

Science Transforming Life®



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

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Molecular Basis of Environmental Disease Susceptibility

*Cystic Fibrosis
(CFTR mutation)*

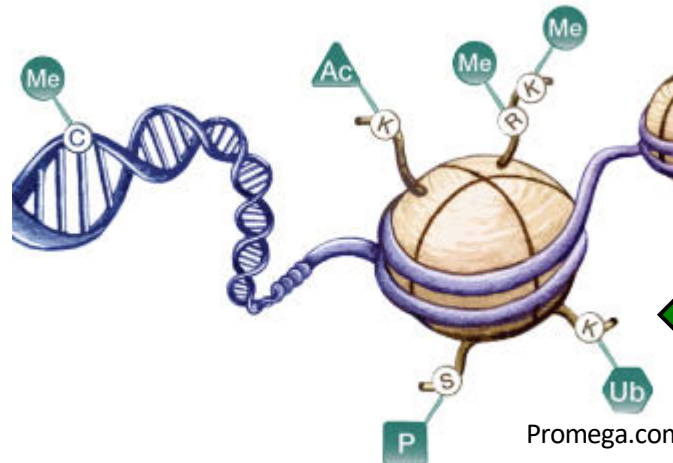
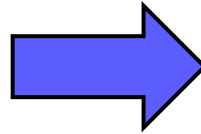
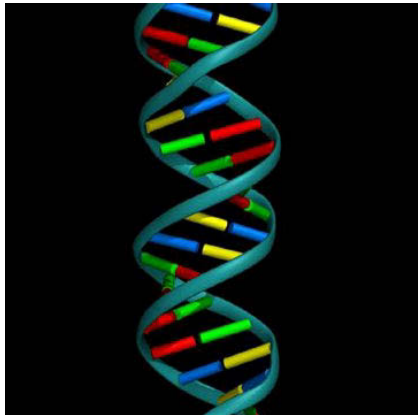
Genes

