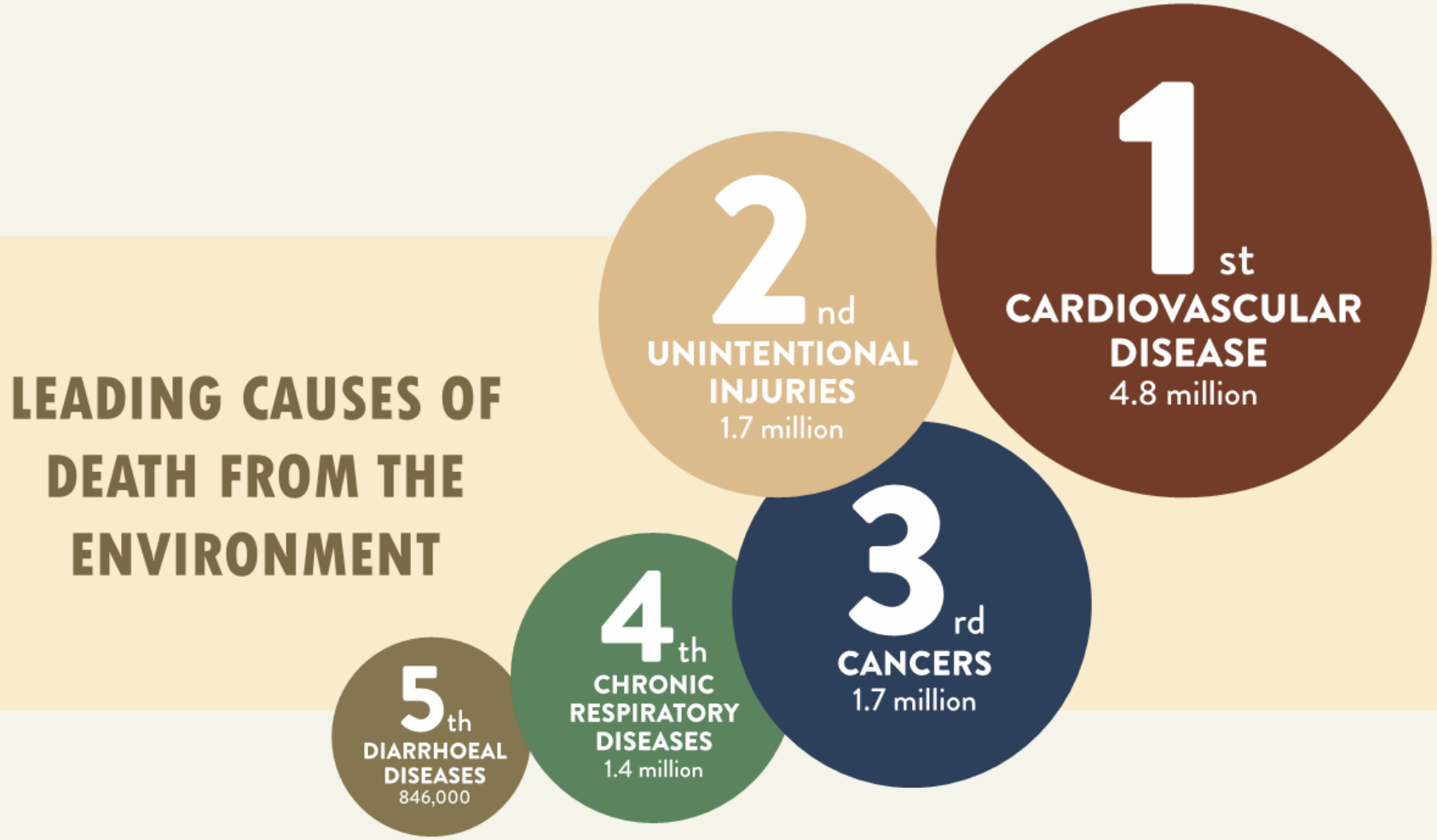
University of Louisville
Superfund Research Center

Volatile Organic Compounds and Cardiometabolic Disease

September 04, 2018



Environmental pollution accounts for 9 million deaths worldwide, out of which 6 million deaths are attributed to air pollution

Louisville and Superfund Sites

Valley of Drums

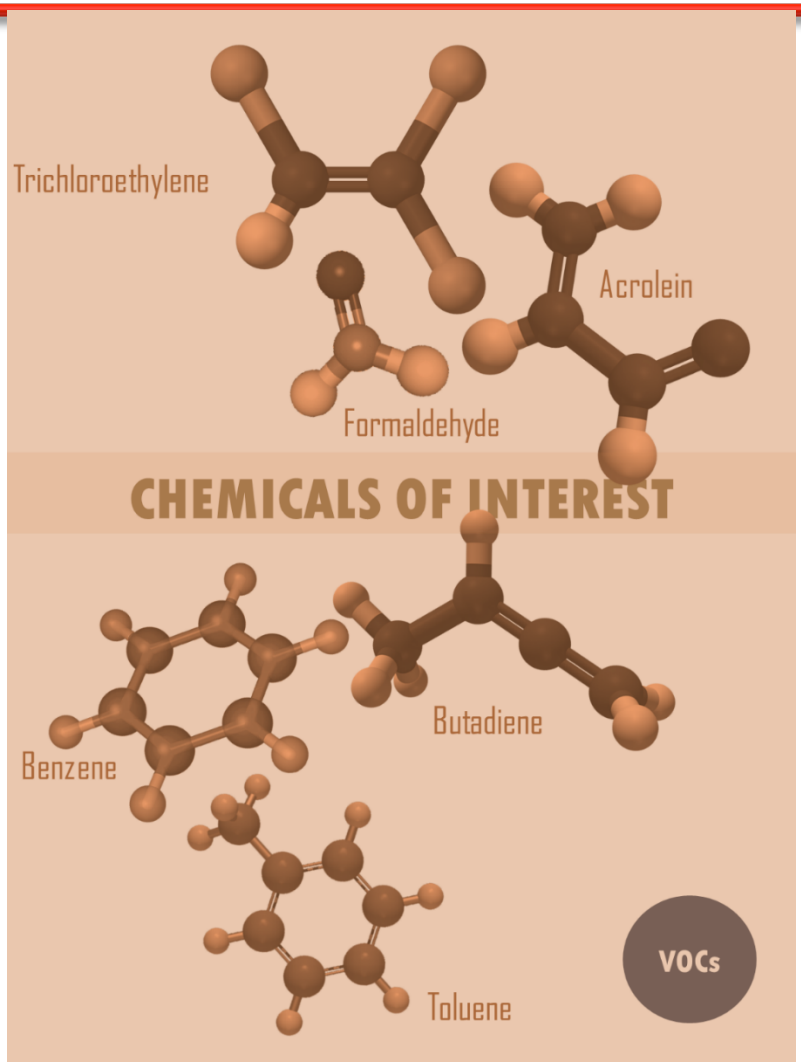
- Hazardous waste in metal drums dumped in open pits and trenches
- Leached into Wilson Creek, a tributary of the Ohio River

