The Exposome and Pediatric Cancer

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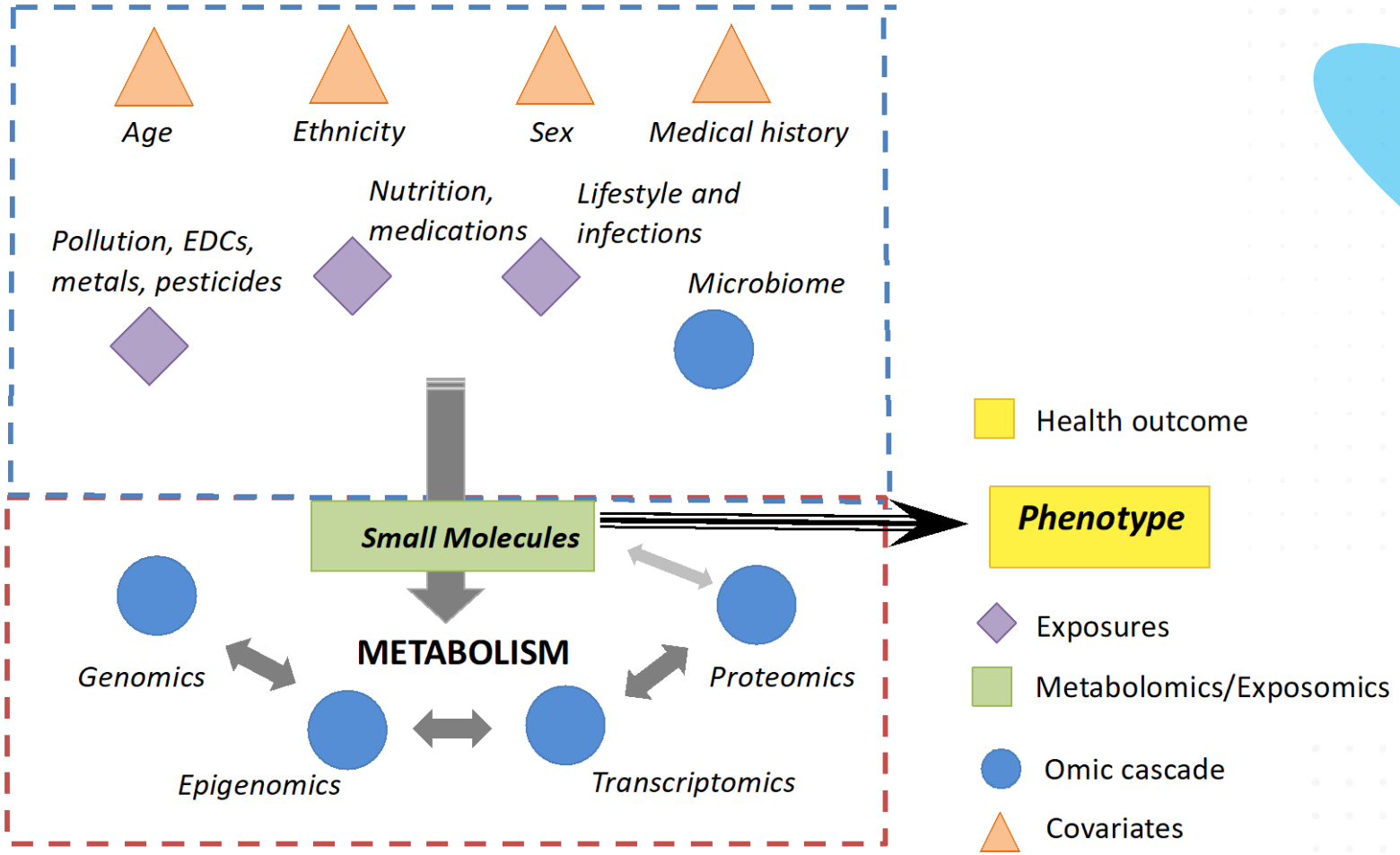
