



DTSC LABORATORY UPDATE

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Environmental Chemistry Laboratory

Scientific Guidance Panel
November 3, 2016
Richmond, CA

Outline

- Current Projects
- Untargeted Suspect Chemical Screening

Current Projects

- California Teachers' Study (CTS)
 - Analyses completed ~2000 (PFASs; PBDEs; PCBs; OCPs)
 - Statistical analyses underway
 - Metabolomics sub-study underway

- FREES (on-going) => PBDEs, OPFRs, hand wipes, foam

- MAMAS (n=540) => Expanded PFASs, PBDEs, PCBs/OCPs, Lipids

- ACE (on-going) => Expanded PFASs

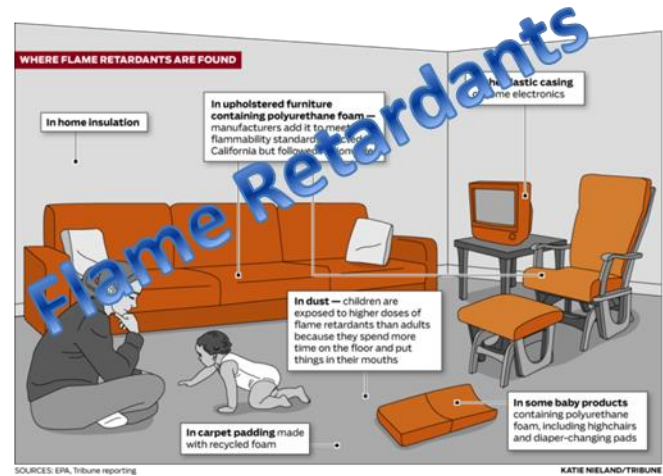
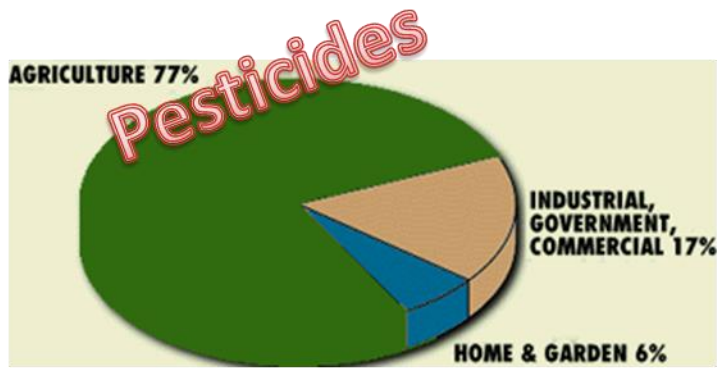
Untargeted Suspect Chemical Screening in Blood using High Resolution LC-QTOF MS