Lee's Lane

- 112 acres wooded and open land
- Flood control levees separate landfill from Riverside Gardens residential area
- 212,400 tons of domestic, commercial, solid municipal and industrial wastes disposed

Priority Ranking of VOCs in Agency for Toxic Substances and Disease Registry

- Vinyl Chloride (#5)
- Benzene (#6)
- Chloroform (#11)
- Trichloroethylene (#16)
- Acrolein (#31)
- Carbon tetrachloride (#50)
- Xylene (#64)
- Toluene (#74)
- 1,3-Butadiene (#153)



Sources: Industrial solvents, gasoline products, wood preservatives, cleaners and disinfectants

Increased Exposure to VOCs near Superfund Sites

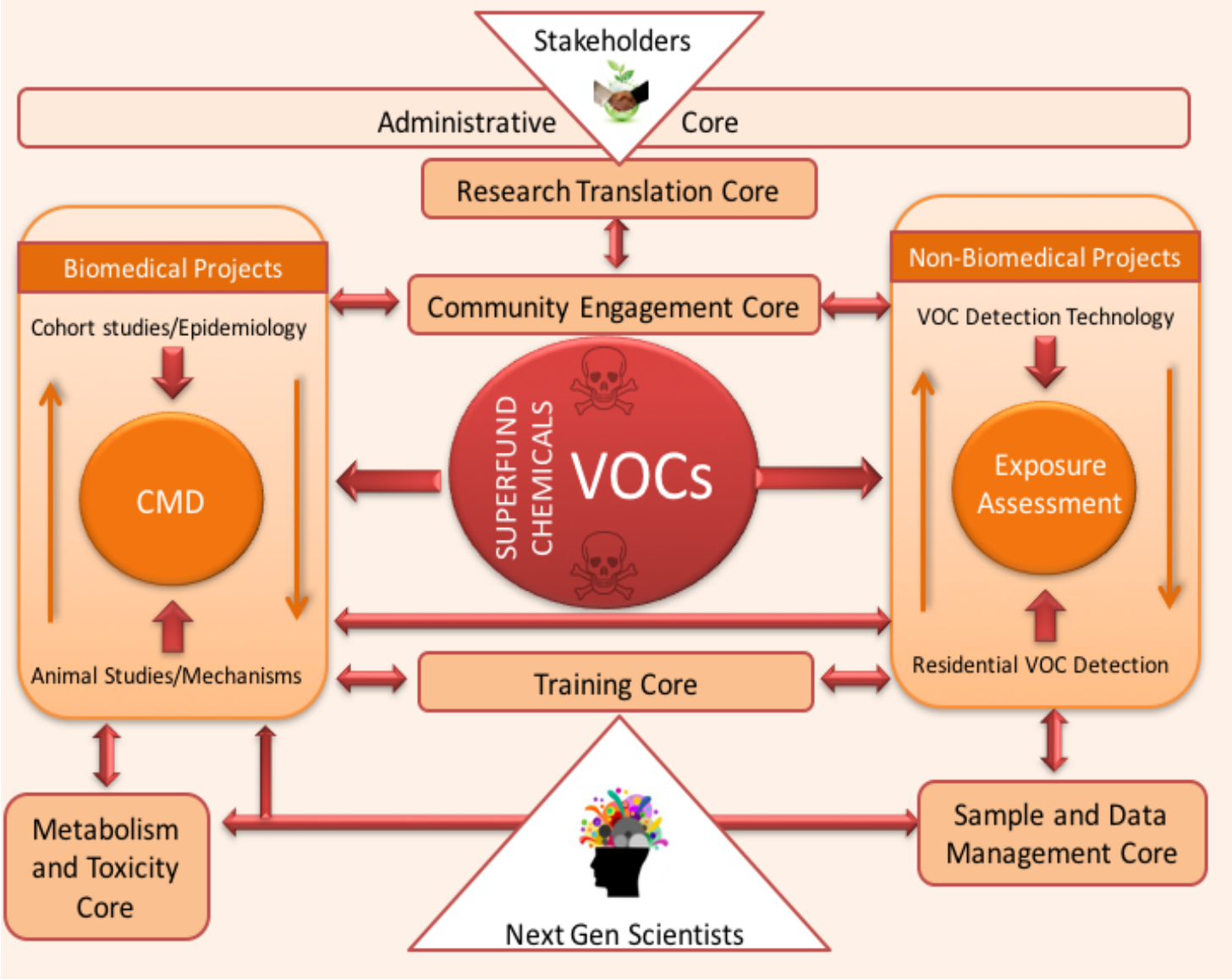
- Excessive rates of T2D (8,200 excessive cases) and stroke (8,600 excessive cases) have been found in an evaluation of 720,000 individuals living within a half-mile of 258 Superfund sites that were associated with excessive VOC in the drinking water.