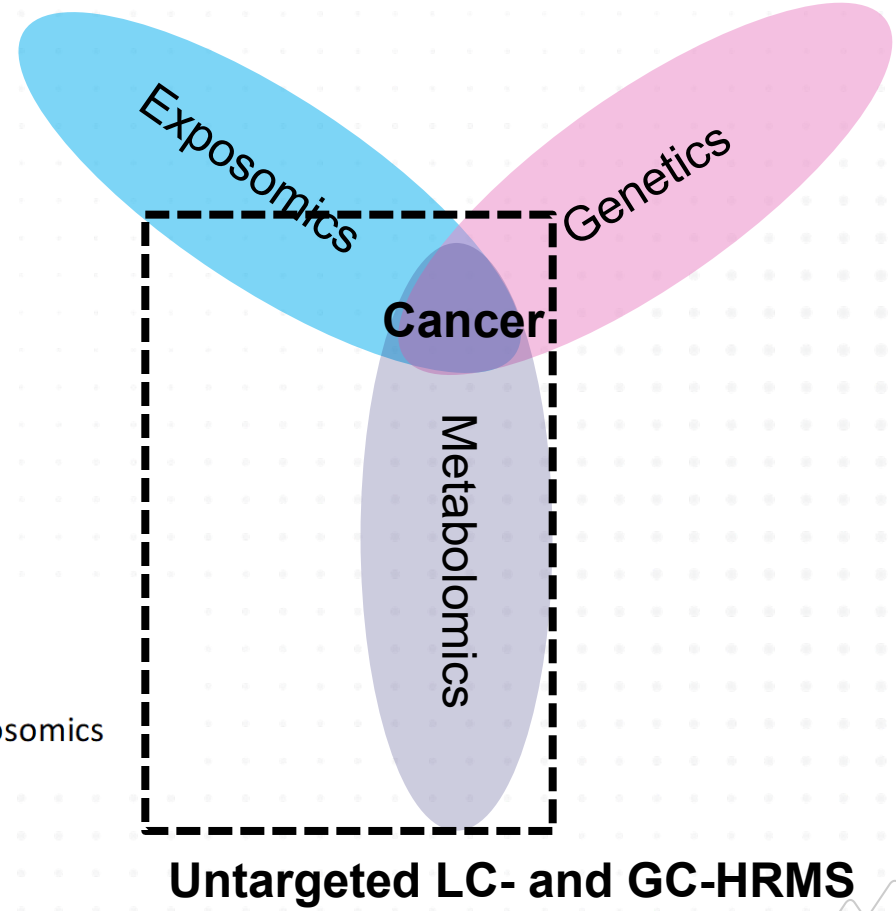
Circulating chemicals represent current and past exposures