1. Background
2. Experimental
3. Workflow
4. Results
5. Current/Future work



Why QTOF Screening? Early Warning

Poly and perfluoroalkyl substances



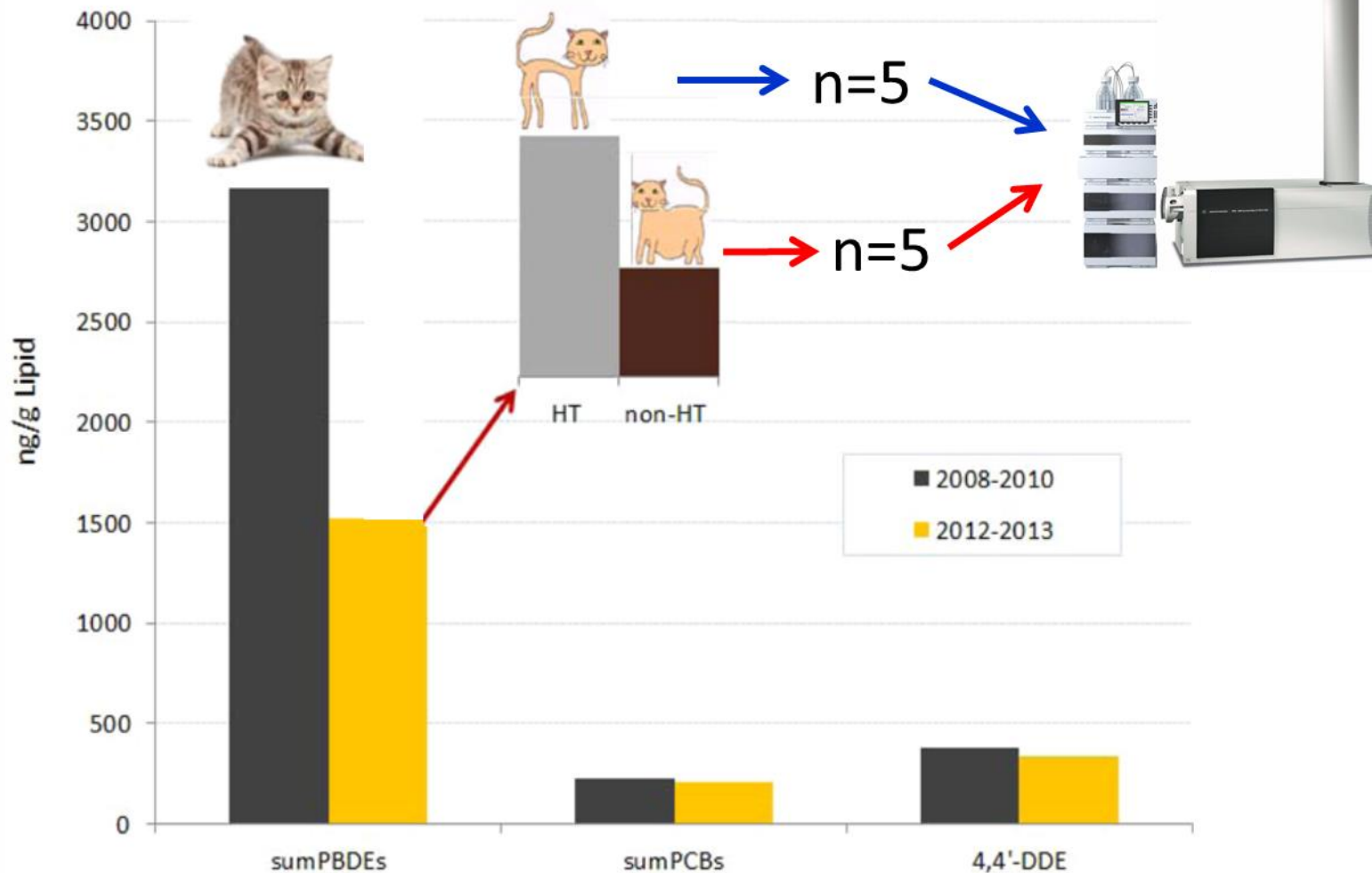
Untargeted Suspect Screening using Cat Serum: Surrogate for Human

- Cats share similar indoor environmental exposure pathways as humans
- 5-10x higher levels of POPs compared to humans
- Samples available from our previous study: Normal and Hyperthyroid (HT) cats (n=22) → only needed ~250 uL
- Good exploratory study that can be easily adapted for human biomonitoring