- Levels of benzene, chloroform, and TCE were found to be appreciably higher than EPA levels in 107 houses near the Del Almo and Montrose Superfund sites in 2016.

- A train (carrying hazardous chemicals) derailment in Louisville caused the release of 1,3-butadiene and forced an evacuation of the neighboring area in 2012.

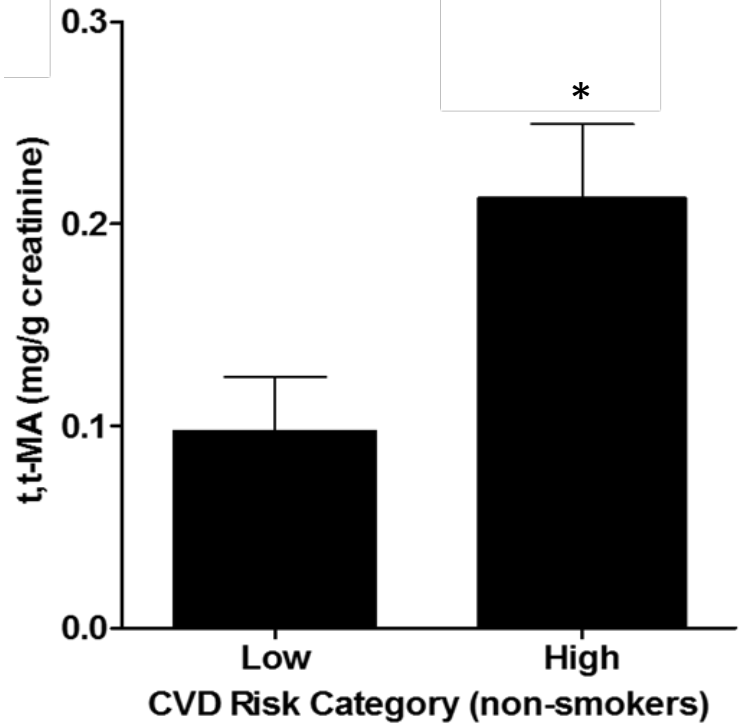
There is very little toxicological data on the cardiometabolic effects of VOCs