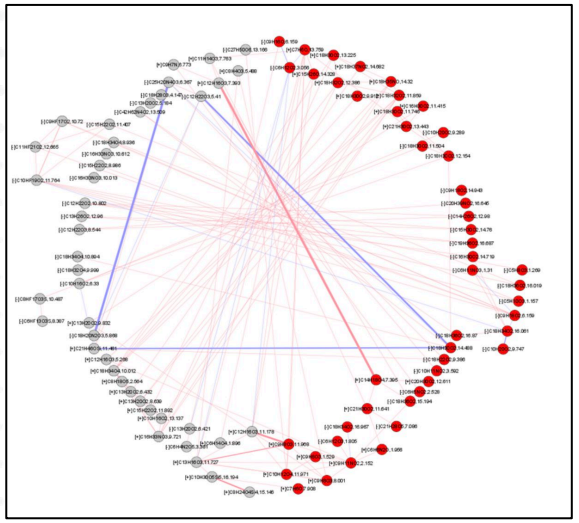
Petrick and Shomron, Cell Rep. Phys. Chem, 2022; Gao and Snyder, Front Genetics; Wishart, Metabolites, 2022

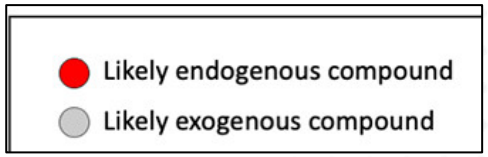
Biomonitoring with mass spectrometry

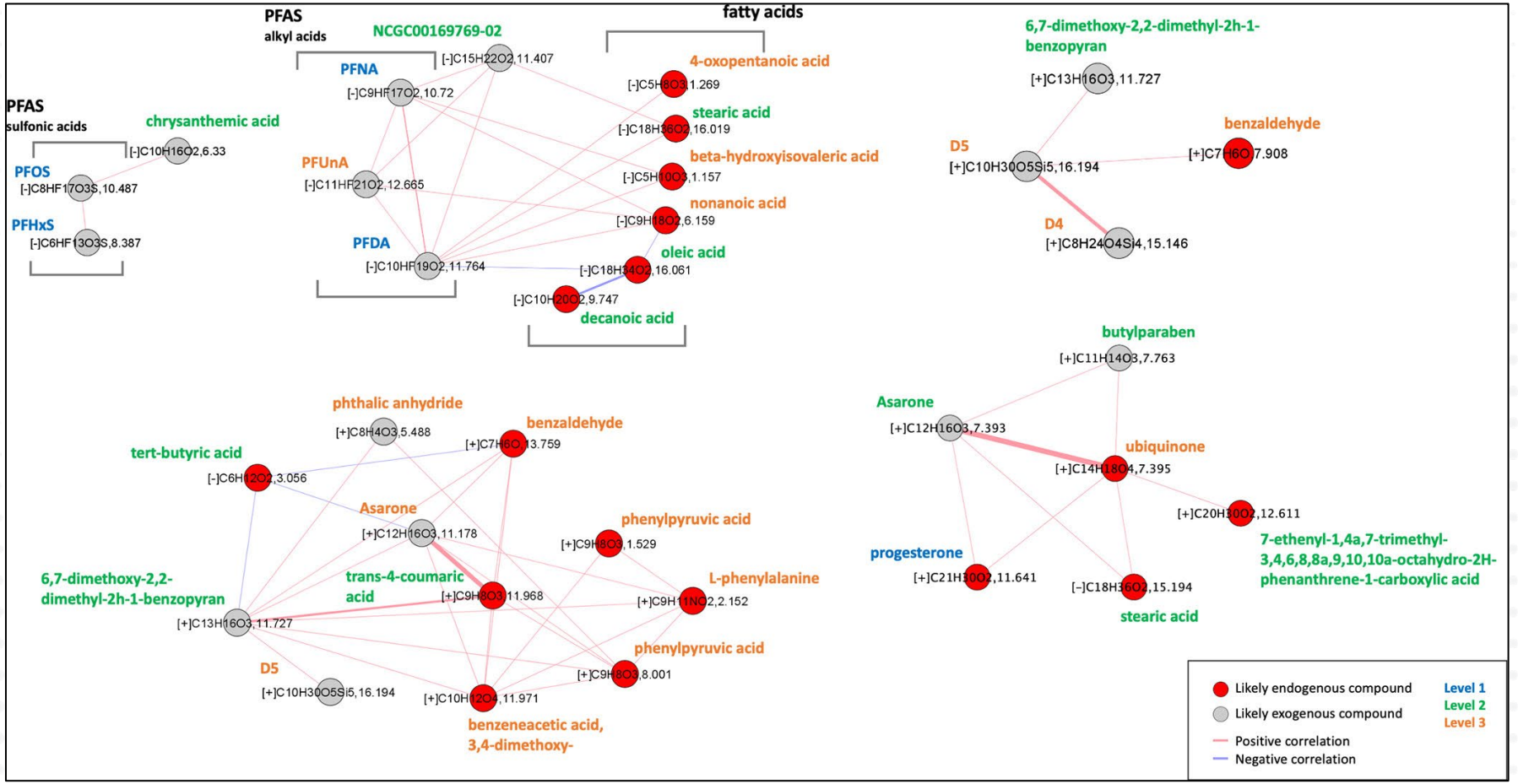
Chemical Class	Typical biofluid	Cancer type
Polychlorinate biphenyls (PCBs)	blood	Cutaneous malignant melanoma
Organochlorine insecticides (OCs)	blood	Breast cancer
Polybrominated diphenyl ethers (PBDEs)	blood	Thyroid cancer
Poly- and per-fluorinated alkyl substances (PFAS)	blood	Renal cell carcinoma
parabens	urine	Breast cancer
phthalates	urine	Endometrial cancer

