AB 617 Biomonitoring Update: Biomarker Research and Potential Study Designs

Susan Hurley, MPH, Julia Varshavsky, PhD, MPH, and Marley Zalay, MPH

Safer Alternatives Assessment and Biomonitoring Section (SAABS)
Office of Environmental Health Hazard Assessment

Presentation to Scientific Guidance Panel Meeting

November 12, 2020

AB 617 background

Photo credit: pxfuel.com

Photo credit: snappygoat.com

- The California Air Resources Board (CARB) established the Community Air Protection Program in response to AB 617, which aims to reduce exposures in communities disproportionately impacted by air pollution
- In collaboration with the University of California (UC), OEHHA is designing targeted biomonitoring studies in selected AB 617 communities to:
  - Complement and validate ongoing air monitoring
  - Increase understanding of exposures and potential health risks faced by residents
  - Evaluate specific emission/exposure reduction measures

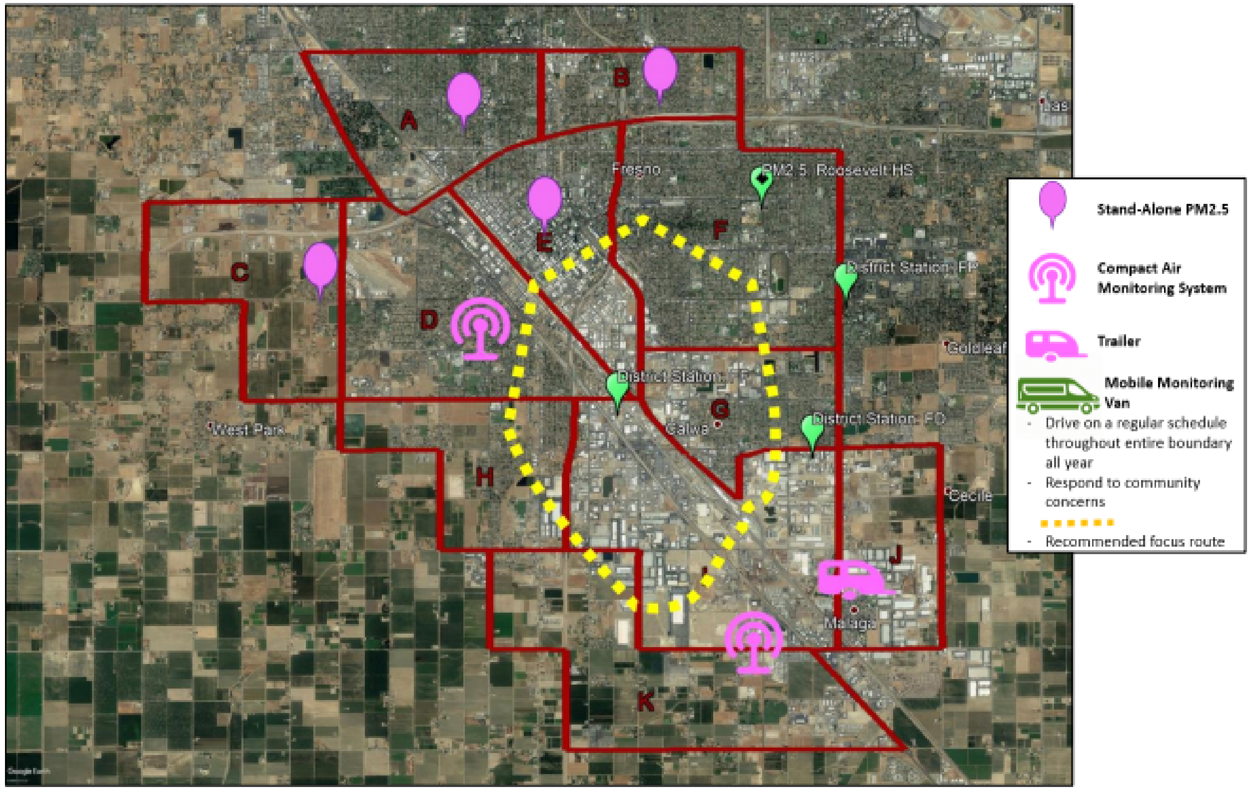
Exposure concerns and reduction strategies