Environment

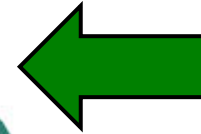
*Asthma/
Sarcoidosis/
HP*

Epigenome

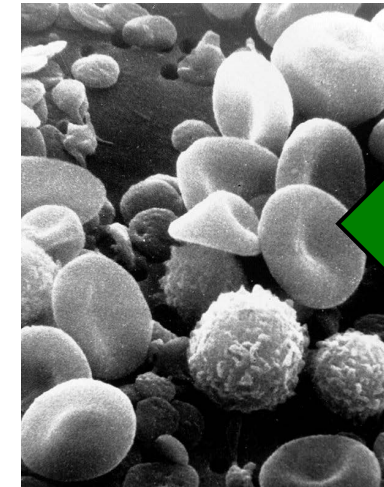
*Genetic
Influence*



Promega.com



*Immune
System
Influence*



*Environmental
Influence*



NIHEIS.com

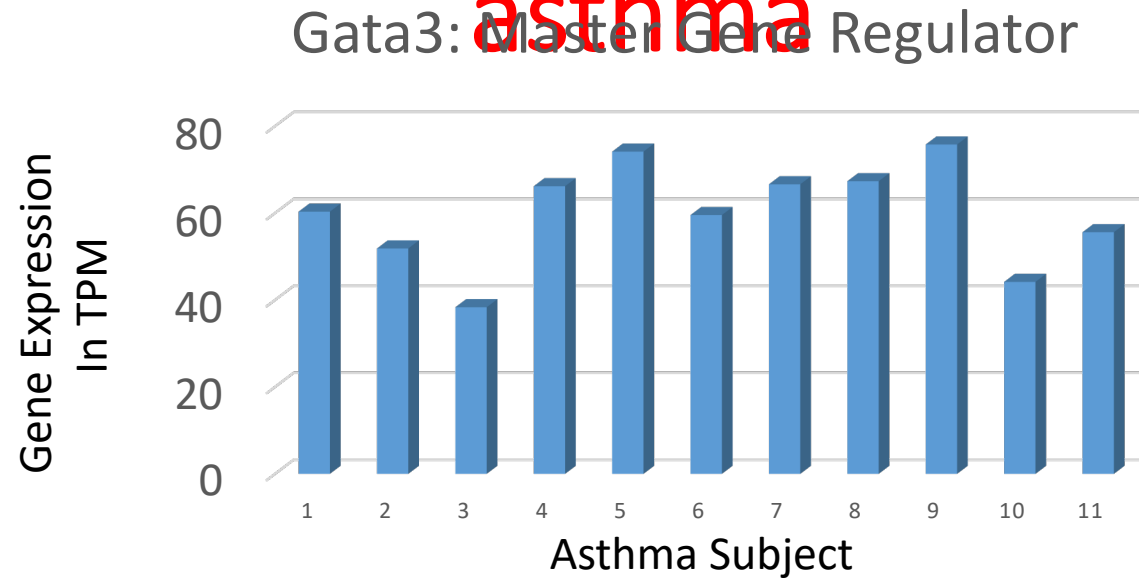
- Ozone
- Pollen
- ETS
- BrC

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

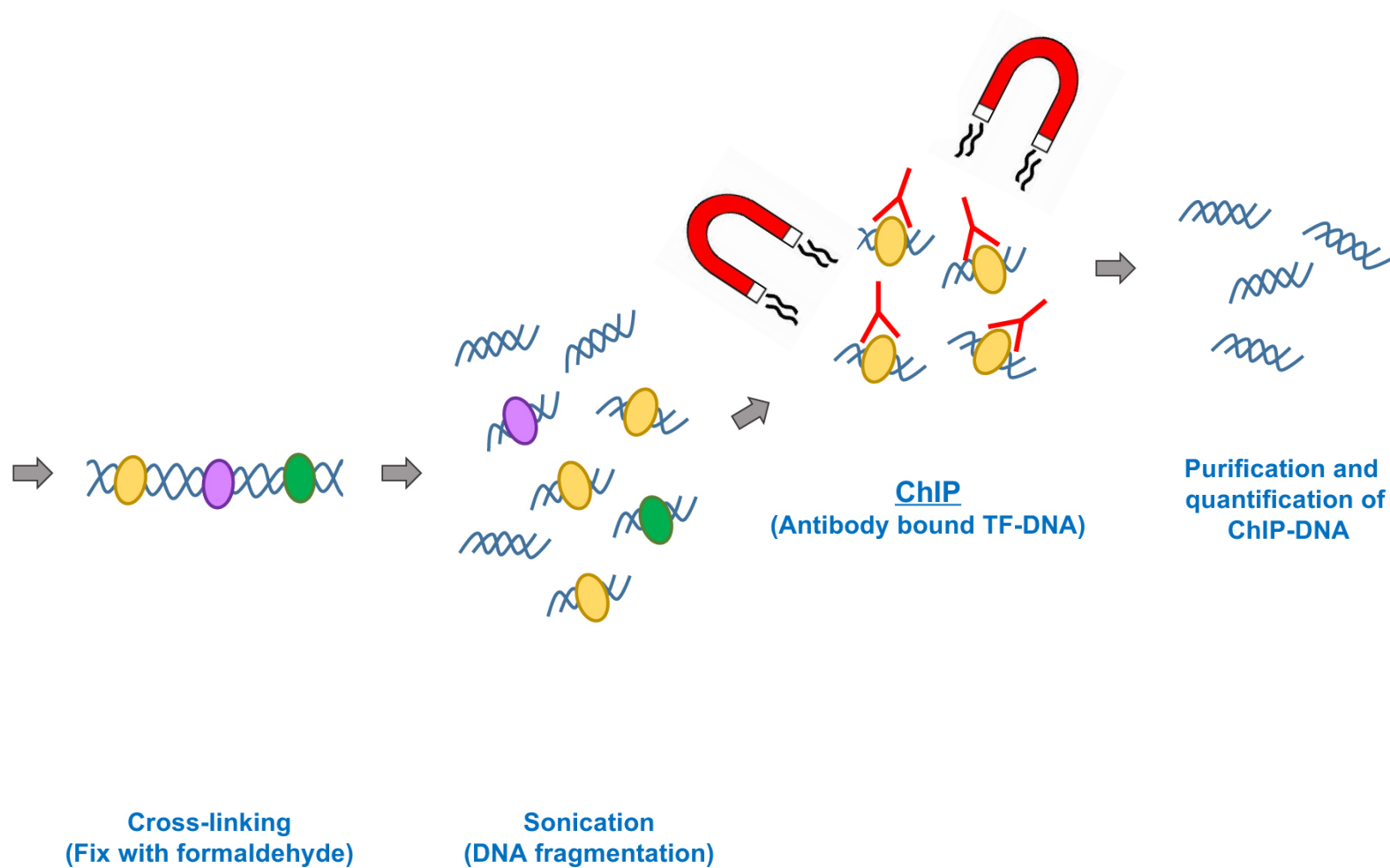
mRNA transcripts are a poor biomarker for asthma

RNA-Seq:

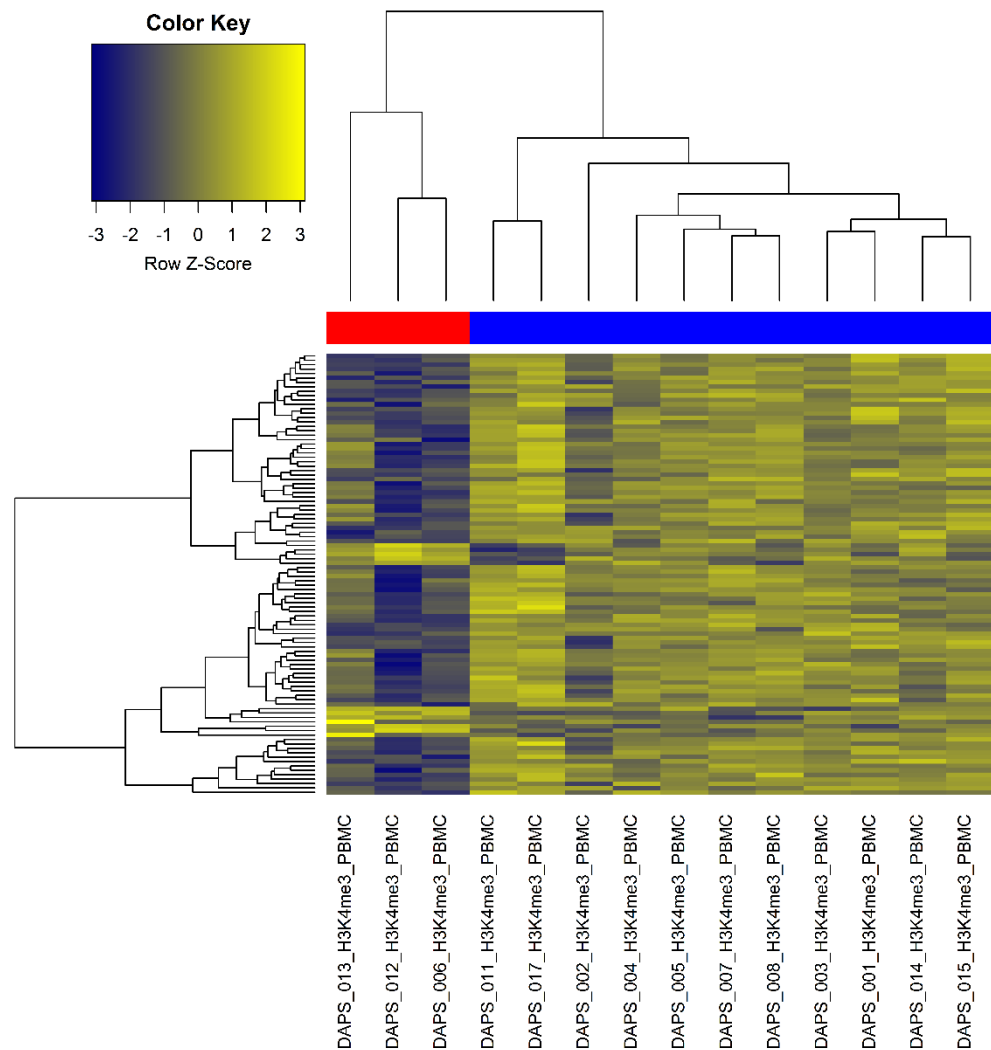


If not mRNA, are epigenetic marks a better biomarker?

ChIP-Seq:



