Ambient air pollution exposures are correlated with DNA modifications in exacerbation prone pediatric asthma

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Molecular Basis of Environmental Disease Susceptibility

Genes

Cystic Fibrosis (CFTR mutation)

Genetic Influence

Epigenome

Environment

Asthma/Sarcoidosis/HP

Immune System Influence

Environmental Influence

- Ozone
- Pollen
- ETS
- BrC

Promega.com

NIHEIS.com
Can epigenetics be a molecular bridge between the environmental exposure and disease susceptibility?

• Blood (PBMCs) from Asthma Prone children
  • Processed and stored, cryopreserved

• Next Generation Sequencing (NGS) to generate molecular data
  • RNA-Seq
  • ChIP-Seq

• Environmental monitors for NO2, Brown Carbon, Ozone, ETS
  • Stationary and personal
mRNA transcripts are a poor biomarker for asthma

RNA-Seq:
If not mRNA, are epigenetic marks a better biomarker?

ChIP-Seq:

Cross-linking (Fix with formaldehyde)  Sonication (DNA fragmentation)

ChIP (Antibody bound TF-DNA)  Purification and quantification of ChIP-DNA
Epigenetic marks are potentially a good biomarker for asthma pathogenesis.
Exposome measurements correlate with epigenetic peaks.
Conclusions

• Epigenetic marks appear to be a good biomarker for asthma
• Environmental monitoring statistically links known exposures with specific epigenetic marks in PBMCs
• Epigenetics can be used as a molecular bridge between environmental exposures and disease susceptibility

Future Directions

• Expand to a larger cohort, which would be too large for personal monitors
• Analyze repressive epigenetic mark in addition to this activating epigenetic mark
Next Steps in Environmental Monitoring and Respiratory Disease

• high-resolution ozone and NOx
• standard particle types (PM10, PM2.5, and major PM2.5 species),
• larger dusts and aeroallergens (pollens, etc...) up to ~100um and ultrafines (<200nm)
  • Right now we can’t study pollen allergies well because the monitor data are sparse and privately held, despite the fact that pollen allergies are one of the most common health complaints

• Next Projects for the Environmental Epigenetics Research (EVER) Program:
  • Hypersensitivity Pneumonitis longitudinal study
  • VA post-deployment lung function and exposome study
  • Interested in disease cohort or healthy cohort collaborations