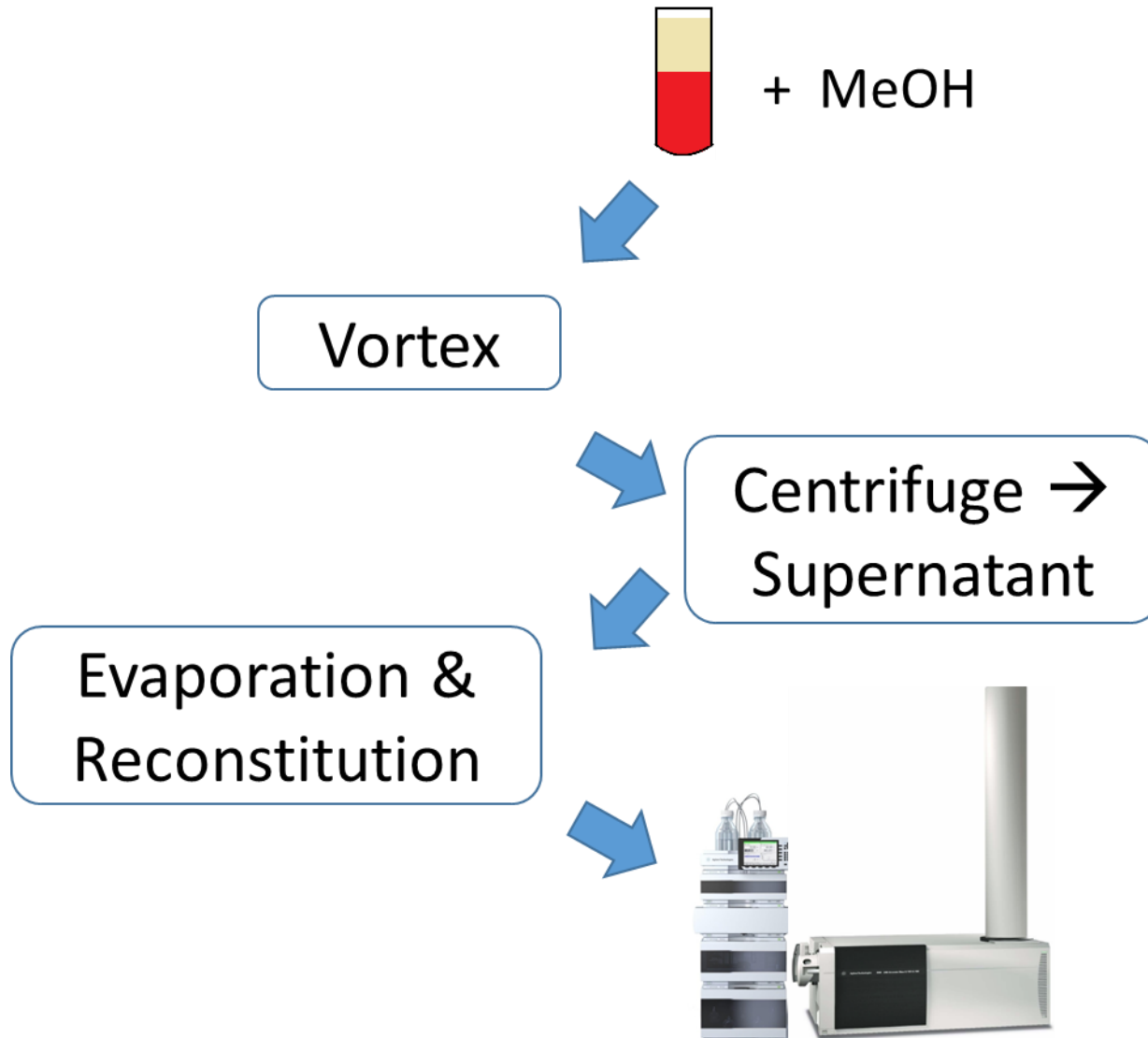
Study Design for Untargeted Suspect Screening

Temporal Changes of PBDE Levels in California House Cats and a Link to Cat Hyperthyroidism

Weihong Guo,^{*,†} Stephen Gardner,[‡] Simon Yen,[§] Myrto Petreas,[†] and June-Soo Park[†]



