Aim 1: Air Quality and Atherosclerosis

- Ambient particulate matter is associated with increased mortality and increased risk of cardiovascular disease (CVD).
- Global Burden of Disease Study 2010: 3.24 premature deaths, 374 healthy life years
- 13,674 deaths annually due to cardiovascular consequences of air pollution exposure
- We examined the effect of air quality on cardiovascular risk factors and cardiovascular disease outcomes in individuals undergoing cardiac catheterization for suspicion of coronary artery disease.
- We performed genome-wide interaction studies in the CATHGEN cohort for cardiovascular disease and air pollution exposure.

Background

Our project is designed to investigate the effects of acute and chronic air pollution on acute and chronic cardiovascular disease (CVD). In part, we are examining gene-by-air quality effects on newly identified cardiovascular risk biomarkers and blood-based metabolic intermediates.

Aim 2: GEOX Interaction Studies

- GWAS with Illumina Omni-Express, 1,000,000 SNPs genotyped in the Duke Center for Human Genetics Molecular Genetics Core Lab
- 2177 individuals with both GWAS and GIS coordinates
- All North Carolina residents (Figure 1)

Results and Conclusions

- We identified a significant (p < 0.05) gene-by-DTR interaction in the FCAD6-PSGR gene, measured by reduced number of diseased vessels (NDV) in CAD (Figure 1). Table 1.
- Evidence for an SNP variant in this locus comes from independent EA and AA ethnic groups (Table 1).
- 2177 individuals with both GWAS and GIS coordinates
- All North Carolina residents (Figure 1)

Table 1. Characteristics of the CATHGEN study cohort for each PM2.5 exposure level

<table>
<thead>
<tr>
<th>PM2.5 Level</th>
<th>Number of Individuals</th>
<th>Mean Age ± SD</th>
<th>Mean Body Mass Index (BMI)</th>
<th>Mean Systolic Blood Pressure</th>
<th>Mean Diastolic Blood Pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>574 (56)</td>
<td>57.3 ± 12.2</td>
<td>29.9 (Overweight)</td>
<td>1199 (58)</td>
<td>500 (24)</td>
</tr>
<tr>
<td>Medium</td>
<td>574 (56)</td>
<td>57.3 ± 12.2</td>
<td>29.9 (Overweight)</td>
<td>1199 (58)</td>
<td>500 (24)</td>
</tr>
<tr>
<td>High</td>
<td>574 (56)</td>
<td>57.3 ± 12.2</td>
<td>29.9 (Overweight)</td>
<td>1199 (58)</td>
<td>500 (24)</td>
</tr>
</tbody>
</table>

Methods

- SNP and gene annotation
- Evaluation of expression in datasets with air pollution exposure
- SNP and gene annotation
- Adjustment for population stratification using principle components (PCs)
- Main effect of PM2.5 (per 1 μg/m³ increase) on CAD adjusted for age, sex and race showed no association, OR = 1.0 (95% CI: 0.89–1.12)
- No significant (p < 0.05) gene-by-PM2.5 interactions in trans-ethnic meta-analysis including CHRM3, CNTNAP2 and SHPK
- Significant eQTLs for lymphocytes
- EPIC now includes the ability to analyze SNPs associated with circulating metabolites

Future Work

- SNPs and gene expression
- Evaluation of expression in datasets with air pollution exposure
- SNP and gene annotation
- Collaborate with EPA on pancreatic studies
- Study epigenetic effects of TGF-PM2.5 and on methylation
- Collaborate with EP-NC on parallel studies of acute and chronic exposure studies.

References