Cao et al., Env. Int., 2019; Wolff et al. J. Natl Cancer Inst. 1993; Huang et al. Am. J. Epidemiol. 2020; Shearer et al. J. Natl Cancer Inst, 2021; Parada et al. Env. Int., 2019; Sarink et al. EHP. 2021

LC-HRMS exposome of maternal blood







Limitations of venous blood in pediatric cancer

1) Described current body burden, timing and magnitude are unknown
2) Retrospective biomonitoring is difficult in pediatric populations
3) Venous blood draw is invasive for infants and children

How can untargeted analysis be used to identify environmental causes of pediatric cancer?

Discovery of metabolites and chemicals in cohort studies

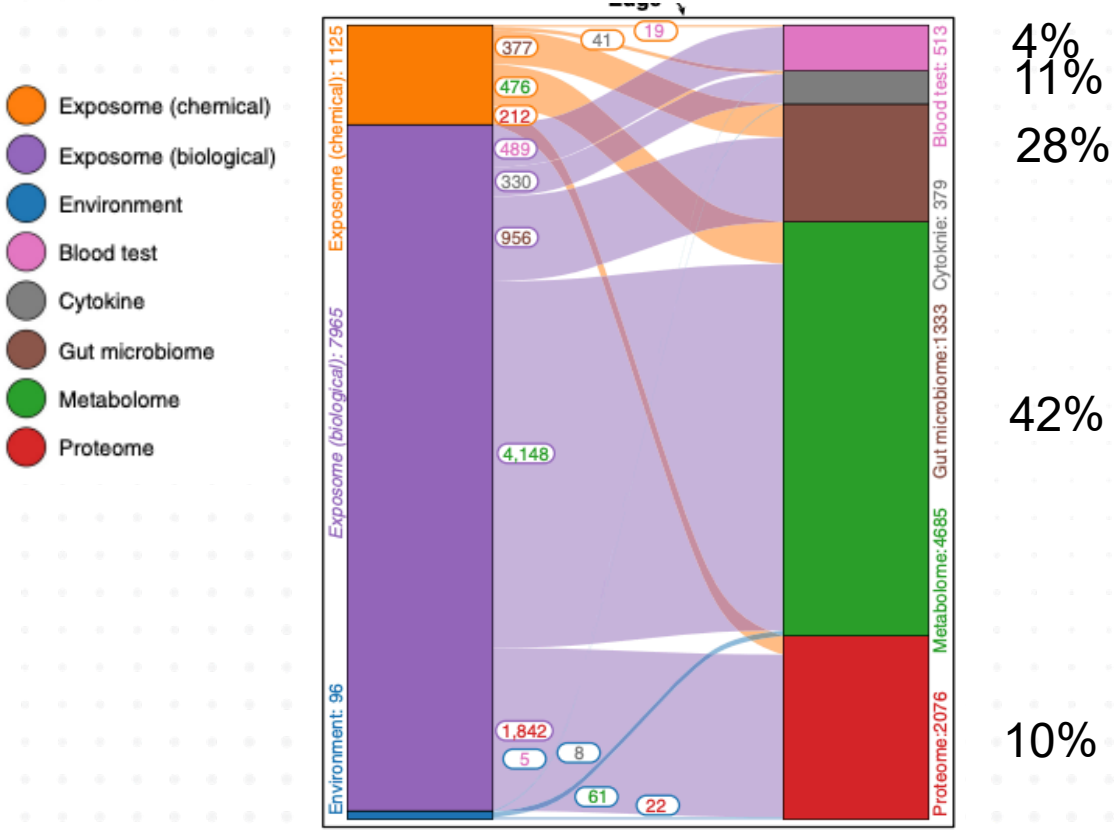
Courtesy of Kelsi Perttula

One-Carbon (Folate) Metabolism Pathway at Birth and Risk of Childhood Acute Lymphoblastic Leukemia: A Biomarker Study in Newborns. Metayer C et al. Cancers (Basel). 2023 Feb 5;15(4):1011.