Center Structure

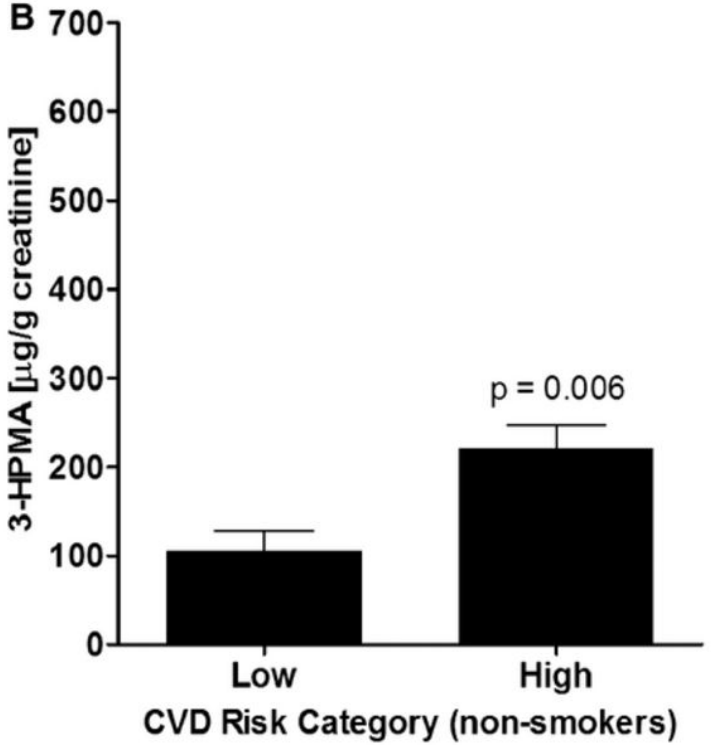


VOCs and Cardiovascular Disease Risk

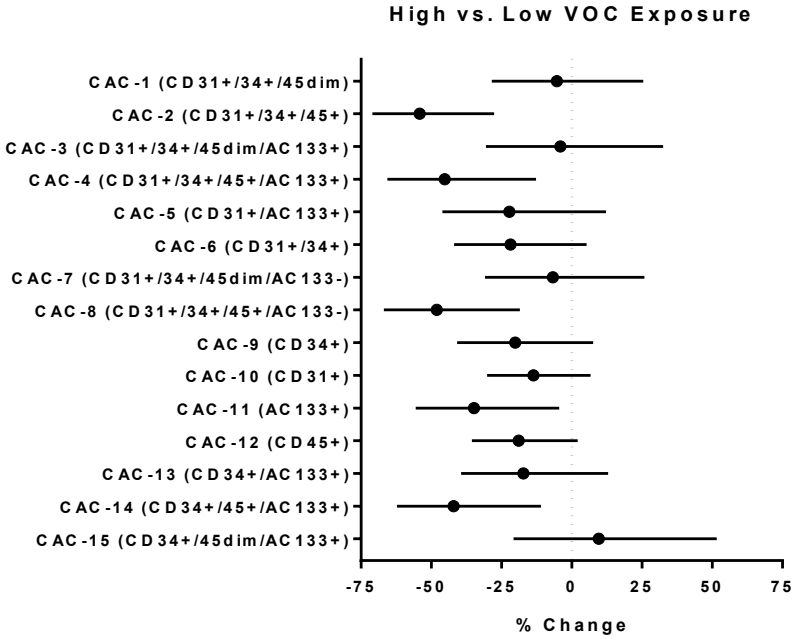
Benzene

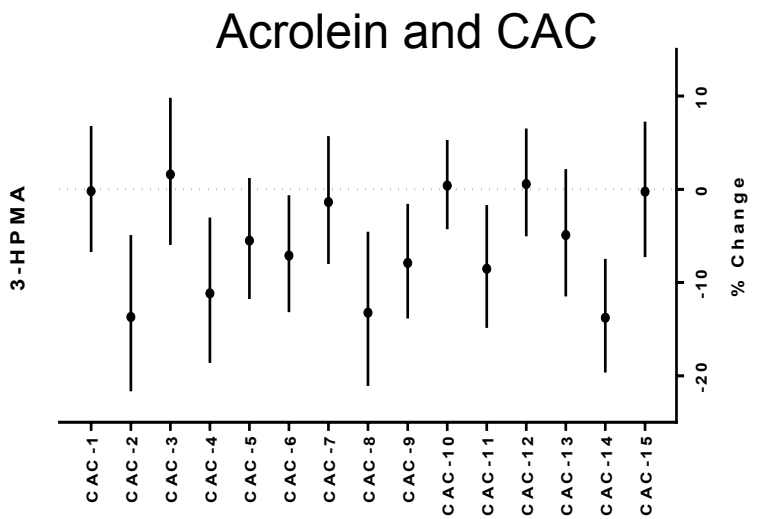


Acrolein

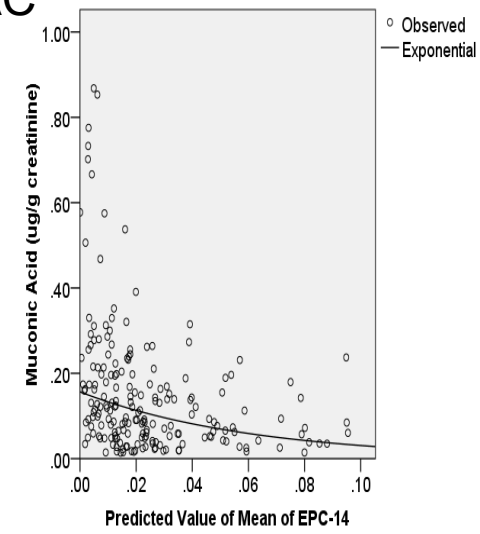


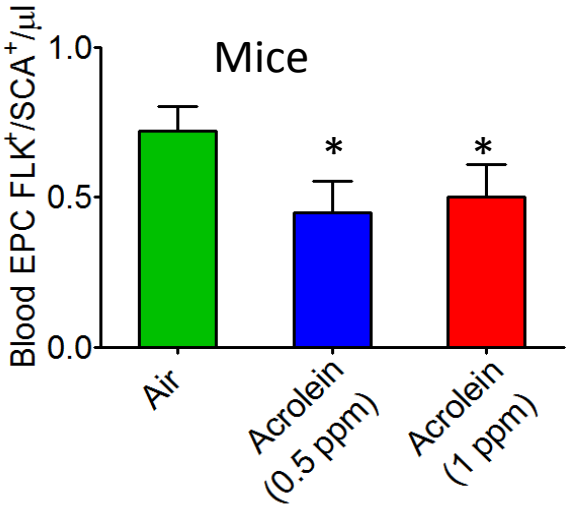
VOCs and Circulating Angiogenic Cells





Benzene and CAC



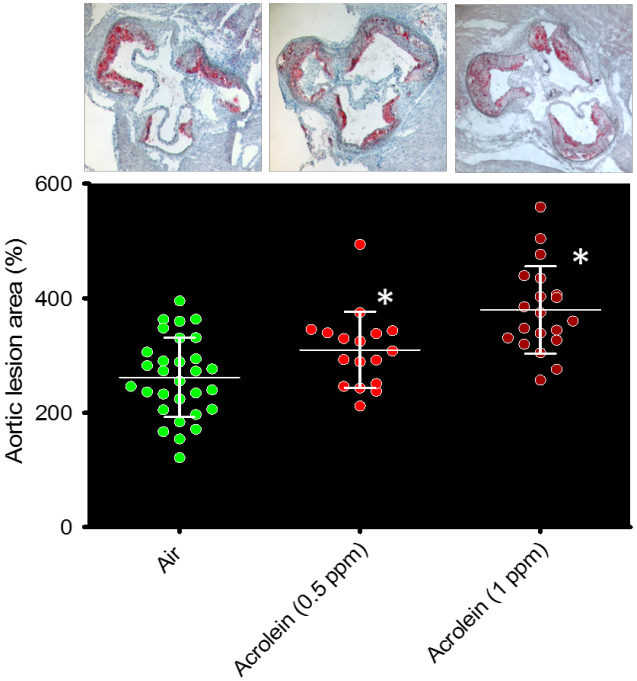


Association of Acrolein and Crotonaldehyde with Atherosclerosis in JHS

Adjusted associations of urinary VOCs with aortic iliac calcification

VOC aldehyde	r	P-value
Acrolein (3HPMA)	0.34	<0.001
Crotonaldehyde (HPMMA)	0.38	<0.001