Sample Preparation and Analysis



LC-QTOF Workflow & Results

Full scan TIC, Negative ion, 3x Injections

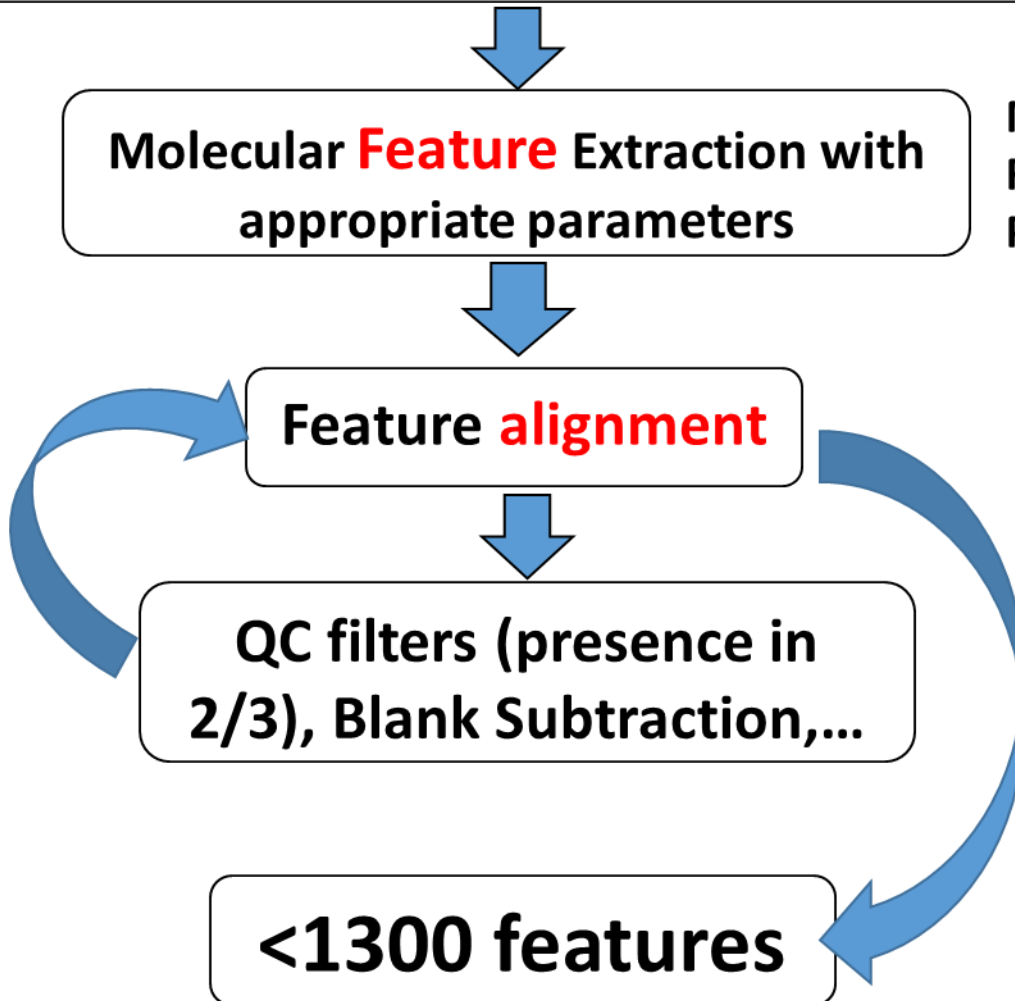
Molecular **Feature** Extraction with appropriate parameters

Mass
RT
Peak Intensity

Feature **alignment**

QC filters (presence in 2/3), Blank Subtraction,...