- Air pollutants of concern include:
  - Criteria air pollutants, such as $PM_{2.5}$, NO_x
  - Polycyclic aromatic hydrocarbons (PAHs)
  - Volatile organic compounds (VOCs)
  - Metals and pesticides
- Community Emissions Reduction Plan (CERP) strategies include:
  - Emission reductions in ports, railyards, and refineries
  - Truck rerouting and prevention of truck idling
  - Vegetation planting
  - Street sweeping
  - Installation of air filtration in facilities like schools and senior centers, as well as in homes

AB 617 community air monitoring

- Aims to characterize local sources
- Will help inform the selection of study area for biomonitoring
- Provides hyperlocal air pollutant measurements to pair with biomonitoring results

Figure 6 Community Recommended Air Monitoring Plan Network Design



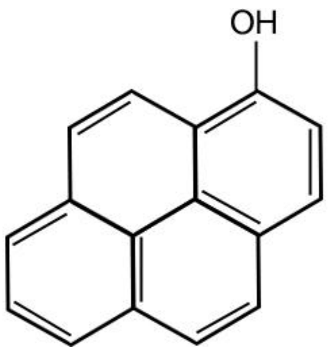
San Joaquin Valley Air Pollution Control District (2019)

Practical considerations

- Limited resources
  - Current contract with UC sufficient to conduct one targeted biomonitoring study
  - Some contract funds can be re-directed to UC labs for biomarker analyses
- COVID-19 emergency
  - Affects potential study design
  - Could impact recruitment

→ Focus on urinary biomarkers only

Options for urinary biomarkers of exposure



1-Hydroxypyrene

- Hydroxy metabolites of PAHs, including:
  - Naphthalene (NAP)
  - Fluorene (FLU)
  - Phenanthrene (PHE)
  - Pyrene (PYR)
- Stable metabolites of VOCs, such as:
  - Acrolein
  - Acrylonitrile
  - Benzene
  - 1,3-Butadiene
  - Ethylbenzene
  - Xylene

Options for urinary measures of effect

- Markers of oxidative stress, including:
  - Malondialdehyde (MDA)
  - 8-Isoprostane
  - 8-Hydroxy-2′-deoxyguanosine (8-OHdG), 8-Oxo-2′-deoxyguanosine (8-oxodG)
- Urinary mutagenicity assays

Challenges with air pollution biomonitoring

- Interpretation of PAH and VOC biomarkers
  - Multiple sources of exposures
  - Short biological half-lives of metabolites (hours to days)
- Spatial and temporal variation in air pollution
  - Affected by season and meteorology
  - Regional air monitoring may not capture hyperlocal exposures






Photo credit: pxfuel.com

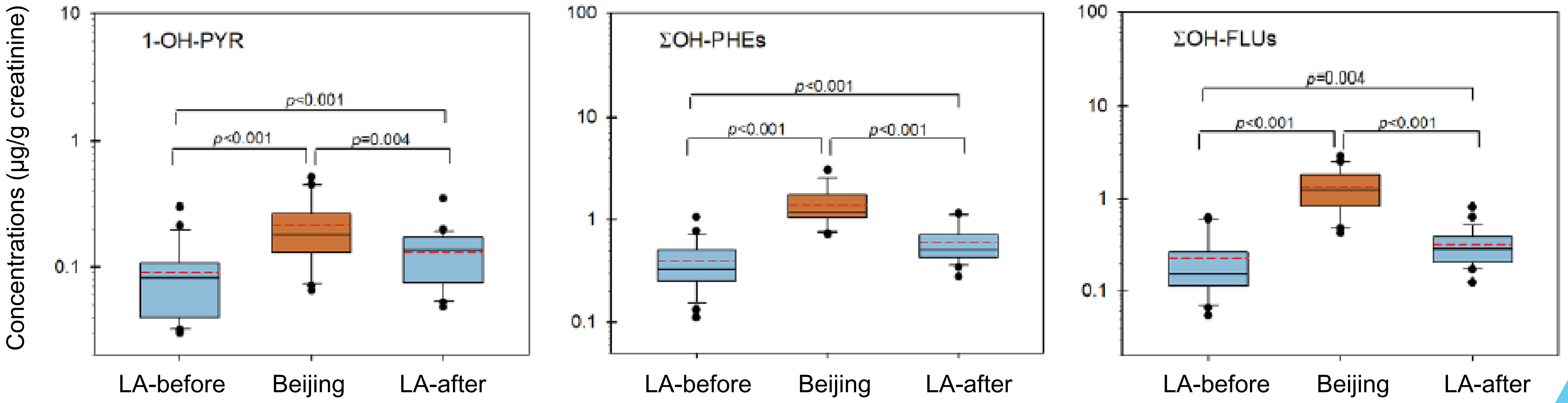
Viability of urinary PAH and VOC biomarkers

