Solving the Puzzle of Asthma Disparities

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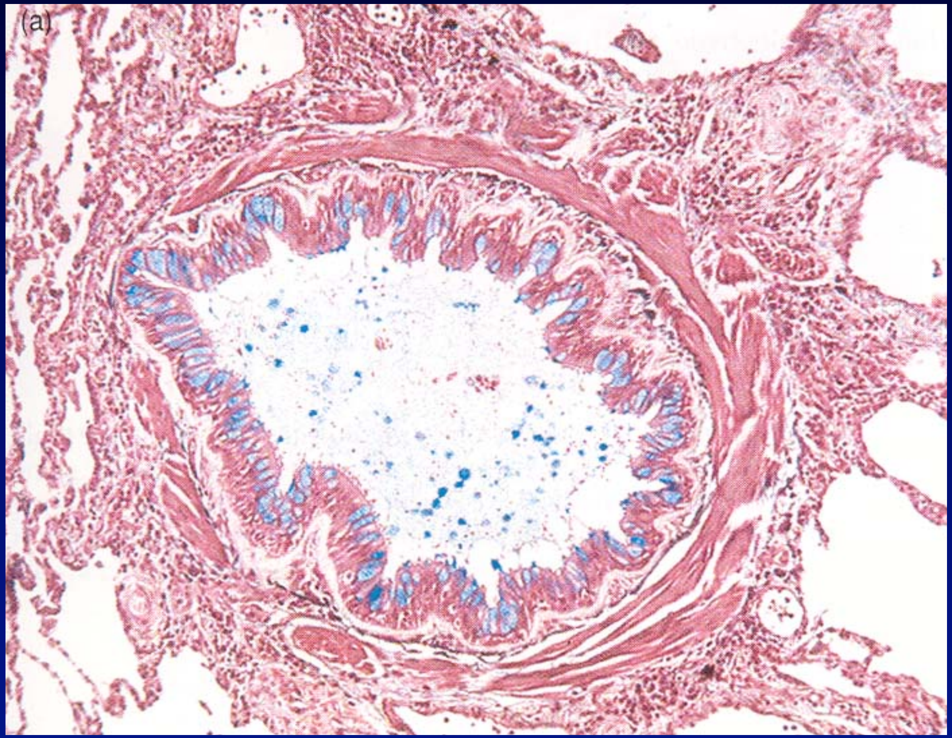
Disclosure of Conflicts of Interest

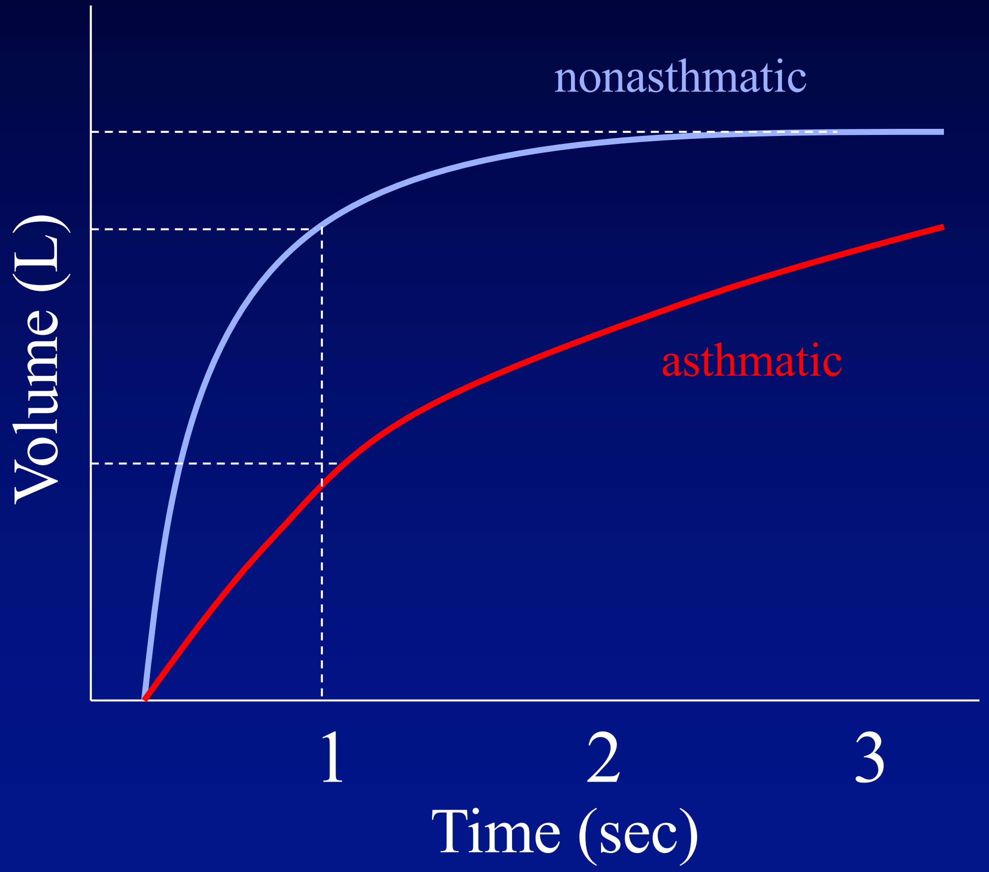
- I have received research materials from Merck, GSK, and Pharmavite (no salary support) to provide medications free of cost to participants in NIH-funded studies.
- I do not intend to discuss unapproved/investigational use of commercial product(s)/device(s) in my presentation