<1300 features



Our Libraries: <20% Features Identified

1. Flame retardants library (~**100 compounds**)
2. PFAS library (~**250**)
3. Consumer product library (~**2500**): consumer product chemicals index, combined with analytes from in-house and up to date literature (*Goldsmith et al.*)
4. US EPA Tox21 library (DSSTox _ToxCastRelease_20151019): ~**9000** (*Richard et al.*)
5. EOA library (~**750**): environmental organic acids (*Gerona et al.*)

3. *Goldsmith et al. Food Chem. Toxicol., 2014, 269-279*

4. *Richard et al. Chem. Res. Toxicol. , 2016, 1225-1251*

Selective Identification

Volcano Plot (Stat Software)

1. HT Cats: Features higher Intensity (>2 fold, $p < 0.05$) than normal cats
2. Matching score > 80

Identification & Confidence

Name	Formula	Mass	RT	Score	comment
Duloxetine <u>3</u>	C18 H19 N O S	343.1241	5.617	96.76	depression drug
PFOSA	C8 H2 F17 N O2 S	498.953	6.568	96.73	PFAS
PFOSAA <u>1</u>	C10 H4 F17 N O4 S	556.9582	6.236	95.59	PFAS
Catechol	C6 H6 O2	110.0368	0.905	87.47	phenol/pesticide
L-leucine	C6 H13 N O2	131.0947	0.619	86.9	dietary supplement
acetaminophen	C8 H9 N O2	151.0634	1.458	86.75	pharmaceutical
texanol	C12 H24 O3	216.1722	5.738	86.44	coalescent for latex paints
myristic acid	C14 H28 O2	228.2093	7.208	85.83	common fatty acid
acetophenone	C8 H8 O	120.0569	5.286	85.56	common fragrant ketone used in fragrance
(S)-hydroprene	C17 H30 O2	266.2239	7.274	85.37	insecticide
dodecyl methacrylate	C16 H30 O2	254.2236	7.644	82.19	an ester that might be used in PCP

3-4

Confidence Levels for Identification (Schymanski et al 2014, ES&T):

