

# Health Update: Influence of Genetic Variants on Ozone Responses of Asthmatic Children

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**California Air Resources Board**

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**California Environmental Protection Agency**

# Background

- Responsiveness to ozone varies widely
- Key question
  - Why are some people more affected than others?
- Gene-based differences may explain Children's Health Study results
  - Genetic differences influence susceptibility to
    - Environmental tobacco smoke
    - Frequency of acute respiratory illnesses

# Defense Against Ozone

- Ozone: a strong oxidant
- Specific enzymes defend against oxidative stress
  - GSTM1\*
    - Variant type: inactive enzyme
  - GSTP1\*\*
    - Variant type: less active enzyme

\*Glutathione S-transferase M1,

\*\*Glutathione S-transferase P1

# Methods

- Study
  - 151 asthmatic children (mild to severe)
  - Mexico City
  - Tested for type of GSTM1 and GSTP1
  - 12 week follow-up
- Symptom endpoints
  - Daily respiratory symptoms
  - Inhaler use (bronchodilator)
  - Lung function

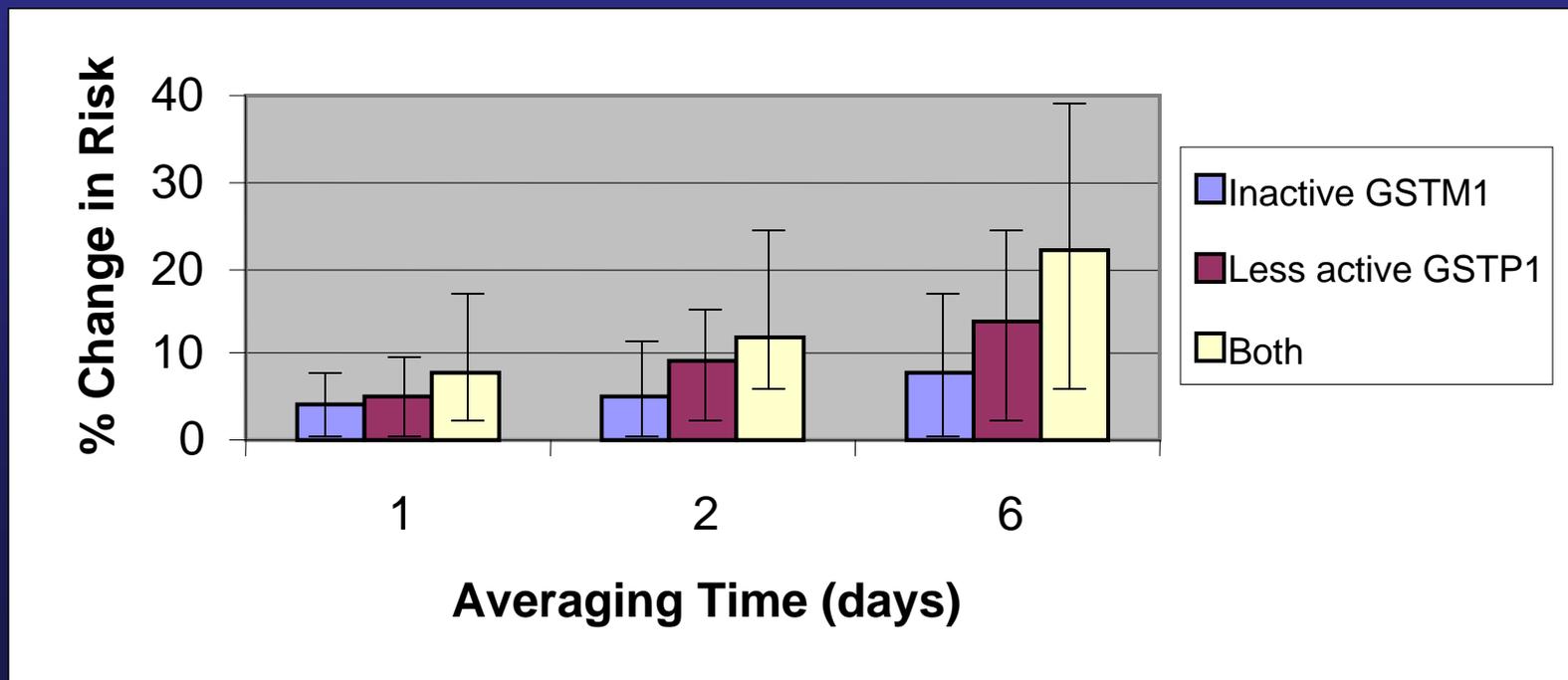
Romieu et al. GSTM1 and GSTP1 and respiratory health in asthmatic children exposed to ozone. *Eur. Respir. J.* 28: 953-959, 2006.

