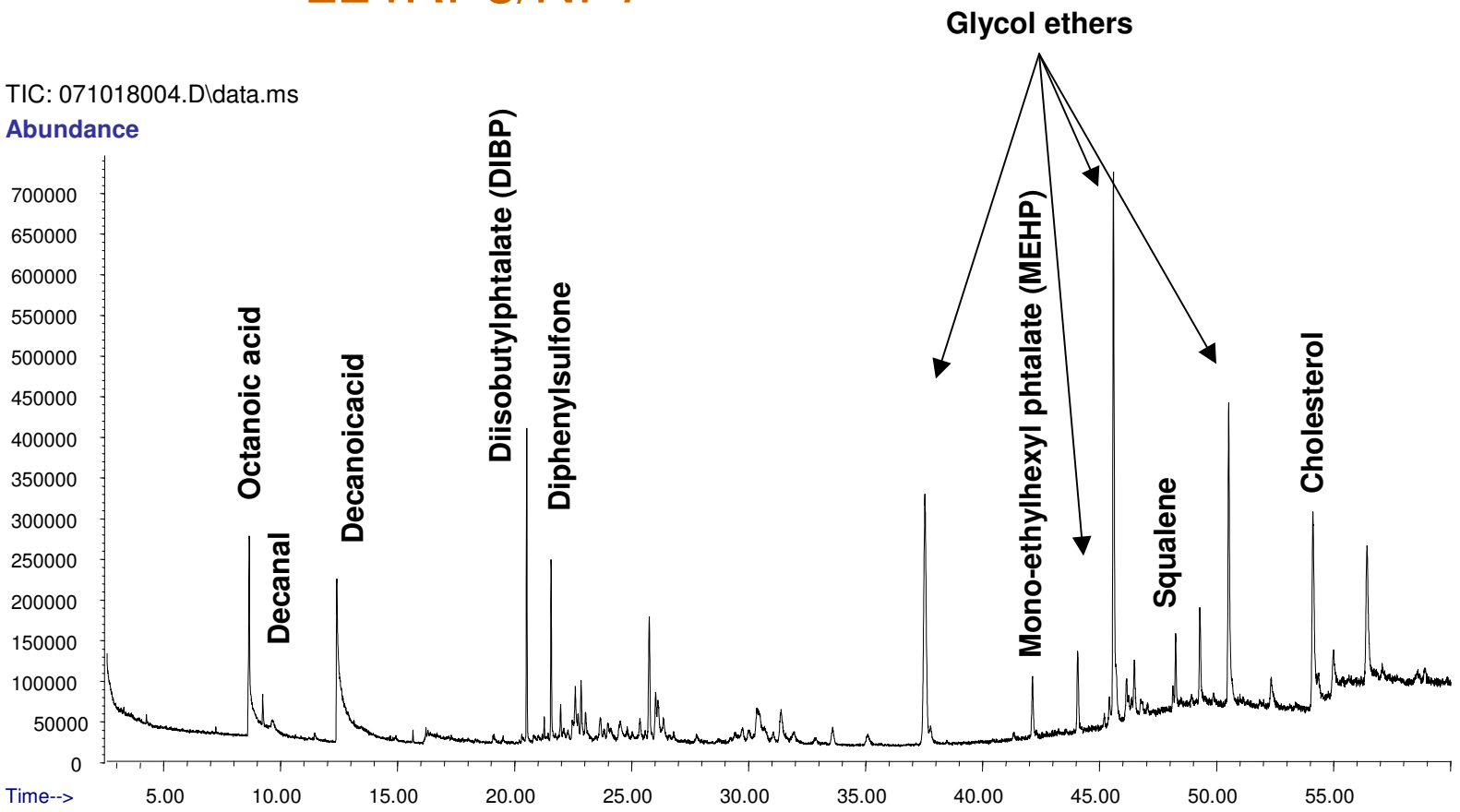
Chemical analysis

GC-MS

- Full scan
- Amdis
- NIST

Chemical analysis

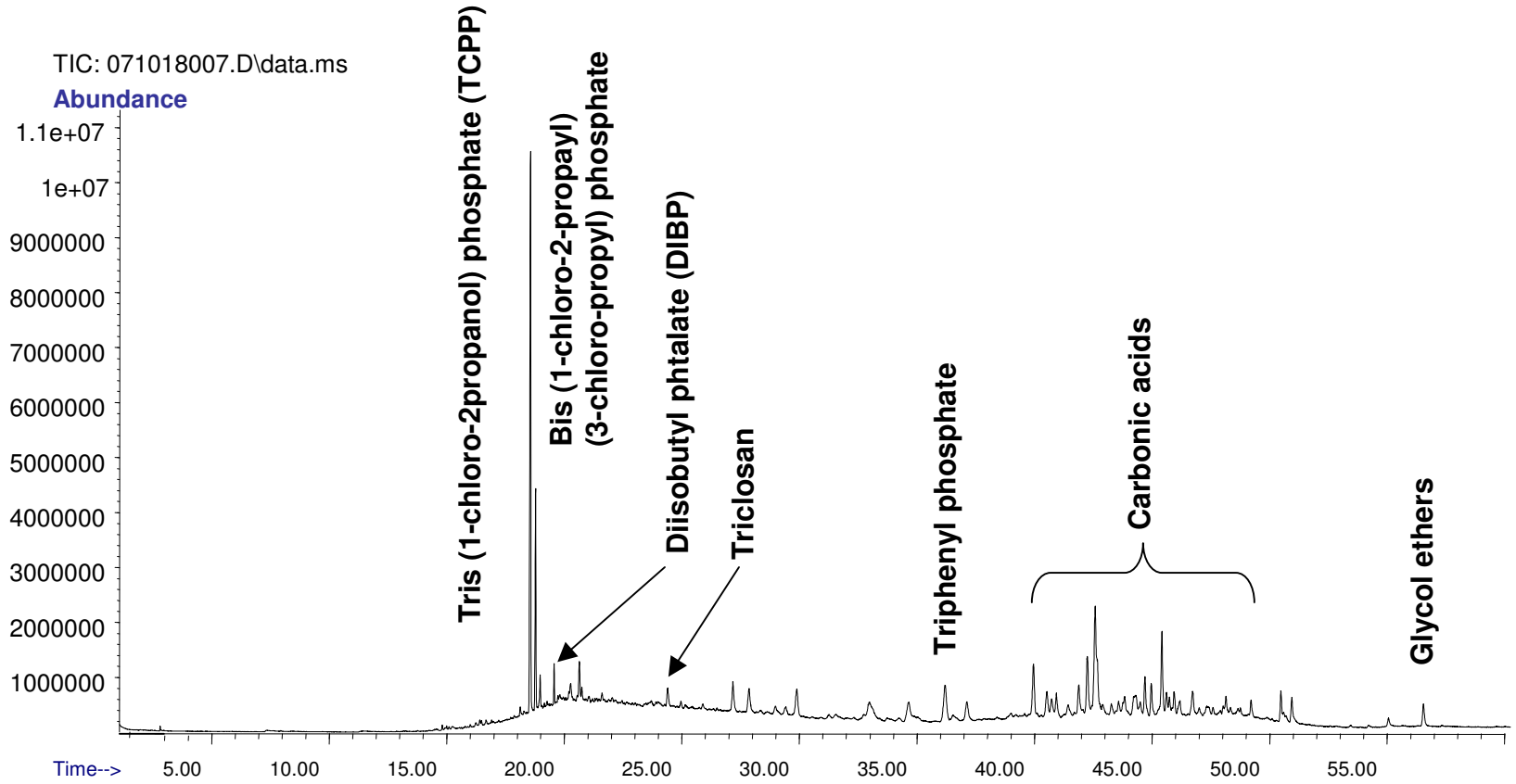
LL4RP3/NP7



modelkey

Chemical analysis

SERP2/NP7



Future Issues

Chemical analysis

GC-MS
- Full scan
- Amdis
- NIST

LC-MS/MS

GCxGC-TOF

Accurate mass

Identification

RT (several columns)