Asthma

- Most common chronic respiratory disease of childhood
- Cost : ~$80 billion per year in USA

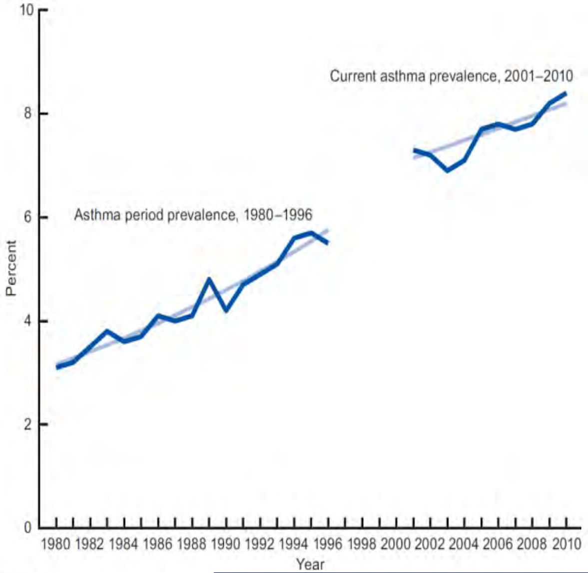


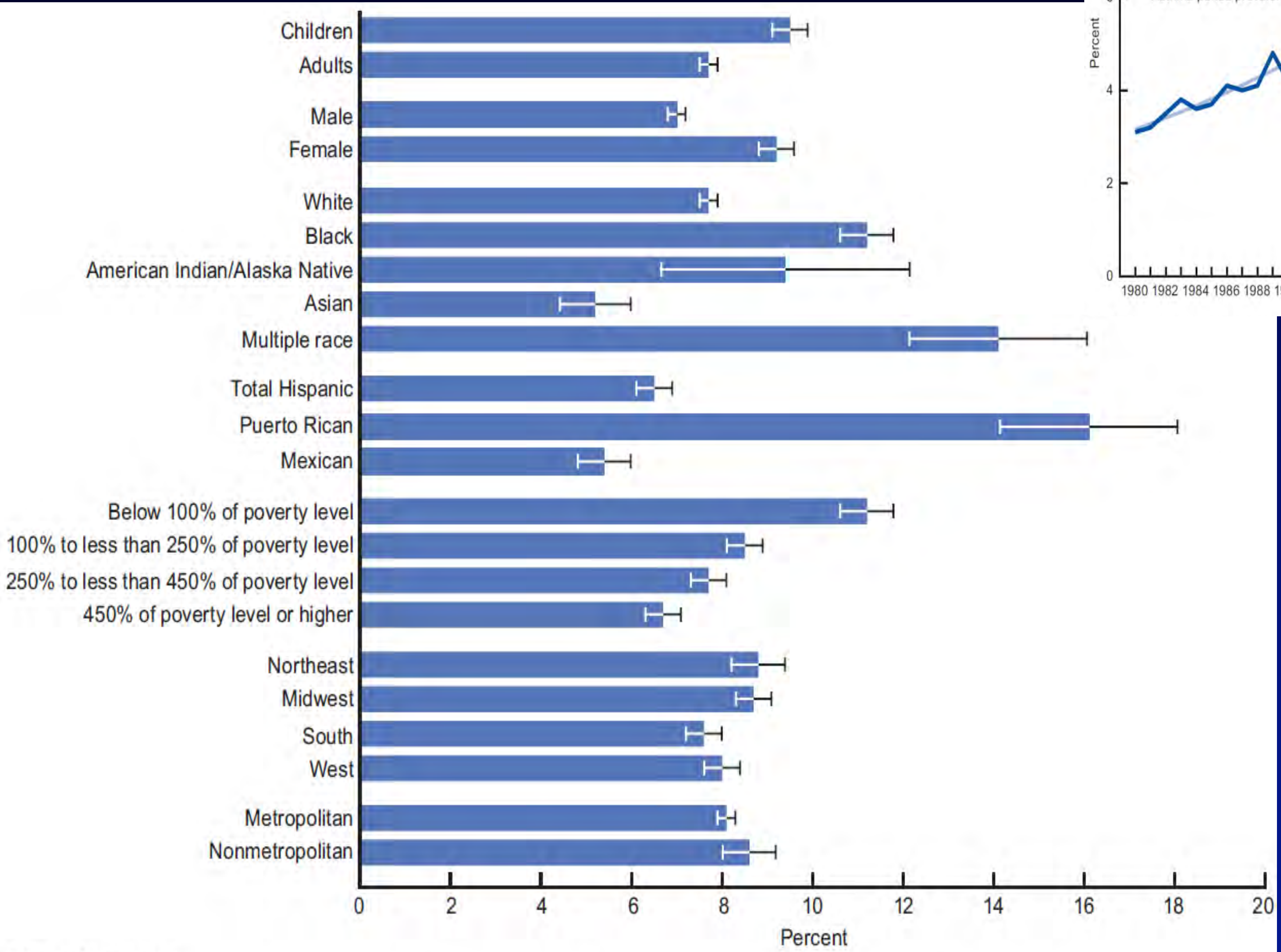
- Airway Inflammation
- Airway Remodeling
- Airway Hypersensitivity
- Reversible Airflow Obstruction



$FEV_1 =$ Forced Expiratory Volume at 1 Second

National Surveillance of Asthma: United States, 2001–2010





I 95% confidence interval.

NOTES: Crude (unadjusted) percentages are presented. See Table 2 for underlying data. The categories "Puerto Rican" and "Mexican" are subcategories of "Hispanic."

SOURCES: CDC/NCHS, National Health Interview Survey and Health Data Interactive (13).

CDC Monitoring the Nation's Health


Patrick Cooper / Retna Ltd.


RED SOX

The "Hispanic Paradox"

- Puerto Ricans have the highest prevalence, morbidity and mortality from asthma of all ethnic groups in the United States
- Mexican Americans have the lowest burden of asthma of all ethnic groups in the United States