Photo credit: pxfuel.com

Selected PAH and VOC biomonitoring studies have shown:

- Correlations with air pollutants
- Differences in exposure profiles between communities
- Correlations with biomarkers of effect
- Links to changes in air pollution exposures

Urinary PAH metabolites before and after travel from Los Angeles to Beijing



- PAH metabolite levels significantly higher while in Beijing
- Daily $PM_{2.5}$: LA=14.6 μg/m^3, Beijing=67.6 μg/m^3
- Smoking: all non-smokers, adjusted for cotinine
- Diet: 8 hour fast prior to urine collection

Adapted from Figure 2, Lin et al. (2019)

Measurements of urinary 1-OHP, 8-oxodG and mutagenic activity among 72 urban Italian traffic policemen

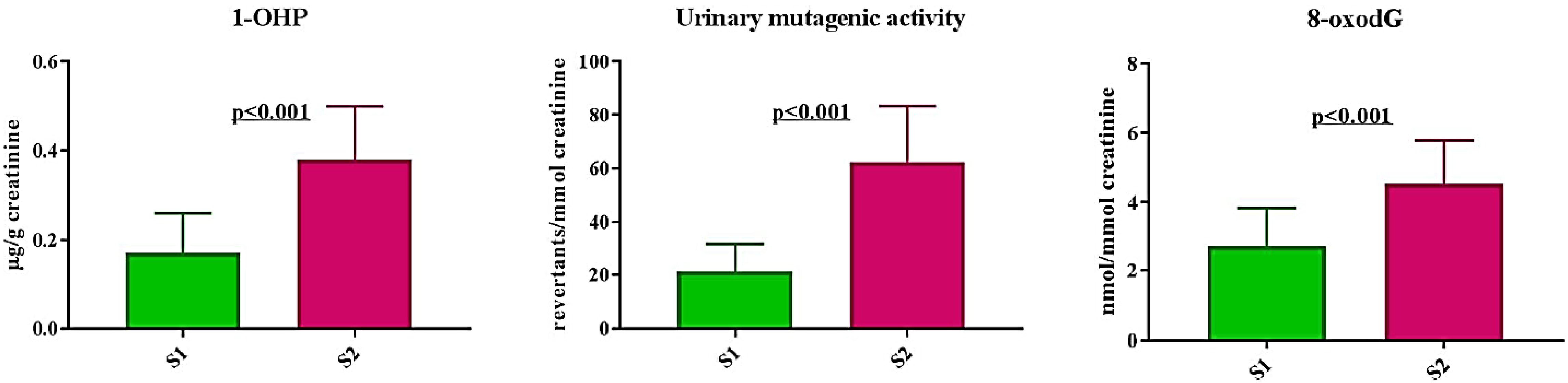


Fig. 1 Plot of 1-OHP, mutagens and oxidative DNA lesions in traffic policemen. S1 collected after 2 days off from work;
S2 collected after 6 consecutive workdays.

- Significant pre/post shift differences in biomarkers of exposure and effect
- Urinary mutagenic activity and 8-oxodG were significantly correlated with 1-OHP
- Prescribed low-PAH diet for 2 weeks prior; all non-smokers

Ledda et al. (2018)

Urinary PAH and VOC metabolites before and after cook stove intervention

Parent compound	% change
NAP	- 38%*
FLU	- 31%*
PHE	- 21%
PYR	- 14%
Benzene	- 40%*
Ethylene oxide	- 12%
Acrylonitrile	- 38%*