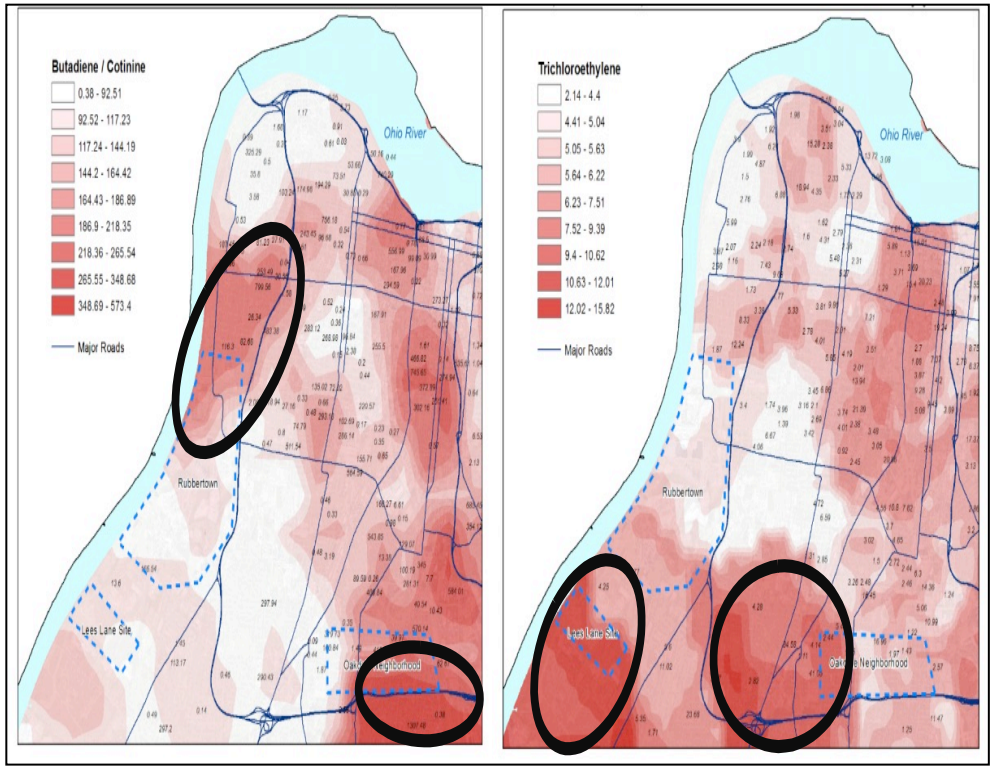
These associations remained significant after adjusting for age, sex, body weight, systolic blood pressure, HbA1c, and estimated glomerular filtration rate, as well as urinary nicotine and cotinine levels.



VOC Levels Near Lee's Lane Superfund Site

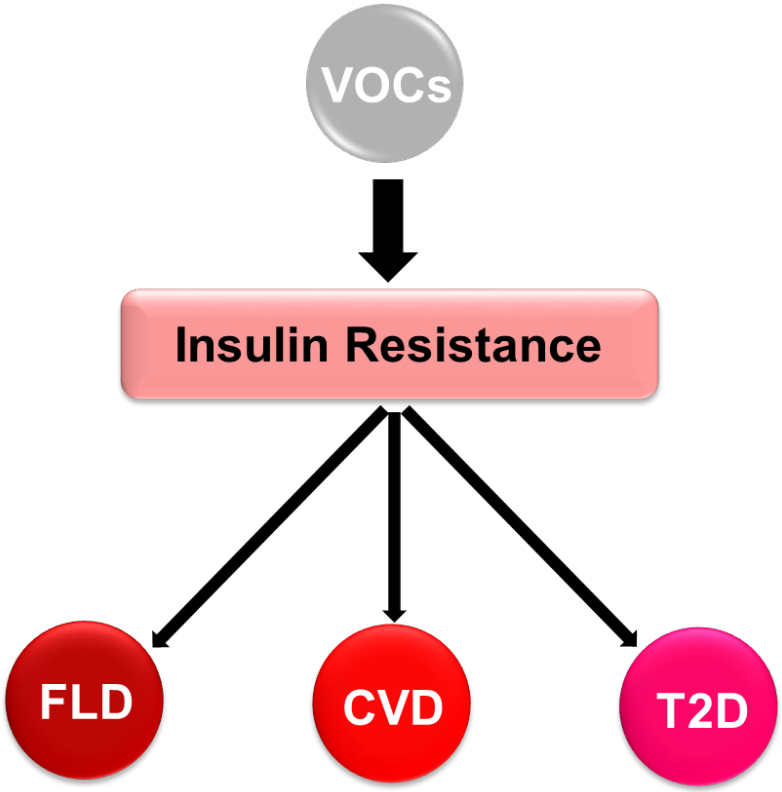
1,3-Butadiene

Trichloroethylene



Highest levels of butadiene were observed in neighborhoods of Rubbertown and Oakdale and TCE levels were highest in residential area near the Lee's lane Superfund site