Epigenetic marks are potentially a good biomarker for asthma pathogenesis



Low Risk CASI Score

High Risk CASI Score

Asthma P1

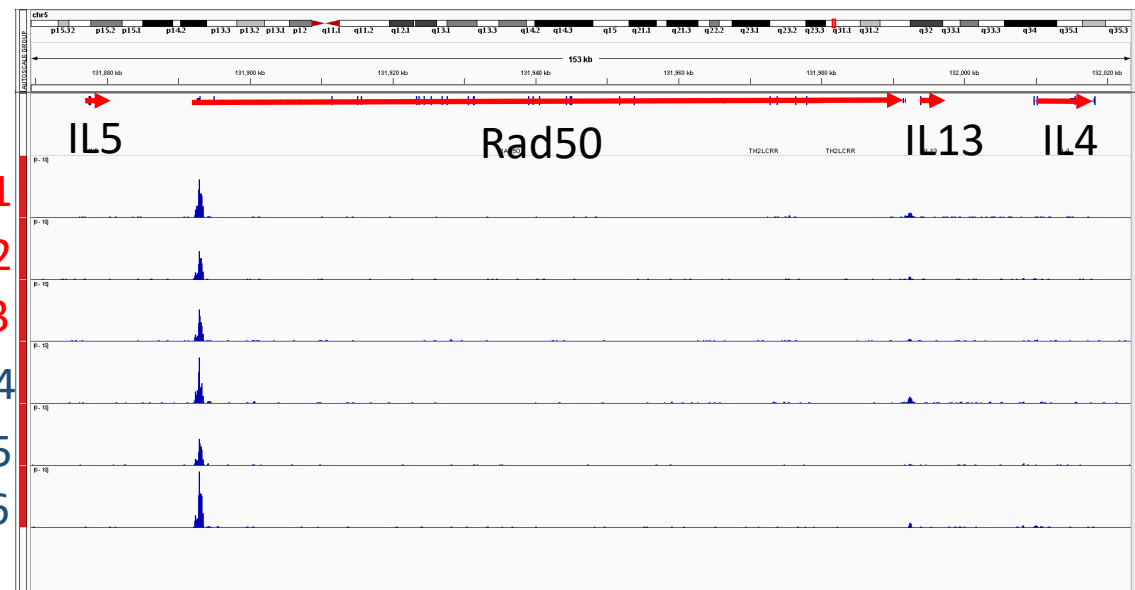
Asthma P2

Asthma P3

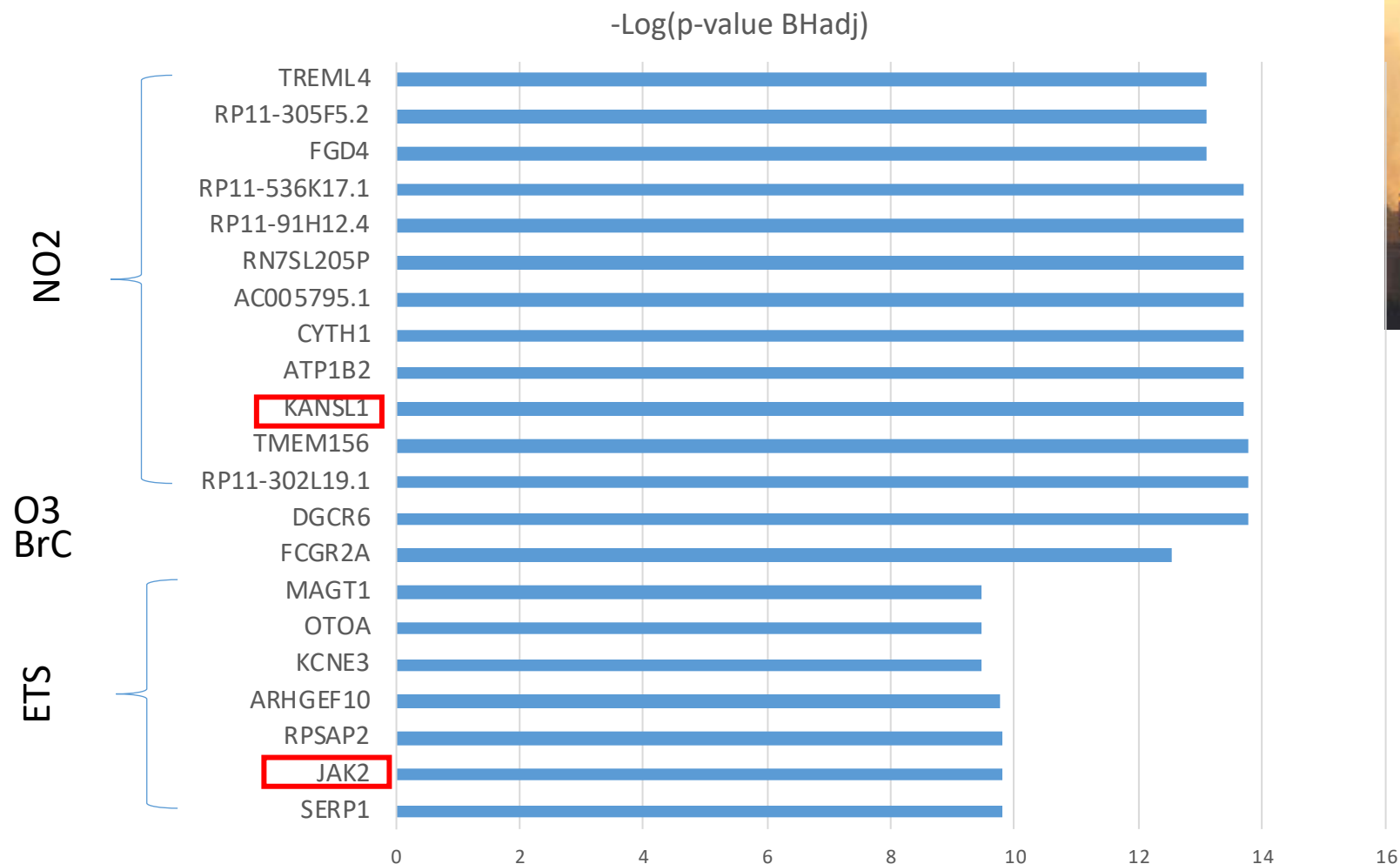
Asthma P4

Asthma P5

Asthma P6



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 NO_x
- standard particle types (PM₁₀, PM_{2.5}, and major PM_{2.5} species),
- larger dusts and aeroallergens (pollens, etc...) up to ~100μm 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