Level 1: Confirmed by reference standard

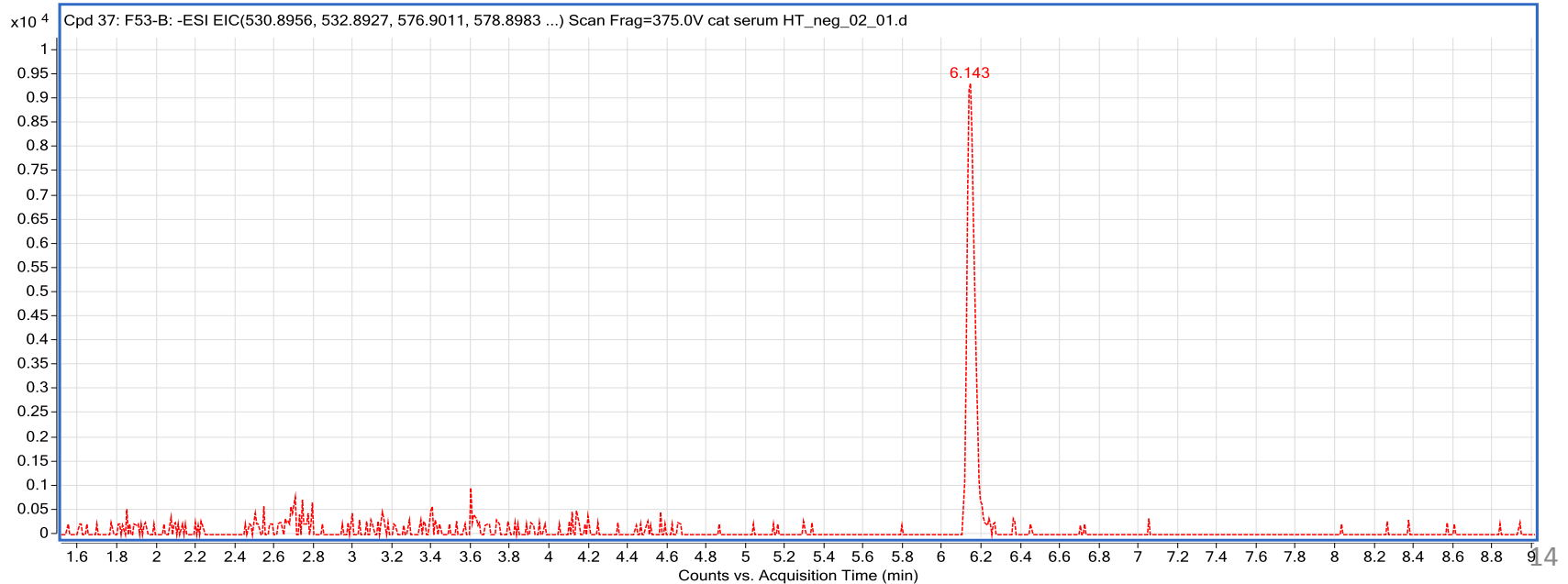
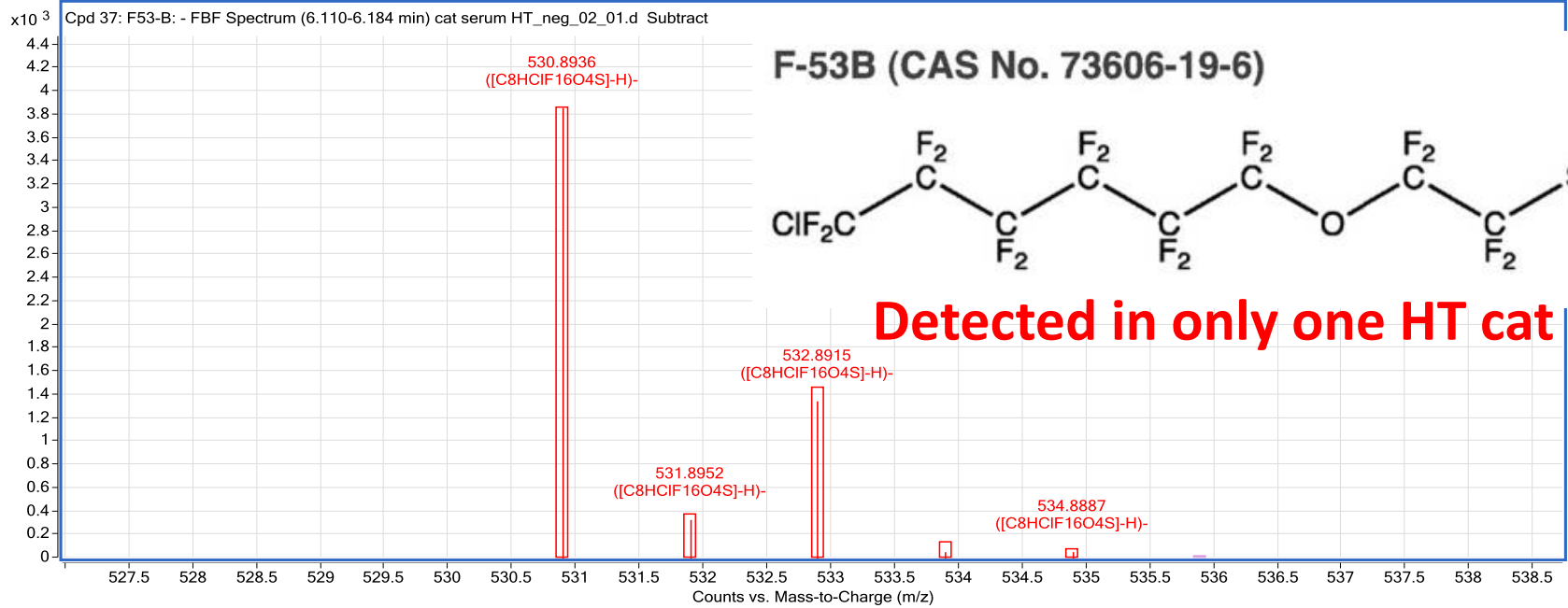
Level 2: MS, MS2, Library MS2, Exp data