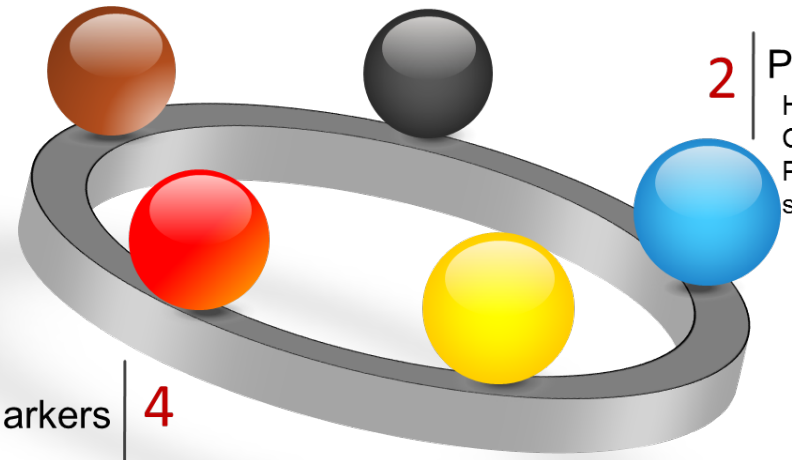
Hypothesis



Project 1: Population Based Study

Five hundred participants followed longitudinally

Is obesity a risk Modifier?
50 obese+100 non-obese



1 Demographic
Age, Race, Gender, SES, detailed medical, family, medication and social history

2 Physical Exam
Height, Weight, Waist Circumference, Blood Pressure, ECG, aortic stiffness, FMD

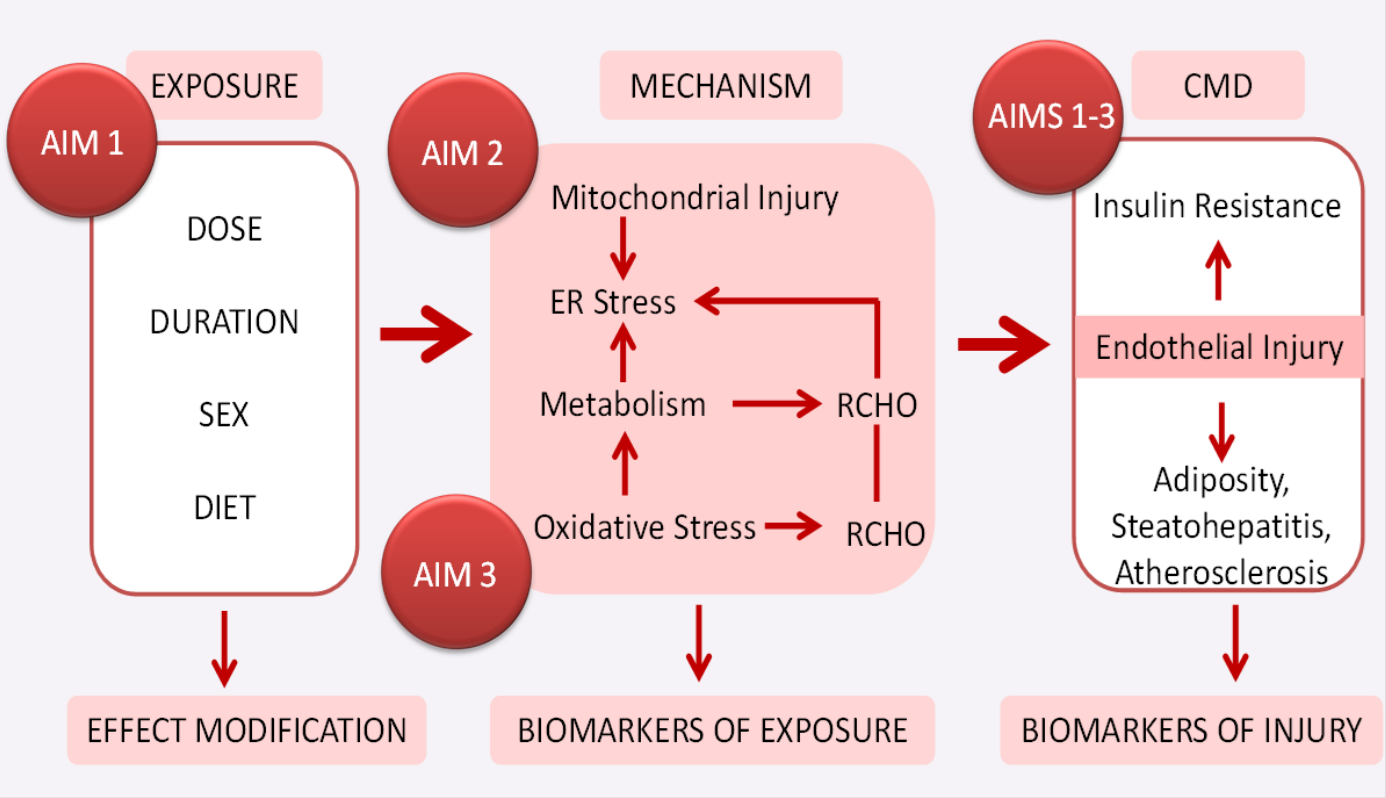
3 Fasting Serum Measurements
LDL cholesterol, HDL cholesterol, Total cholesterol, Triglycerides, Glucose, HbA1c, Serum Creatinine, vWF, CRP, t-PA, PAI-1, Ascorbic acid, Uric Acid, SAA, fibrinogen

4 Biomarkers
EPC, Platelet-monocyte aggregates, Microparticles, PF4, t-PA, TxA2, Factor VII, IL-2, IL-6, D-dimer, PAI-1, s-ICAM-1, s-thrombomodulin, s-TNFR1, MMP-3, MMP-9, endothelin, E-selectin, P-selectin, oxidized LDL.

5 Tobacco Exposure
Nicotine, cotinine, 3HC etc

Project 2: Pre-clinical Studies

- Examine the effects of VOCs exposure on endothelial function and insulin resistance.
- Delineate the contribution of endothelial UPR to the cardiometabolic toxicity of VOCs.



Project 3: VOC Sensor Development

- **Challenge**

  Ambient VOC concentrations normally range from a few parts per trillion (ppt) to a few parts per billion (ppb)

  - These trace levels strain the detection limits of GC-MS

- **Objective**

  Develop novel technologies for quantitative analysis of VOCs to improve both lab and on-site measurements

