Targeted and untargeted analysis of per- and polyfluoroalkyl substances (PFAS) in human plasma from Nunavik (northern Quebec)

Sophia Schreckenbach[1], Pierre Dumas[2], Gabriel Muñoz[3], Sébastien Sauvé[3], Pierre Ayotte[1,2]

[1]Centre de recherche du CHU de Québec, Université Laval, Axe santé des populations et pratiques optimales en santé

[2]Centre de Toxicologie du Québec, Institut National de Santé Publique du Québec

[3]Département de chimie, Université de Montréal, Montréal, QC, Canada

Introduction

- Per- and polyfluoroalkyl substances (PFAS)
  - Widely used in industrial and consumer products
  - Linked to adverse health outcomes
  - Subject to long-range transport (LRT)
  - Highly persistent ("forever chemicals") and bioaccumulative

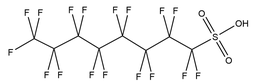

Fig. 1 Examples of regulated PFAS

Transport to Arctic → Deposition → Bioaccumulation and biomagnification → Elevated concentrations in high-trophic-level consumers → Exposure risk for Indigenous populations

- Multiple PFAS have been phased out and regulated
- Phase-outs → development and use of replacement PFAS
- New PFAS often not monitored → unknown health and environmental risks
- Need for new targeted and untargeted methods to detect and identify novel PFAS
- First application of a method of 70 PFAS to human serum from Arctic populations

Materials and methods

- Samples from *Qanuilirpitaa?* health survey (Nunavik, 2017)
- ~1300 human serum samples, pooled by:
  - Age (16-19, 20-29, 30-39, 40-59, 60+)
  - Sex (M and F)
  - Region (Hudson Bay, Hudson Strait, Ungava Bay)

Fig. 2 Map of the study area indicating the individual communities (reproduced from Makivik Corporation)

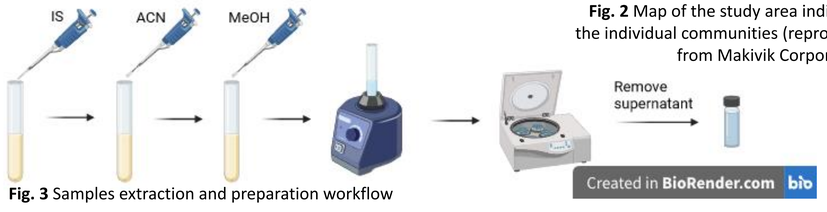

Fig. 3 Samples extraction and preparation workflow

- Analysis using liquid chromatography and Thermo Fisher Orbitrap mass spectrometer
  - Full scan mode (negative and positive electrospray ionization, *m/z* 150-1000)
- Quantification in Thermo Fischer instrument software
- Statistical analysis in R
  - Non-detected values replaced with ½ LOD values
  - ANOVA for comparison between groups
  - Pearson correlation coefficient for correlation between compounds
- Suspect screening data processed in MzMine 2.53
  - Peak picking, chromatogram deconvolution, alignment, suspect screening
  - Blank subtraction of suspect screening data performed in Excel
  - $Mean_{sample} \geq 5 \times mean_{blank}$

Fig. 4 Orbitrap (Thermo Fisher)

Results and discussion

Targeted analysis:

Table 1 Identities and human serum concentrations of PFAS identified in study participants