Level 3: MS, MS2, Exp data

Level 4: MS Isotope, adduct

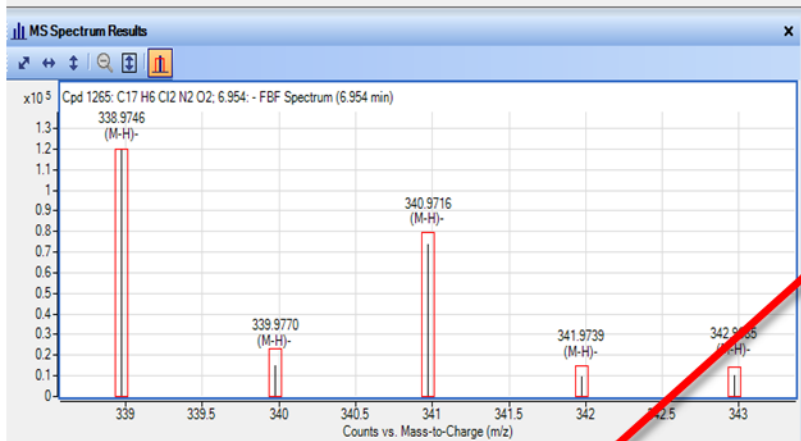
Level 5: Exact mass

Replacement PFAS: F-53B



>80% Features: No Database Match

Formulas generated using CI →



Formula	Score	Mass
C17 H6 Cl2 N2 O2	90.7	339.9816
C9 H10 Cl2 N4 O4 S	86.7	339.9818
C6 H14 Cl2 N4 O4 S2	83.05	339.9819
C14 H10 Cl2 N2 O2 S	81.95	339.9817
C14 H9 Cl3 N3 O	76.92	339.9817
C16 H11 Cl3 O2	75.43	339.9817
12 more formulas < 70		