Untargeted metabolomics of newborn dried blood spots reveals sex-specific associations with pediatric acute myeloid leukemia. Petrick L, et al. .Leuk Res. 2021 Jul; 106:106585.

Metabolomics of neonatal blood spots reveal distinct phenotypes of pediatric acute lymphoblastic leukemia and potential effects of early-life nutrition. Petrick LM et al. .Cancer Lett. 2019 Jun 28;452:71-78.

Integrating untargeted analysis with other omics: suggesting causation



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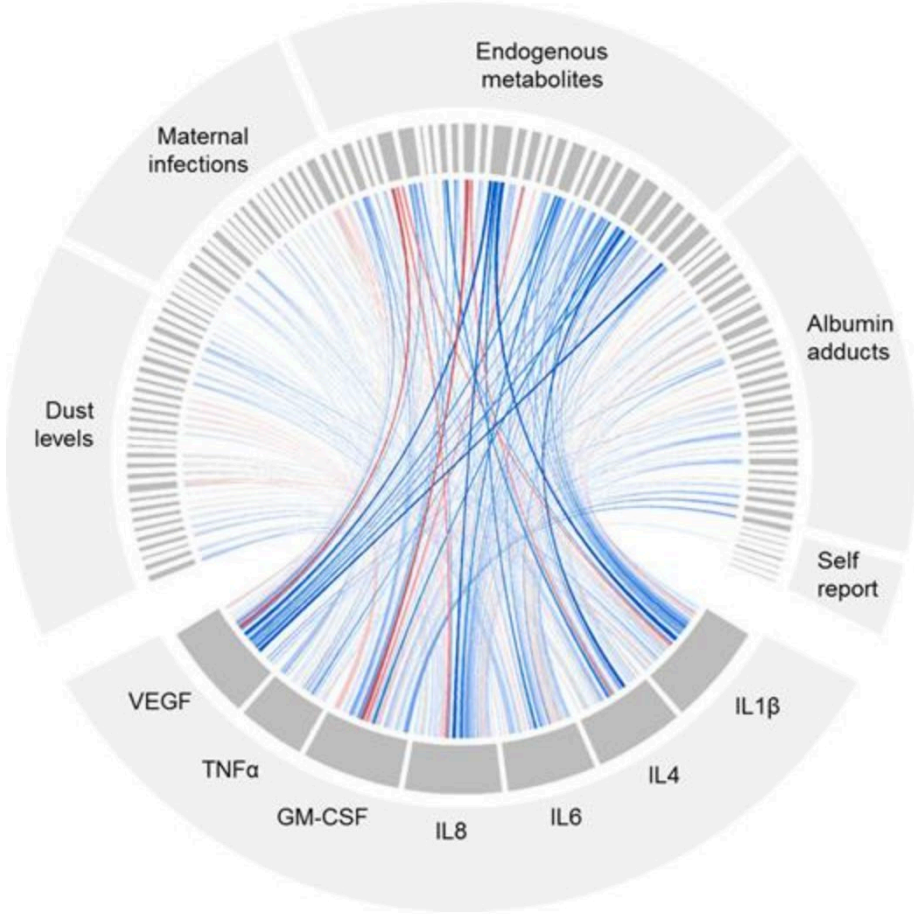
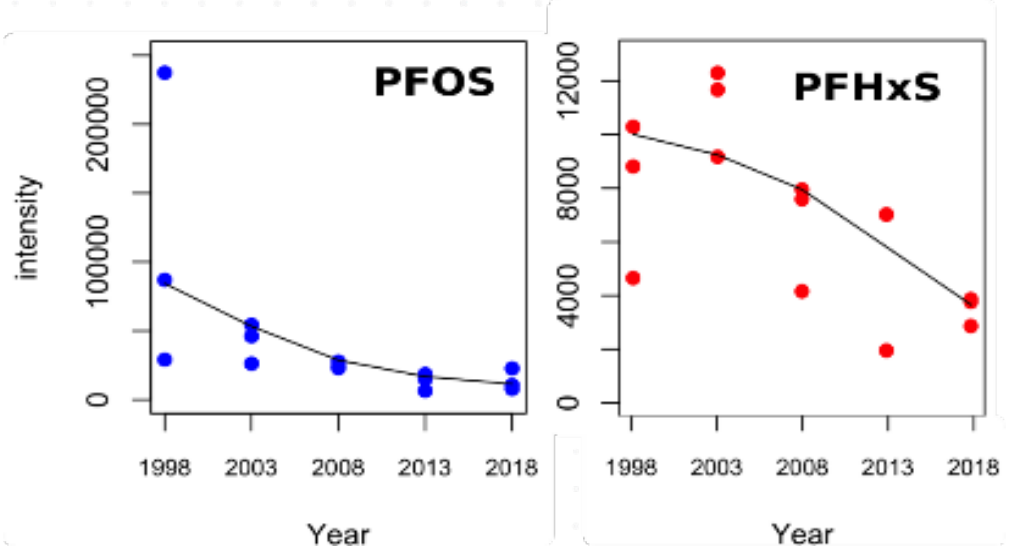
Gao et al., Genome Research , 2022