# Single Gene Effects

- Active forms of GSTM1 and GSTP1
  - No associations with ozone
- Inactive form of GSTM1 associated with
  - Difficulty breathing
- Less active form of GSTP1 associated with
  - Cough
  - Difficulty breathing
  - Inhaler use

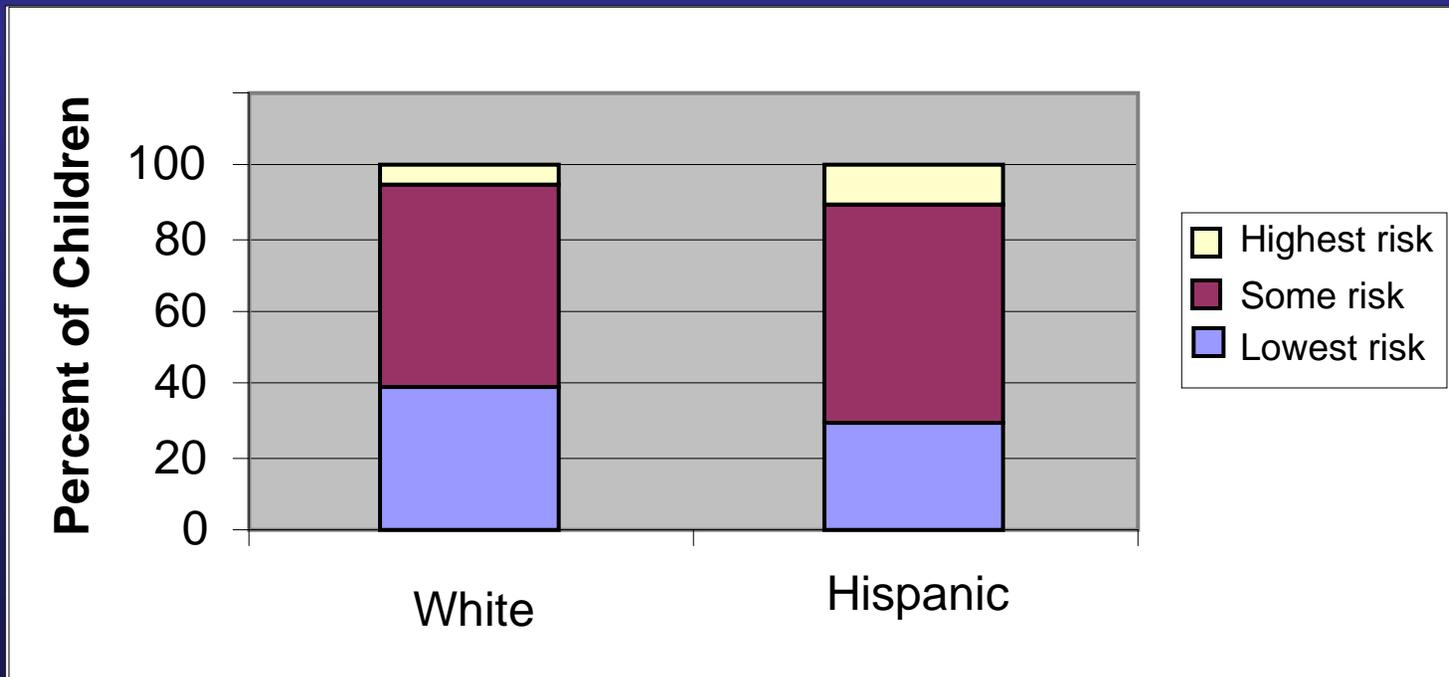
# Combined Gene Effect

- Children with both inactive form of GSTM1 and less active form of GSTP1
  - Greatest risk of breathing difficulty



20 ppb change in 1-hr maximum ozone concentration

# Distribution of Gene Types and Risk in Children\*



\*Data from Children's Health Study cohort

# Conclusions

- Genetics influences susceptibility to ozone
- Implications
  - Need to reconsider how we think about susceptibility to air pollution
  - Susceptibility includes more than baseline health status
- Ongoing research
  - ARB-funded study at U.C. San Francisco
  - Additional studies in Mexico City