



DTSC LABORATORY UPDATE

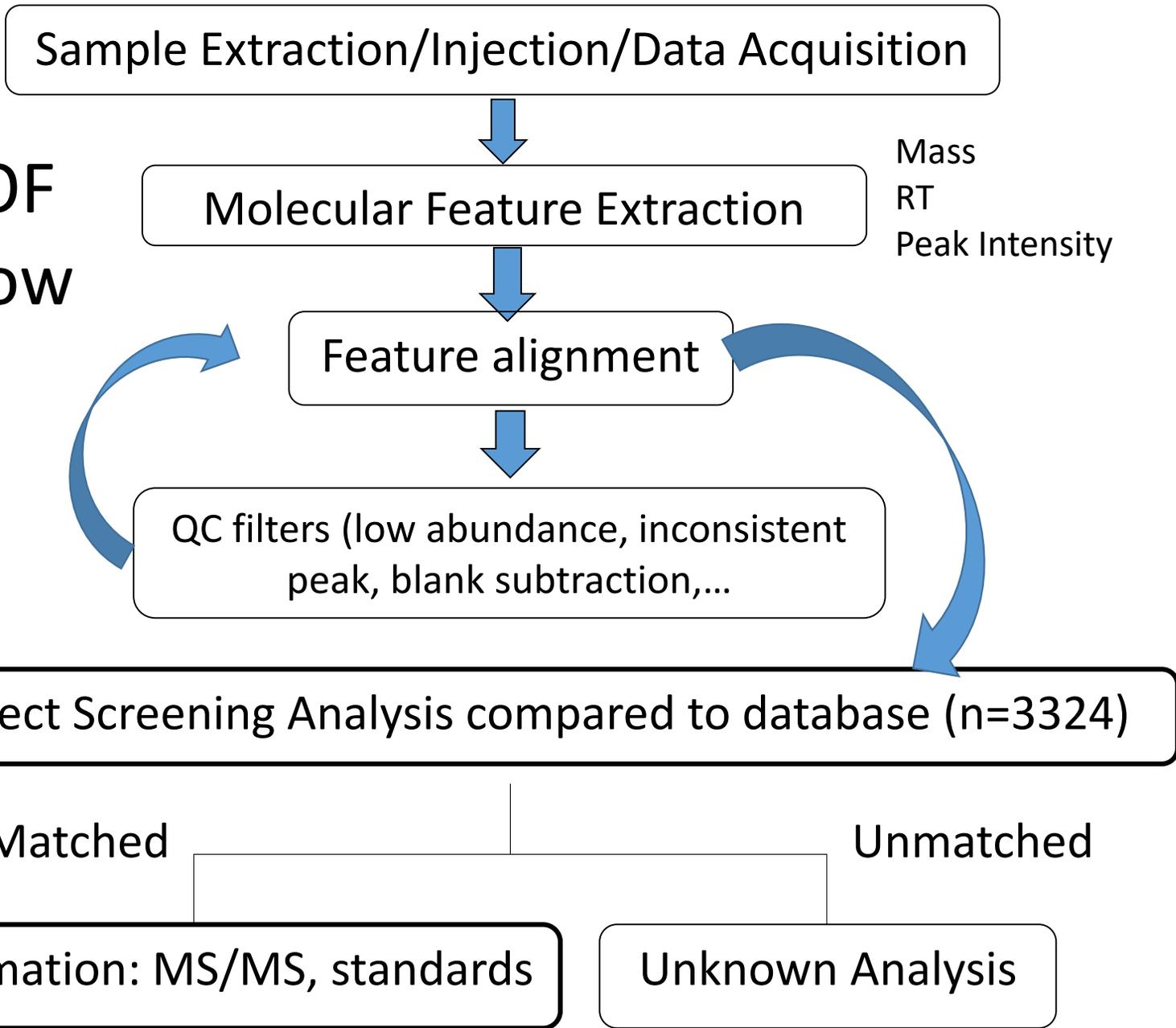
NON-TARGETED ANALYSIS (NTA)

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Scientific Guidance Panel
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LC-QTOF Workflow