Chemspider → 352 hits →

1-(2,4-Dichlorobenzyl)-3-methyl-1H-thieno[2,3-c]pyrazole-5-carboxylic acid

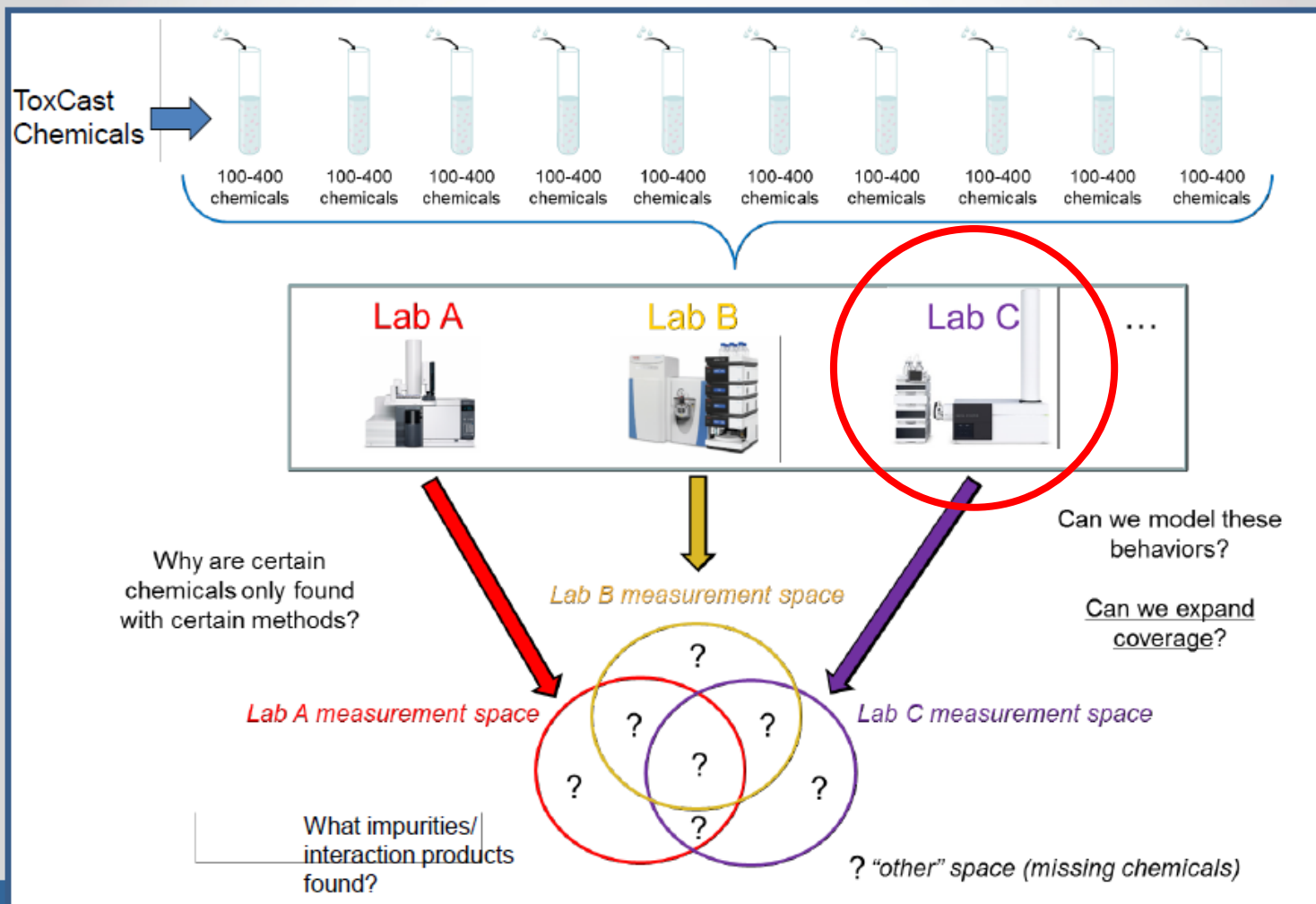
Molecular Formula C₁₄H₁₀Cl₂N₂O₂S
Average mass 341.212 Da
Monoisotopic mass 339.984009 Da
ChemSpider ID 1817854

Next Steps

1. Continue identification
2. Confirmatory → Confidence level 1 or 2
3. Select 5-10 compounds of concern (working with OEHHA for designation) -> Target analysis & Quantitation
4. Standard Operating Procedure (SOP)
5. Apply to human studies

Collaboration 1: US EPA Round Robin

ORD-led NTA Research Trial



Collaboration 2: UCSF (NIH R01): “Discovery of Novel Environmental Contaminants”

1. Develop and apply LC-QTOF MS screening method for over 700 Environmental Organic Acids (EOA) in matched umbilical cord and maternal serums (n=600).
2. Develop and apply targeted LC-MS/MS methods to confirm and quantify 10 priority EOAs.
3. Assess demographic and maternal-neonatal differences in exposure to 10 priority EOAs.

Pesticide metabolites	365
Phenols	270
Pesticides	60
PFASs	46
Phthalate metabolites	38
Phthalates	27
OH-PBDEs	12
OH-PCBs	12

Collaboration 3: Uppsala University, Sweden (Dr. Samira Salihovic)

1. Variation in metabolomics profile against POPs already measured in CTS (n=325)
2. Metabolomics profile comparison: CTS vs. “Uppsala Senior Population”

Annotation:

-Primary database: In-house library **Uppsala University/ Colorado State University** (Dr. Jessica Prenni) with >1000 standard spectra and RT available.

-Secondary database: METLIN, HMDB, LIPIDMAPS

Acknowledgements

- ECL's Non-targeted Analysis Team (Drs. Miaomiao Wang, Swati Anand & Samira Salihovic)
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Questions/Comments?

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