

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

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California Air Resources Board

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

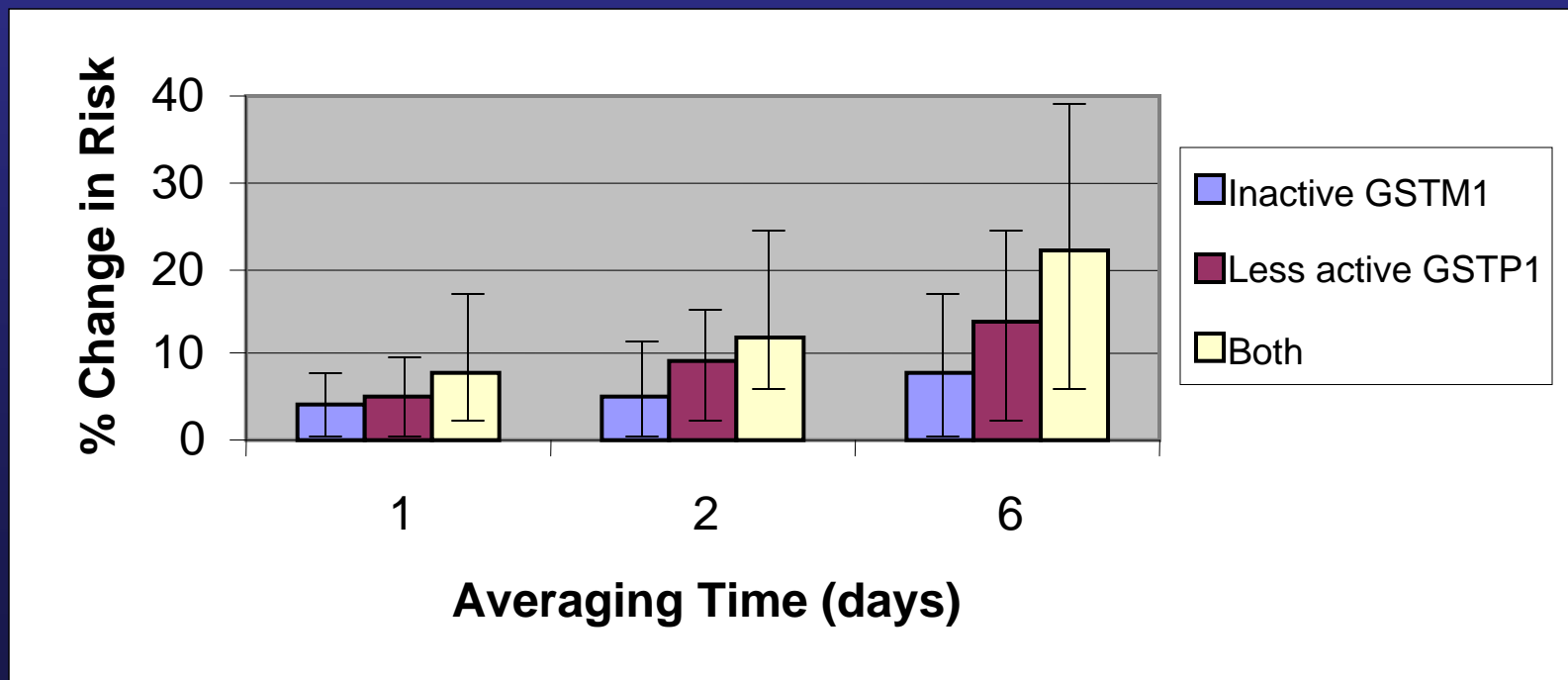
Romieu et al. GSTM1 and GSTP1 and respiratory health in asthmatic children exposed to ozone. *Eur. Respir. J.* 28: 953-959, 2006.

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

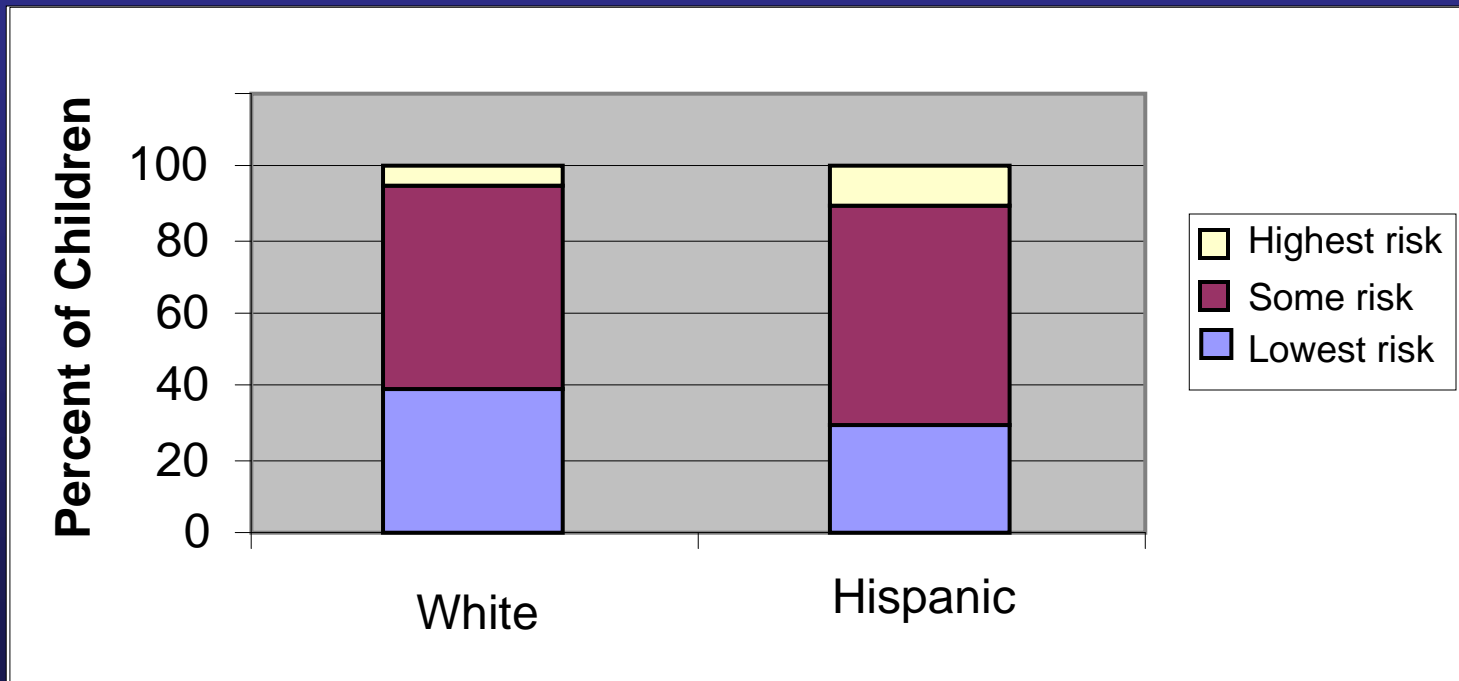
Combined Gene Effect

- 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