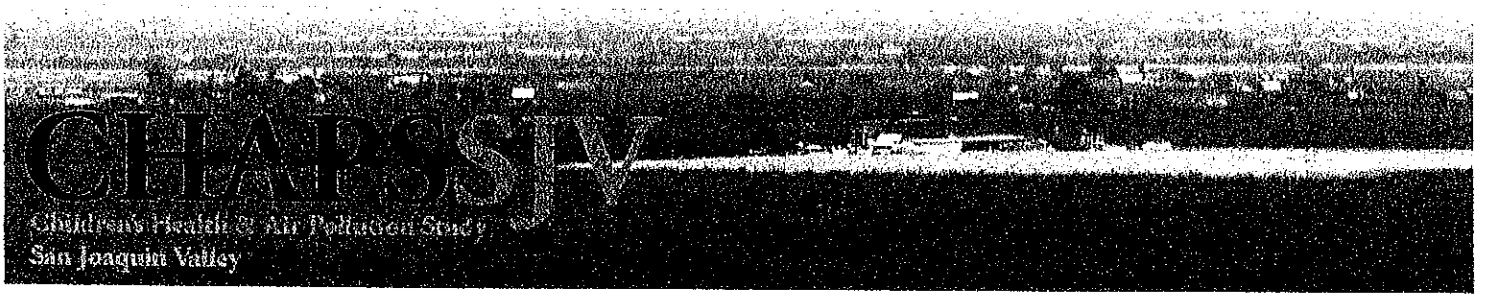


Ambient air pollution impairs regulatory T-cell function in asthma

Journal of Allergy and Clinical Immunology. 2010 Oct;126(4):845-852.e10.
Nadeau K, McDonald-Hyman C, Noth EM, Pratt B, Hammond SK, Balmes J, Tager I.

BACKGROUND:
Asthma is the most frequent chronic disease in children, and children are at high risk for adverse health consequences associated with ambient air pollution (AAP) exposure. Regulatory T (T_{reg}) cells are "peace-keeping" cells that prevent excessive immune responses and they suppress immune responses specific to asthma. DNA methylation results in the decreased expression and function genes. T_{reg}-cell impairment is associated with increased methylation of the Foxp3 gene, a key transcription factor in T_{reg}-cell activity. Children lacking Foxp3 are found to have greater incidence of severe allergies, asthma, gastrointestinal disease and type 1 diabetes. Because AAP exposure can induce epigenetic changes (changes in genetic expression without changes in the underlying DNA sequence), we hypothesized that T_{reg}-cell function would be impaired by AAP, allowing amplification of an inflammatory response.

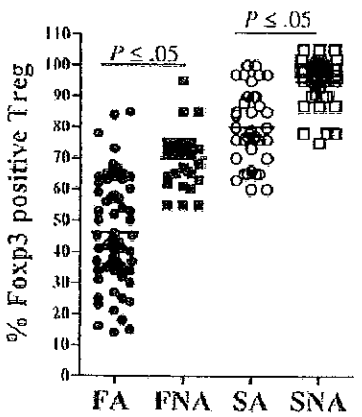
OBJECTIVES:
To assess whether T_{reg}-cells are dysfunctional by the hypermethylation of the Foxp3 gene in subjects exposed to high levels of AAP exposure, leading to worsened asthma symptom severity. Understanding biological mechanisms is an important step towards developing target-driven treatments to reduce the burden of asthma in children who are exposed to high levels of air pollution.

METHODS:
Children with and without asthma from Fresno, CA (high pollution, Fresno Asthma Group [FA] and Fresno Non Asthmatic Group [FNA]) and from Stanford, CA (low pollution, Stanford Asthma Group [SA] and Stanford Non Asthmatic Group [SNA]), were enrolled in a cross-sectional study. Peripheral blood T_{reg} cells were used in functional and epigenetic studies. Asthma severity was assessed by a score derived from severity criteria in the Global Initiative for Asthma.

RESULTS:
In the FA Group, T_{reg}-cell suppression was impaired and FA T_{reg}-cell mobility was reduced compared with other groups. T_{reg}-cell dysfunction was associated with more pronounced decreases in asthma severity in FA versus the SA Group. Foxp3 was decreased in FA compared with the FNA Group. FA also contained significantly higher levels of Foxp3 methylation .

CONCLUSION:
Increased exposure to AAP is associated with hypermethylation of Foxp3, impairing T_{reg}-cell function and increasing asthma morbidity. AAP could play a role in mediating epigenetic changes in T_{reg} cells, which may worsen asthma by an immune mechanism. Foxp3 was measured in respect to genetic expression, T_{reg}-cells function and asthma symptom score. In all 3 measurements, Foxp3 expression was measured lowest for the FA group, next lowest for FNA, higher for SA and highest for the SNA group.

T_{reg} Foxp3 expression is associated with asthma severity



Most Polluted Cities in U.S. 2011: Short-Term Particulate Pollution	
Metropolitan Area	Rank
Bakersfield	1
Fresno	2
Los Angeles	4
Visalia	7
Hanford	9
Sacramento	9
Modesto	12
Merced	13
Stockton	16
San Jose, San Francisco, Oakland	24
American Lung Association: State of the Air 2011	

CHAPS-SJV is a project of UC Berkeley and Stanford University and is in partnership with various Fresno-based environmental, health and academic organizations. jennysaklar@berkeley.edu; http://chaps-sjv@berkeley.edu