Mass spectra

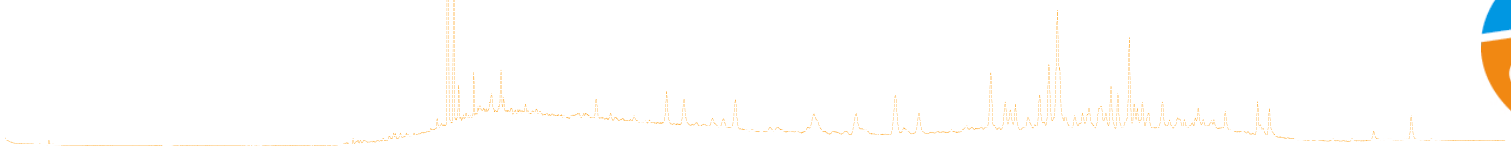
NMR

Accurate mass

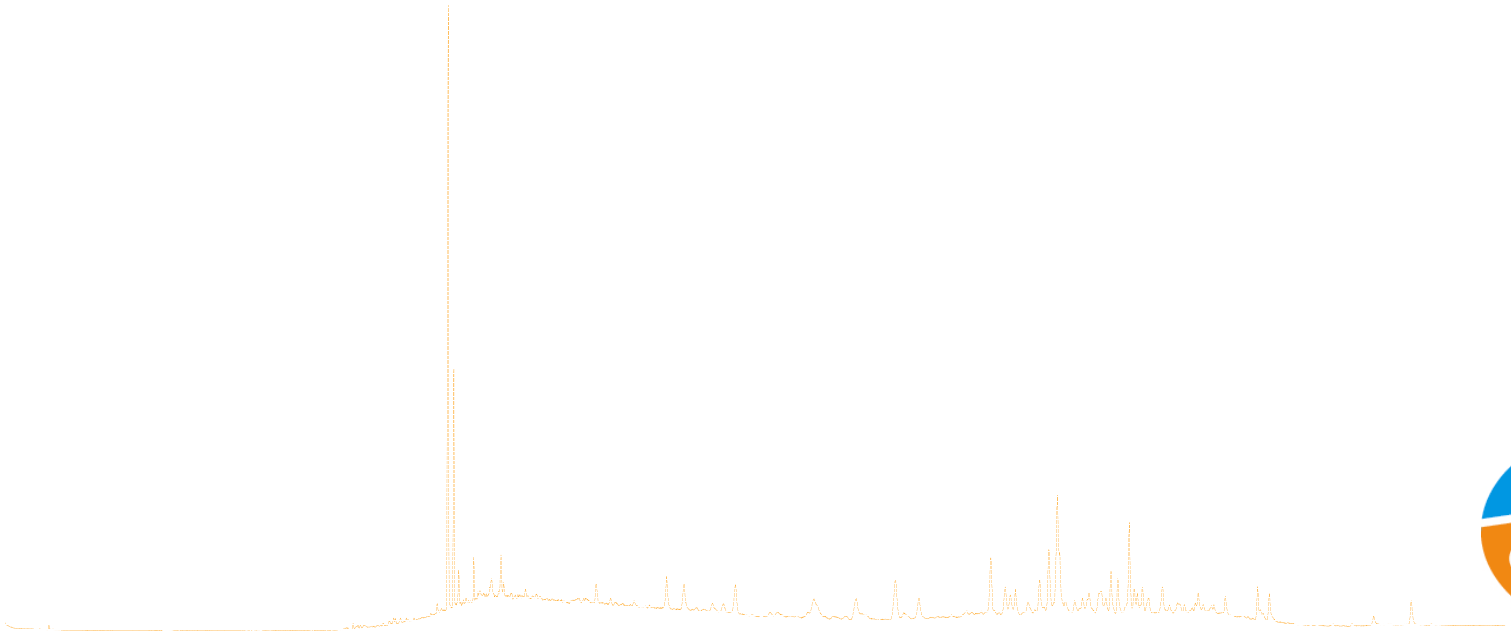
Confirmation

Analytical
- recovery
- mass balance approach

Toxicity
- *in vivo/ in vitro*
- *spiking approach*



Thank you for your attention!



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