Maitre et al., MedRxiv, 2021



Whitehead et al. Cancer Epidemiol Biomarkers Prev (2021)

Re-mining data for chemicals of emerging concern



PFAS and cancer

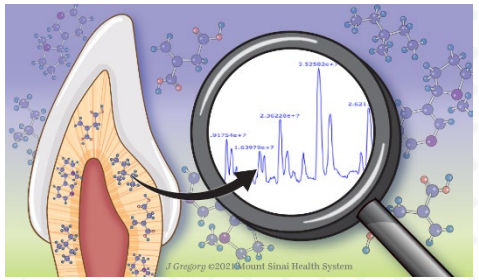
Serum Concentrations of Per- and Polyfluoroalkyl Substances and Risk of **Renal Cell Carcinoma**. Shearer et al..J Natl Cancer Inst. 2021

Exposure to perfluoroalkyl substances and risk of hepatocellular carcinoma in a multiethnic cohort. Goodrich JA et al. JHEP Rep. 2022 Aug 8;4(10):100550.

Per- and Polyfluoroalkyl Substances (PFAS) Exposure and Thyroid Cancer Risk. van Gerwen et al. 2023. Not peer reviewed preprint at SSRN: https://ssrn.com/abstract=4397033

Selected PFAS measurements in 100 DBS samples from the CA Biobank Detection			
Compound[a]	**Non-detects (%)**	**Median[10%,90%][b]**	**Ratio 90/10**
Perfluorohexanesulphonic acid (PFHxS)	6	17150 [7180,35200]	19.78
Perfluorooctanoic acid (PFOA)	2	13120 [9400,19250]	2.04
Perfluorooctanesulfonic acid (PFOS)	0	50950 [15710,128350]	8.16
Perfluoroheptanesulfonic acid (PFHpS)	59	4735 [2694,8118]	3.01

Alternatives for biosampling children and infants



Criteria	Urine	Plasma	DBS	Microsamplers	Teeth	Hair
Non-invasive	++	-	+/-	+/-	++	++
Stable for short-term room-temperature storage (e.g., transport)	--	--	++	++	++	++
Stable for long-term room-temperature storage	--	--	--	--	++	++
Provides retrospective analysis	--	--	+/-[a]	--	++	++
Captures exposure timing	--	--	--	--	++ (long-term)	++ (short-term)
Direct comparison to analysis of traditional urine or plasma samples	n.a.	n.a.	+/-	+/-	--	--
Allows for at-home sampling	++	--	++	++	++	++
Point-of-care sample collection	++	++	++	++	--	++

++ fully compliant, +/- partially compliant, -- not compliant, n.a. not applicable or unknown

[a] Compliant for archived DBS following newborn screening

Yu et al., Environ Int., 2021; Lupo et al. BioEssays, 2021, Petrick et al, CEHR, 2020

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