In-house Suspect Screening Database: Environmental Organic Contaminants in Human (N=3324)

Category	# of chemicals
Consumer products	1285
PFAS (per- and polyfluoroalkyl substances)	308
Environmental phenols	192
Agrochemicals	182
Personal care products	121
Food additives and packaging	120
Flame retardants	88
Plasticizers	86
Phthalates	74
Other industrial chemicals	868

Non-Targeted Analysis: Challenges and Lessons Learned

NIH-funded (R01) Study
in partnership with UC San Francisco

“Discovery of Novel Chemicals in Humans”
(300 cord and 300 maternal serum samples)

Identified Features (<15%) Uncertain

Name	Formula	Mass	RT	Score	comment
Duloxetine 3	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 1	C10 H4 F17 N O4 S	556.9582	6.236	95.59	PFAS
Catechol	C6 H6 O2	110.0368	6.905	87.47	phenol/pesticide
L-leucine	C6 H13 N O2	131.0947	6.619	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

Identified Feature Confirmatory Process

Feature Prioritization for MS/MS (A.Wang et al in prep)

1. Detection frequency & peak intensity:

- ✓ 100% DF
- ✓ Median intensity rank among top 50%

2. Demographic difference:

- ✓ Intensity of cord or maternal sample different by at least one demographic variable assessed ($p < 0.05$)

3. Maternal/cord serum correlation ($r > 0.5$, $p < 0.05$):

- ✓ >50% cord serums have intensity $\geq 2 \times$ median of maternal serums
- ✓ >50% maternal serums have intensity $\geq 2 \times$ median of cord serums

Target features selected for MS/MS test = 208

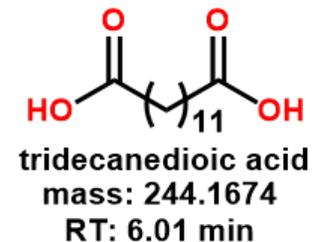
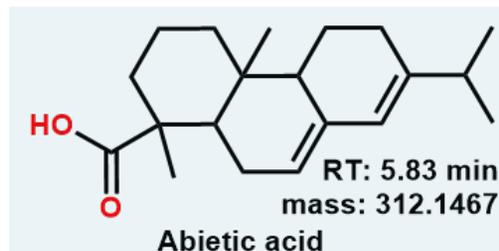
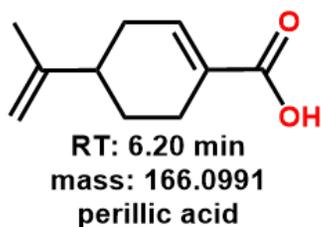
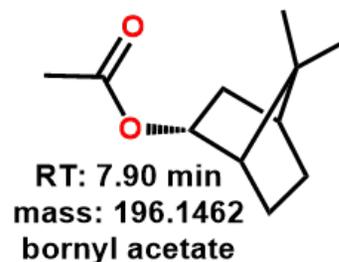
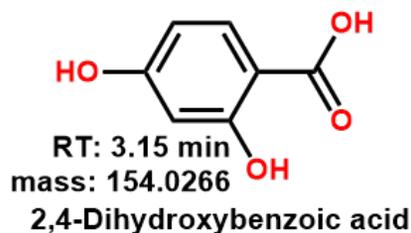
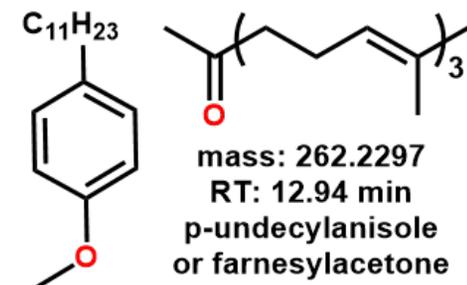
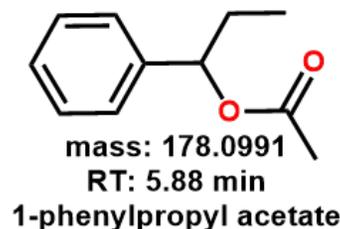
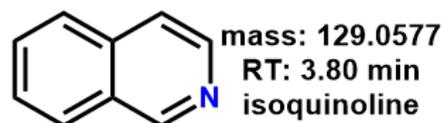
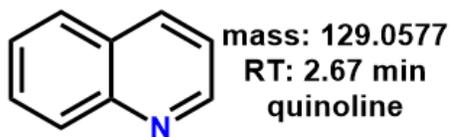
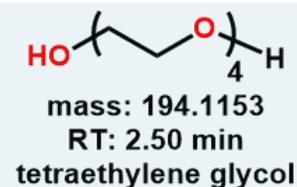
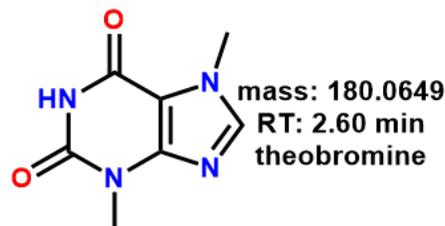
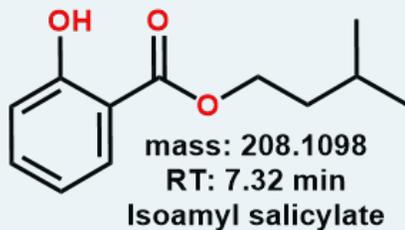
Level 2 Identification Rate