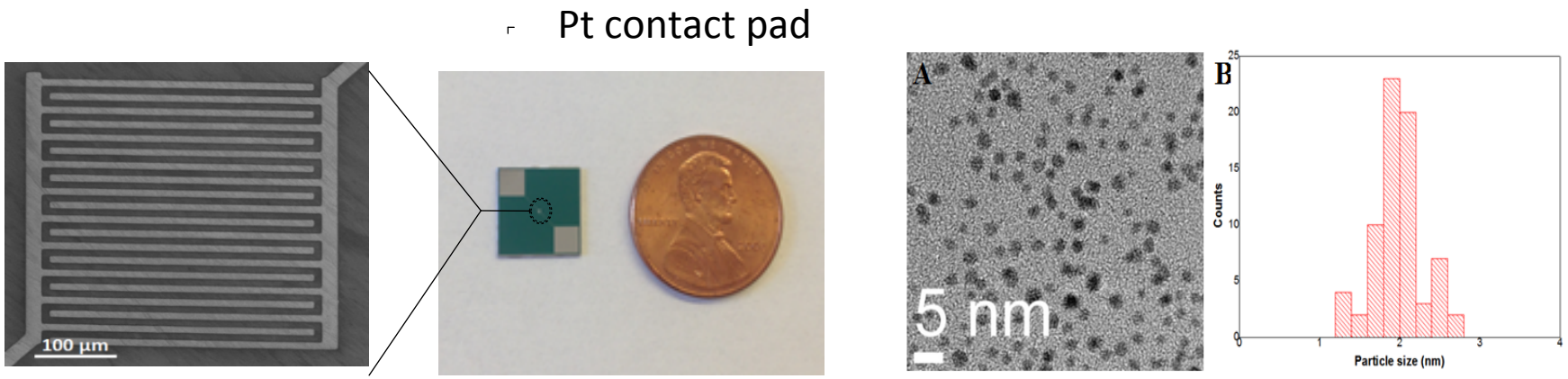
- **Approach**

  Microfabricated gold-based gas sensors and sensor arrays

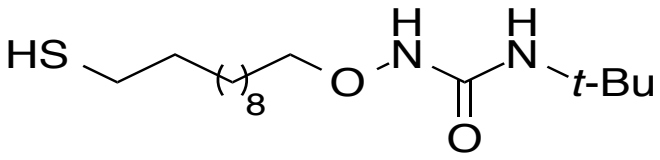
  - Initially focus on detection and quantification of vinyl chloride, acrolein, benzene and 1,3-butadiene

Project 3: Chemiresistor Platform Technology

Microfabricated Pt interdigitated electrode coated with surface-functionalized gold nanoparticles



Urea thiol-functionalized gold nanoparticle sensor for sensing acetone



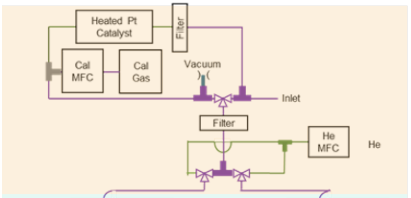
Project 4: VOC Spatial Variability

- **Hypothesis**

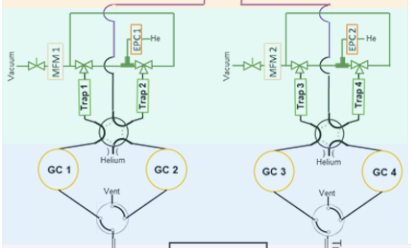
  VOCs of interest may exhibit high spatial variability at urban, and possibly neighborhood, scales because of differential patterns in emission sources and their zones of influence

- **Objective**
  - Characterize urban- and finer-scale spatial variability for select VOCs
- **Approach**
  - Design, construct and validate a novel portable field gas chromatograph (GC) suitable for mobile-based monitoring
  - Measurements in neighborhoods identified by the urinary metabolites study
  - Land use regression model to quantify the small-area variation in VOCs and to estimate residential level exposures