* $p < 0.05$

- Intervention resulted in:
  - Significant 56% decline in $PM_{2.5}$ (measured by personal air monitoring)
  - Significant declines in urinary metabolites of NAP, FLU, benzene, and acrylonitrile
- $PM_{2.5}$ significantly correlated with all PAH metabolites and some VOC metabolites

Adapted from Table 3 of Weinstein et al. (2020)

Urinary PAH metabolites correlated with PAHs in air

Parent PAH in air	Urinary metabolite	Low PAH diet ρ*	High PAH diet ρ*
NAP	∑ OH-NAP	**0.87**	**0.63**
	1-OH-NAP	**0.89**	**0.76**
	2-OH-NAP	0.42	0.20
FLU	∑ OH-FLU	0.55	0.41
	9-FLU	0.22	0.27
	3-FLU	**0.67**	0.52
	2-FLU	**0.68**	0.54
PHE	∑ PHE	-0.09	0.13
PYR	1-OH-PYR	0.38	0.11

* ρ=Pearson correlation coefficient; bolded numbers statistically significant ($p < 0.05$)

- N=8 non-smoking CDC employees
- PAHs in air measured via personal monitoring
  - Medians ranged from 0.4 ng/m^3 for PYR to 921 ng/m^3 for NAP
- Selected metabolites of NAP and FLU strongly correlated with modeled air exposures

Adapted from Table 5, Li et al. (2010)

Important elements for air pollution biomonitoring

- Designing a well-controlled intervention that produces a sufficiently large change in exposure (~50%)
- Accounting for smoking and dietary exposures
- Measuring multiple biomarkers of exposure and effect
- Collecting spatially and temporally appropriate measures of air pollution

Potential Biomonitoring Study Designs

Multi-pronged approach

Key study design elements

Intervention

- Air filtration in an elder care facility and/or school

Biomonitoring

- Samples collected pre- and post-intervention
- Biomarkers of exposure: PAH and VOC metabolites
- Biomarkers of effect (e.g., oxidative stress, mutagenicity)
- Smoking exposure biomarkers
- Specific gravity, creatinine