- MS/MS matching rates in our study (T. Jiang et al*) = ~ 15%
 - Matched through:
 - empirical check of fragmentation peaks
 - online experimental database eg. Massbank, PubChem
 - In silico fragmentation tools: e.g. MetFrag, CFM-ID

- Similar to other study in wastewater (Gago-Ferrerro et al *ES&T* 2015) = ~ 9%

*T. Jiang et al. "Confirmation of Contaminants from Serum Suspect Screening Analysis". 68th ASMS Conference on Mass Spectrometry May 31 - June 4, 2020. On-line oral presentation.

Example Features Confirmed by MS/MS



Other Ongoing Human Biomonitoring NTA Projects

1. Cumulative exposure in Fresno population
(with OEHHA)

Fresno N=70 cord/70 maternal serums vs. Bay Area (R01)

2. Women Firefighters/Nurses/Office Workers
(with UC Berkeley)

FFs (N=62), nurses (N= 63), office workers (N=43)

NTA Manuscripts in Progress

1. M.Wang et al. Non-targeted screening: Analysis and Review of Results from EPA's Non-Targeted Analysis Collaborative Trial (ENTACT). first draft ready.
2. A.Wang et al. Suspect screening of environmental chemicals in maternal-newborn pairs from San Francisco. Ready to submit.
3. T.Jiang et al. Confirmation of Contaminants from Serum Suspect Screening Analysis. In progress.
4. A.Miralles et al. Applicability of a non-targeted workflow approach to explore PFASs in wastewater: Sample stability in inter-laboratory studies. In progress.
5. M.Wang et al. Suspect screening and profile analysis of stormwater runoff following 2017 wildfires in northern California. First draft ready.
6. M.Wang & C.Ranque et al. Exposomic approach on cat hyperthyroidism (ECL). In prep.
7. S.Smith et al. Target and non-targeted PFAS in firefighters accidentally exposed to AFFF. In prep.
8. S. Salihovic et al. Geographical differences in metabolomic profile and epidemiology aspect between women in the California Teachers Study (n=100) and an Uppsala population (n=100) at age ~70. Pending.

Next Steps

1. Level 2 features are being compared to authentic standards purchased (n=30): MS/MS and retention time
2. Quantitate 5-10 chemicals selected using calibration curves
3. Continue to work on how to improve identification rate and confidence

Also big challenges:

1. Continue identification expanding to unknown chemicals (>85% not identifiable by database → unknown identification)
2. Non-targeted volatile and semivolatile analysis using GC-QTOF-MS just installed.

Acknowledgements



(R01 ES 027051)



**Many
Others...**

Disclaimer: The views expressed herein are those of the authors and do not necessarily reflect those of the California Department of Toxic Substances Control.