	Name	Abbreviation	Mean (Min-Max) (ng/ml)	Detection frequency (%) (n = 30)	LOD (ng/mL)
Perfluoro-carboxylic acids	Perfluoroheptanoic acid	PFHpA	0.06 (<LOD-0.20)	73	0.006
	Perfluorooctanoic acid	PFOA	1.01 (0.45-2.08)	100	0.004
	Perfluorononanoic acid	PFNA	3.49 (1.24-9.59)	100	0.004
	Perfluorodecanoic acid	PFDA	0.66 (0.25-1.99)	100	0.002
	Perfluoroundecanoic acid	PFUnDA	0.65 (0.030-1.86)	100	0.004
	Perfluorododecanoic acid	PFDoDA	0.02 (<LOD-0.04)	30	0.01
	Perfluorotridecanoic acid	PFTrDA	0.09 (0.04-0.18)	100	0.006
	Perfluorotetradecanoic acid	PFTeDA	0.01 (<LOD-0.02)	73	0.003
Perfluoro-sulfonic acids	Perfluorohexanesulfonic acid	PFHxS	0.64 (0.19-1.79)	100	0.001
	Perfluoroheptanesulfonic acid	PFHpS	0.17 (0.04-0.48)	100	0.001
	Perfluorooctanesulfonic acid	PFOS	7.16 (2.30-21.9)	100	0.002
Novel PFAS	7:3 fluorotelomer carboxylic acid	7:3 FTCA	0.13 (<LOD-0.44)	50	0.01
	Perfluoro-4-ethylcyclohexane	PFECHS	0.04 (<LOD-0.10)	83	0.001

Comparisons between pools:

- Pools differ significantly only by age
  - No significant differences by sex or region
  - 60+ age group significantly different
- Most compounds display increase with age
- C_7-C_9 PFCAs and 7:3 FTCA display a U-shaped distribution

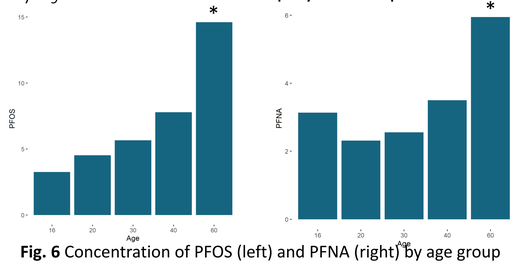

Fig. 6 Concentration of PFOS (left) and PFNA (right) by age group

- U-shaped distribution observed in women but not men
  - May represent different PFAS sources, and/or losses from breastfeeding
  - Not statistically significant (ANOVA)

Preliminary suspect screening results:

- 18 hits that were also present in targeted method (10 detected, 8 < LOD)
- 58 hits representing potential novel PFAS (identification level 4 according to Schymanski *et al.*: accurate mass and chemical formula only[5])
  - 27 detected in all pools
  - 33 detected in < 100% and > 50% of pools
- Need to collect fragment data to determine validity of potential identifications

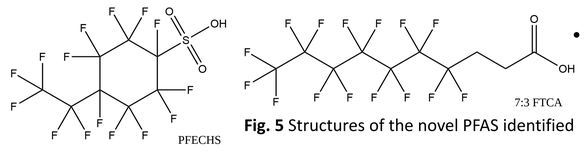

Fig. 5 Structures of the novel PFAS identified

- Many non-detects = probably good news
- PFOS highest concentration
  - Common in human populations
- PFNA > PFOA
  - Odd-even pattern in PFCAs, where PFCAs with odd-numbered chains > their even-numbered counterparts
  - Contrary to general Canadian population, but in line with previous work in Canadian Arctic[1]
- First detection of PFECHS in Nunavik
  - Cyclic PFOS analogue
  - Detected in all except youngest age group
  - Correlates with PFOS (R = 0.93) but low concentrations (200x < PFOS)
- Limitations:
  - Method not optimized for shorter-chain compounds (non-detection of short chain PFCAs may be false negatives due to poor sensitivity)
  - Pools of different size

Conclusions and Future Work

Summary:

- Detected 13/70 targeted PFAS including 2 novel PFAS (PFECHS and 7:3 FTCA)
  - Many non-detected compounds = likely good news for Nunavik population
- Concentrations ↑ with age

Future Work:

- Collect fragmentation data
- Attempt to confirm suspects using isotope peaks, fragmentation, and ideally standards
- Further work on nontarget data (comparison with other populations, searching for common PFAS fragments, etc.)

References and Acknowledgements

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Thank you to INSPQ for providing samples and lab space, to the residents of Nunavik for their participation in this study, and to Université de Montréal for providing lab space, instrumentation, and technical assistance. Thank you to A. O. de Silva, A. Aker, and T. Smythe for helpful discussion. This work was funded by Sentinelle Nord and an NSERC doctoral fellowship.