Air monitoring

- Indoor and outdoor air measurements of PAHs, VOCs, and other pollutants

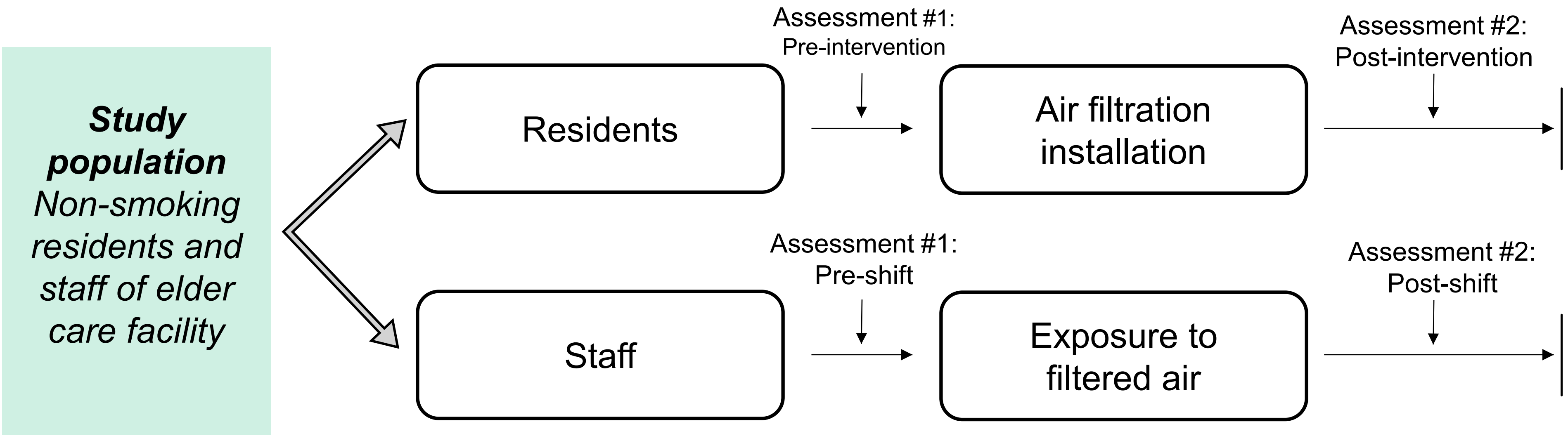
Study tools

- Questionnaire on diet, smoking, and other potential sources
- Activity diary

Effectiveness of indoor air filtration

- Most air filtration systems filter out particulate matter only; others also capture VOCs
- Air filtration can reduce particulate matter 50-90%, depending on the system (Polidori et al. 2013, Bennett et al. 2018, San Francisco Department of Public Health et al. 2018)
- Previous studies suggest urinary PAH biomarkers can detect changes in $PM_{2.5}$ exposures as small as 50% (Weinstein et al. 2020)

Proposed intervention study design



Advantages of residents

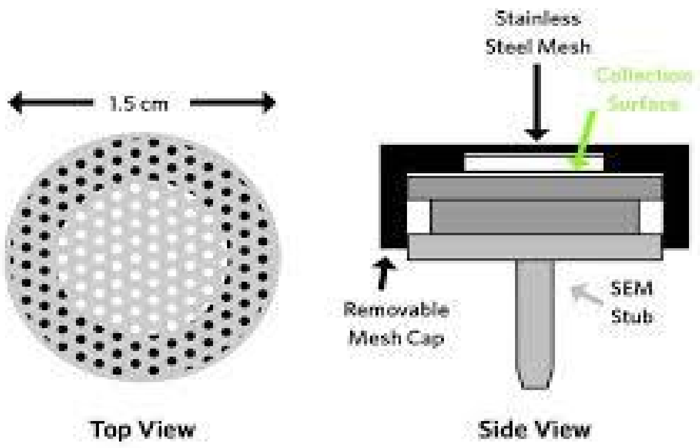
- Assess exposures before and after installation of air filtration
- Control for diet and indoor vs outdoor activity

Advantages of staff

- Assess "cross-shift" changes in exposures (pre-shift + post-shift)
- Expanded demographics

Other design elements

- Indoor and outdoor air monitoring
  - Both gas-phase and particle-bound air pollutants
  - Compare to hyperlocal community monitoring levels
- Ultrafine particle analysis to examine likely sources



Wagner and Leith, 2001

Other approaches for consideration

- Non-targeted screening
  - New analytical methods that can more broadly screen for VOCs in ambient air
- Unmetabolized parent PAHs
  - Higher detection frequencies – capture additional PAHs
- Diagnostic ratios for PAHs

Diagnostic ratio	Value	Source	Reference
FLU/(FLU+PYR)	> 0.5 < 0.5	Diesel Gasoline	Ravindra et al. 2008
$\Sigma PAH_{LMW}/\Sigma PAH_{HMW}$	> 1.0 < 1.0	Petrogenic Pyrogenic	Oliveira et al. 2017

Keys to success for air filtration intervention study design

- Design intervention that will result in sufficiently large reduction in particles and VOCs ($\geq$50%) and that is appropriate for short half-life exposure biomarkers
- Pair indoor and outdoor air pollution measurements with multiple biomarkers of exposure and effect
- Conduct study at a time and place with high ambient air pollution (e.g., winter months)
- Control for and/or assess the influence of other exposure sources (e.g., smoking, diet)

Other collaborative opportunities

Collect and biobank urine samples as part of existing longitudinal or cross-sectional studies to:

- Compare exposures over time (e.g., before and after emission reduction strategies are implemented)
- Compare exposures within communities (e.g., examine impact of proximity to local emission sources)
- Compare exposures between AB 617 communities and with other communities
- Examine relationship between air pollution exposures and health effects (e.g., asthma, lung inflammation)

Next steps

- Identify potential facilities for intervention study
- Continue research on biomarkers of exposure and effect
- Develop specific study strategies with collaborators at UC and CDPH
  - Secure additional funding for enhanced air monitoring and VOC filtration
- Ongoing engagement with communities and CARB
- Continue conversations about other collaborative opportunities