Project 4: VOC Mobile Monitor

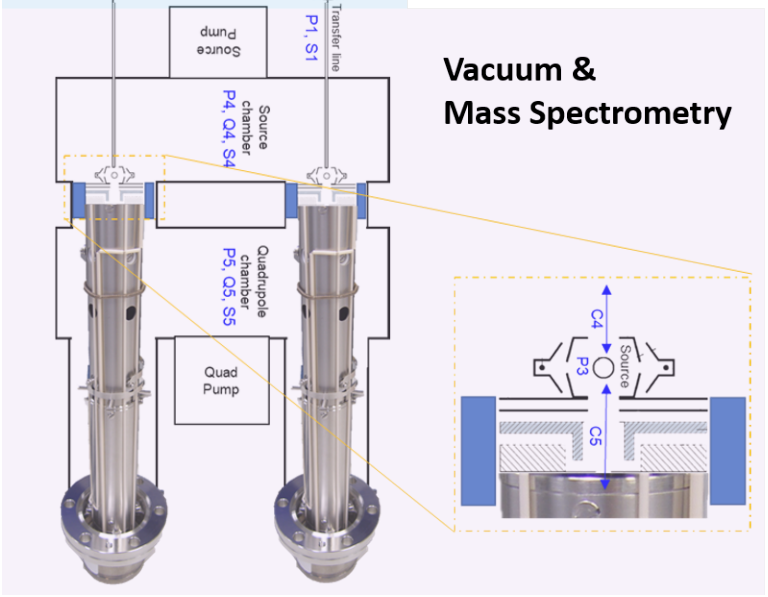


Sample Inlet and Calibration

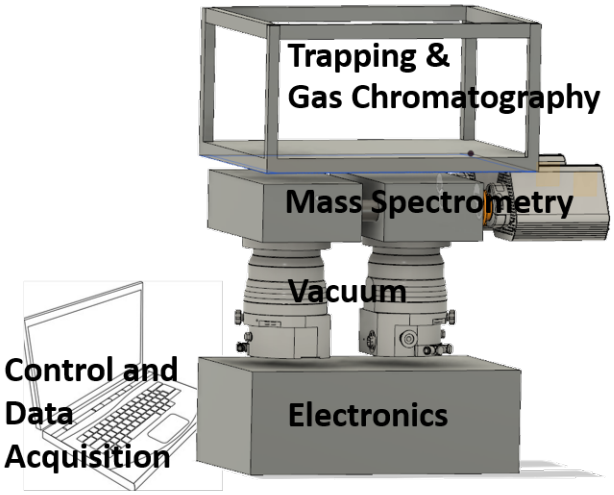


Trapping

Gas Chromatography

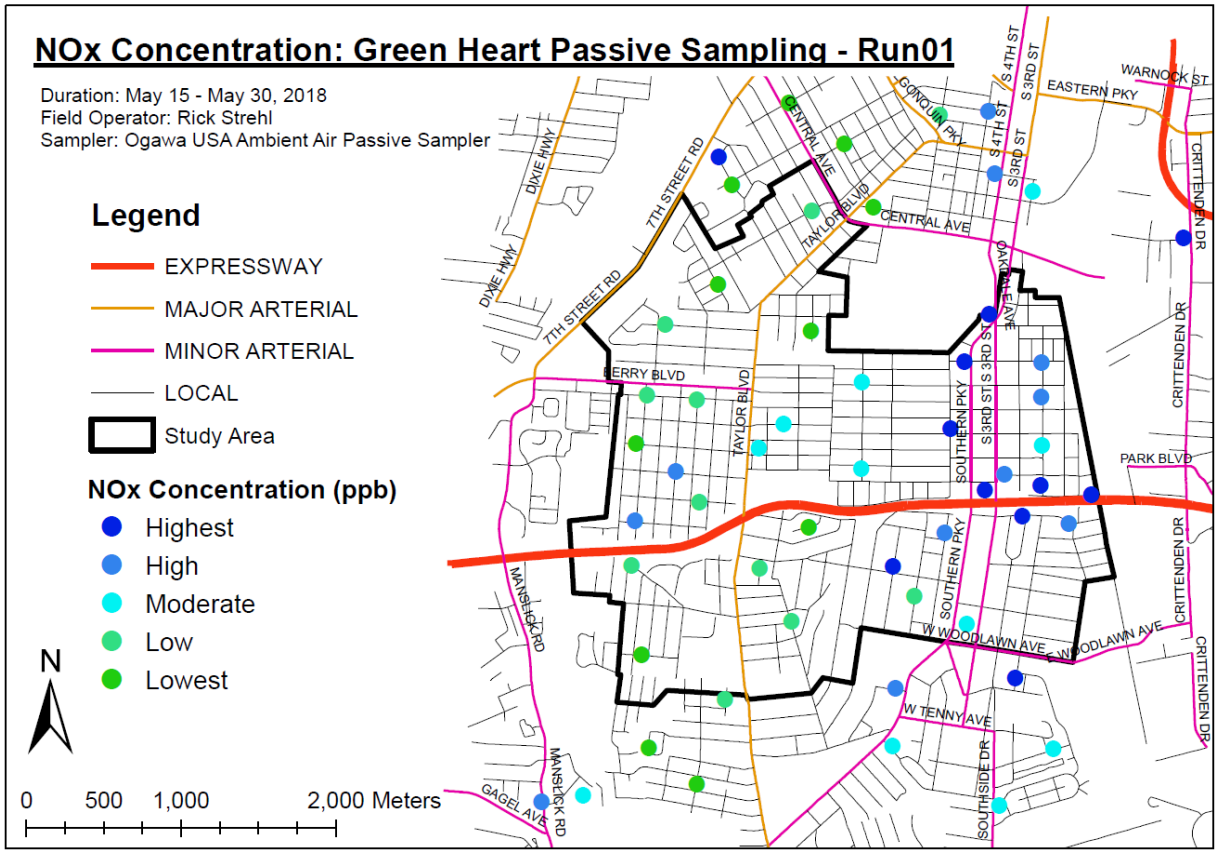


Vacuum &
Mass Spectrometry



Project 4: VOCs in Context

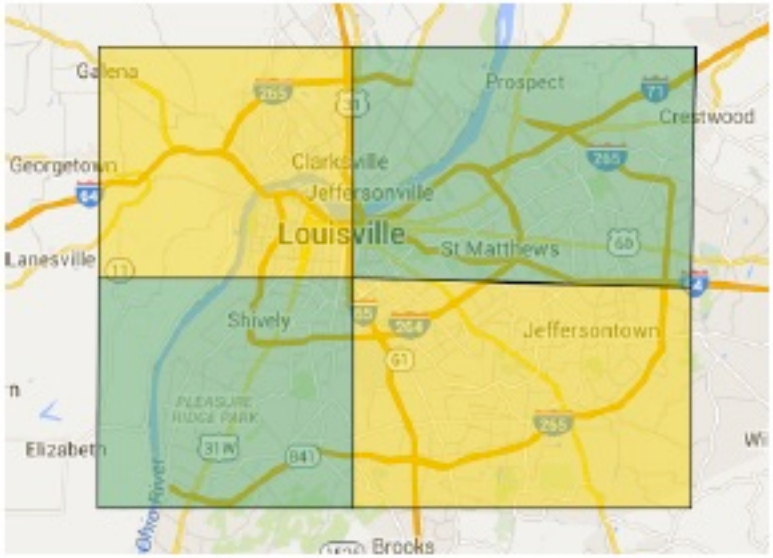
- How will VOCs spatial variability differ from NOx?
  - NOx passive sampling (figure) and NOx mobile measurements (forthcoming) to provide a context for VOCs, including insights into VOC sources



RESEARCH TRANSLATION CORE

1. Facilitate communication between Louisville Superfund Center, the community, policy makers and public health organizations
2. Disseminate research findings
3. Furnish educational information to the CEC and Training Core

Air Quality Daily Report For Louisville *(Last 24 Hours)*



We are currently monitoring the parameters of PM2.5 (small particulate matter), PM10 (large particulate matter) and O3 (Ozone)

The best Air Quality was in Southwest Louisville Kentucky with an AQI value of 9 which is GOOD

The worst Air Quality was in Southeast Louisville Kentucky with an AQI value of 58 which was MODERATE

The average Air Quality for Louisville, Kentucky was 28 which is GOOD

Air Quality Index (AQI) Values	Levels of Health Concern	Colors
When the AQI is in this range:	...air quality conditions are:	...as symbolized by this color:
0-50	Good	Green
51-100	Moderate	Yellow
101-150	Unhealthy for Sensitive Groups	Orange
151-200	Unhealthy	Red
201-300	Very Unhealthy	Purple
301-500	Hazardous	Maroon

About The Metrics

Best Air Quality: This is the lowest AQI value accross all quadrants and parameters monitored

Worst Air Quality: This is the highest AQI value accross all quadrants and parameters monitored

Average Air Quality: This is the average AQI value accross all quadrants and parameters monitored. This metric averages all hourly recorded values for all sensors over the last 24 hours

AIR BARE

REMEDIATION

PLANTING TREES TO PREVENT POLLUTION AND IMPROVE HEALTH

GREEN HEART PROJECT

CENTRAL HYPOTHESIS

Exposure to neighborhood greenery diminishes the risk of cardiovascular disease by decreasing the levels of air pollution