Collaborating institutions

OEHHA
California Office of Environmental Health Hazard Assessment

Berkeley
UNIVERSITY OF CALIFORNIA

BIOMONITORING CALIFORNIA

California Department of PublicHealth

cerch
Center for Environmental Research & Children's Health

Questions and Discussion

References cited

- Bennett DH, Kenyon N, Tancredi D, Schenker M, Moran R, Roudneva K, Wu X, Krakowiak P, Fisk WJ. (2018). Final Report: Benefits of High Efficiency Filtration to Children with Asthma. Sacramento, California: California Environmental Protection Agency, California Air Resources Board, Research Division. Available at: https://ww2.arb.ca.gov/sites/default/files/classic//research/apr/past/11-324.pdf.
- Ledda C, Loreto C, Bracci M, Lombardo C, Romano G, Cinà D, Mucci N, Castorina S, Rapisarda V (2018). Mutagenic and DNA repair activity in traffic policemen: A case-crossover study. J Occup Med Toxicol 13(1):24. Available at: https://doi.org/10.1186/s12995-018-0206-9.
- Li Z, Mulholland JA, Romanoff LC, Pittman EN, Trinidad DA, Lewin MD, Sjodin A (2010). Assessment of non-occupational exposure to polycyclic aromatic hydrocarbons through personal air sampling and urinary biomonitoring. J Environ Monit 12(5):1110-18. Abstract available at: https://www.ncbi.nlm.nih.gov/pubmed/21491629.
- Lin Y, Ramanathan G, Zhu Y, Yin F, Rea ND, Lu X, Tseng CH, Faull KF, Yoon AJ, Jerrett M, Zhu T, Qiu X, Araujo JA (2019). Pro-oxidative and proinflammatory effects after traveling from Los Angeles to Beijing: A biomarker-based natural experiment. Circulation 140(24):1995-2004. Available at: https://www.ncbi.nlm.nih.gov/pubmed/31744317.
- Oliveira M, Slezakova K, Delerue-Matos C, do Carmo Pereira M, Morais S (2017). Assessment of exposure to polycyclic aromatic hydrocarbons in preschool children: Levels and impact of preschool indoor air on excretion of main urinary monohydroxyl metabolites. J Hazard Mater 322(Pt B):357-69. Abstract available at: https://www.ncbi.nlm.nih.gov/pubmed/27776859.
- Polidori A, Fine PM, White V, Kwon PS (2013). Pilot study of high-performance air filtration for classroom applications. Indoor Air.23(3):185-95. Available at: https://www.ncbi.nlm.nih.gov/pubmed/23137181.

References cited (cont.)

- Ravindra K, Sokhi R, Van Grieken R (2008). Atmospheric polycyclic aromatic hydrocarbons: Source attribution, emission factors and regulation. Atmospheric Environ.42(13):2895-921. Available at: http://www.sciencedirect.com/science/article/pii/S1352231007011351.
- San Francisco Department of Public Health, Bay Area Air Quality Management District, and Lawrence Berkeley National Laboratory (2018). Measurement Study to Evaluate Controls for Reducing In-Home Pollutant Exposures at Homes Near High Trafficked Roadways. Available at: https://www.sfdph.org/dph/files/EHSdocs/ehsPublsdocs/Mirant_Indoor_Air.pdf.
- San Joaquin Valley Air Pollution Control District (2019). Community Air Monitoring Plan: South Central Fresno AB 617 Community. Available at: http://community.valleyair.org/media/1308/fresno_camp_v1_2019_july-1.pdf.
- Wagner J and Leith D (2001). Passive aerosol sampler. Part I: Principle of operation. Aerosol Sci Technol.34(2):186-92. Available at: https://doi.org/10.1080/027868201300034808.
- Weinstein JR, Diaz-Artiga A, Benowitz N, Thompson LM (2020). Reductions in urinary metabolites of exposure to household air pollution in pregnant, rural Guatemalan women provided liquefied petroleum gas stoves. J Exp Sci & Environ Epidemiol 30(2):362-73. Available at: http://www.ncbi.nlm.nih.gov/pubmed/31477781.
- Wu X, Lintelmann J, Klingbeil S, Li J, Wang H, Kuhn E, Ritter S, Zimmermann R (2017). Determination of air pollution-related biomarkers of exposure in urine of travellers between Germany and China using liquid chromatographic and liquid chromatographic-mass spectrometric methods: A pilot study. Biomarkers 22(6):525-36. Abstract available at: https://www.ncbi.nlm.nih.gov/pubmed/28330376.