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- Forno E, Celedón JC. Curr Opin Allergy Clin Immunol. 2009 ;9:154-160.
- Forno E, Celedón JC. Am J Respir Crit Care Med 2012; 185:1033-1035.
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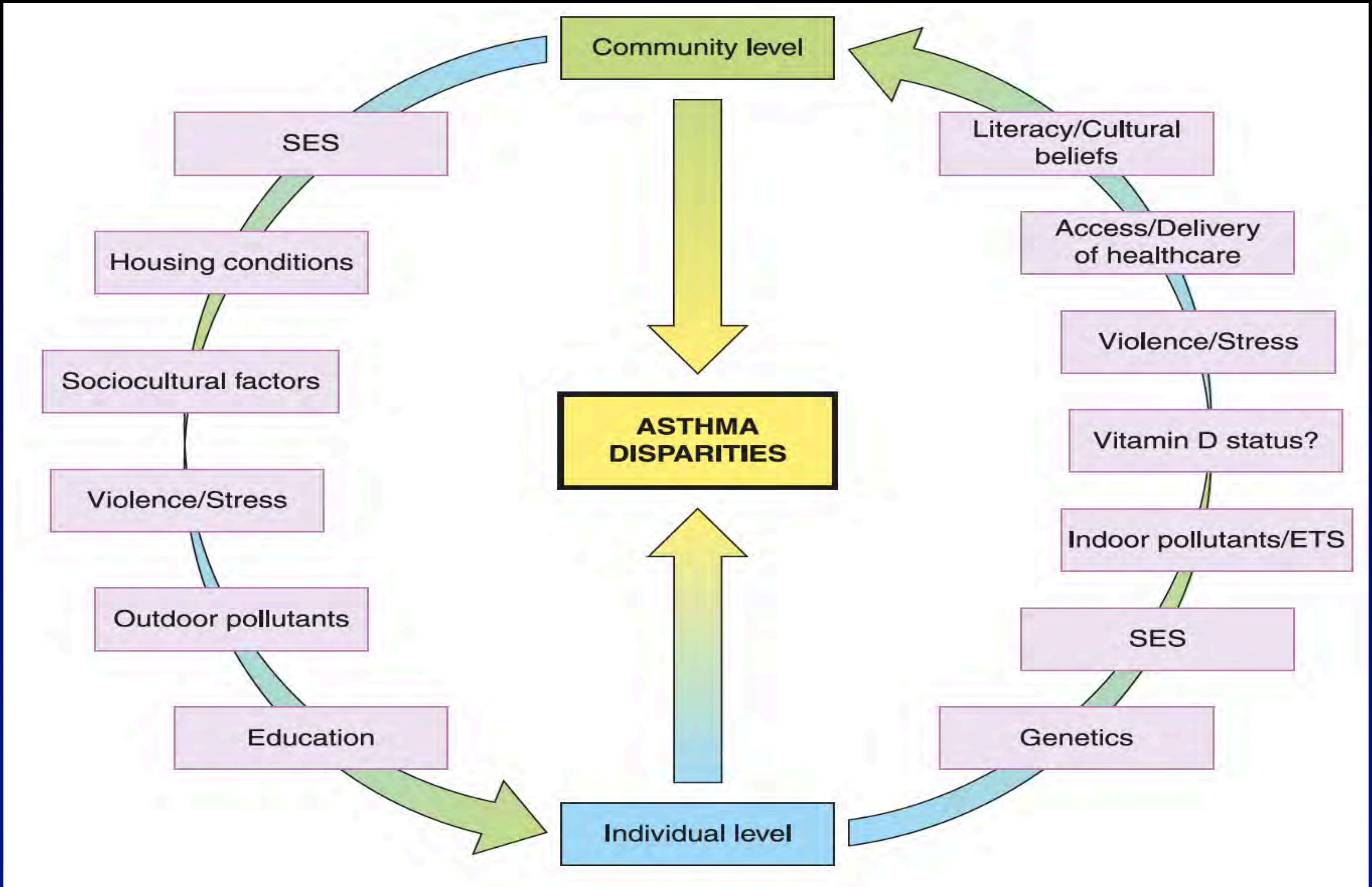
- Szentpetery S,…, Celedón JC. J Allergy Clin Immunol 2016;138:1556-1558.



Forno E, Celedón JC. Am J Respir Crit Care Med 2012; 185:1033-5.

1.

Racial Ancestry

African ancestry and lung function in Puerto Rican children

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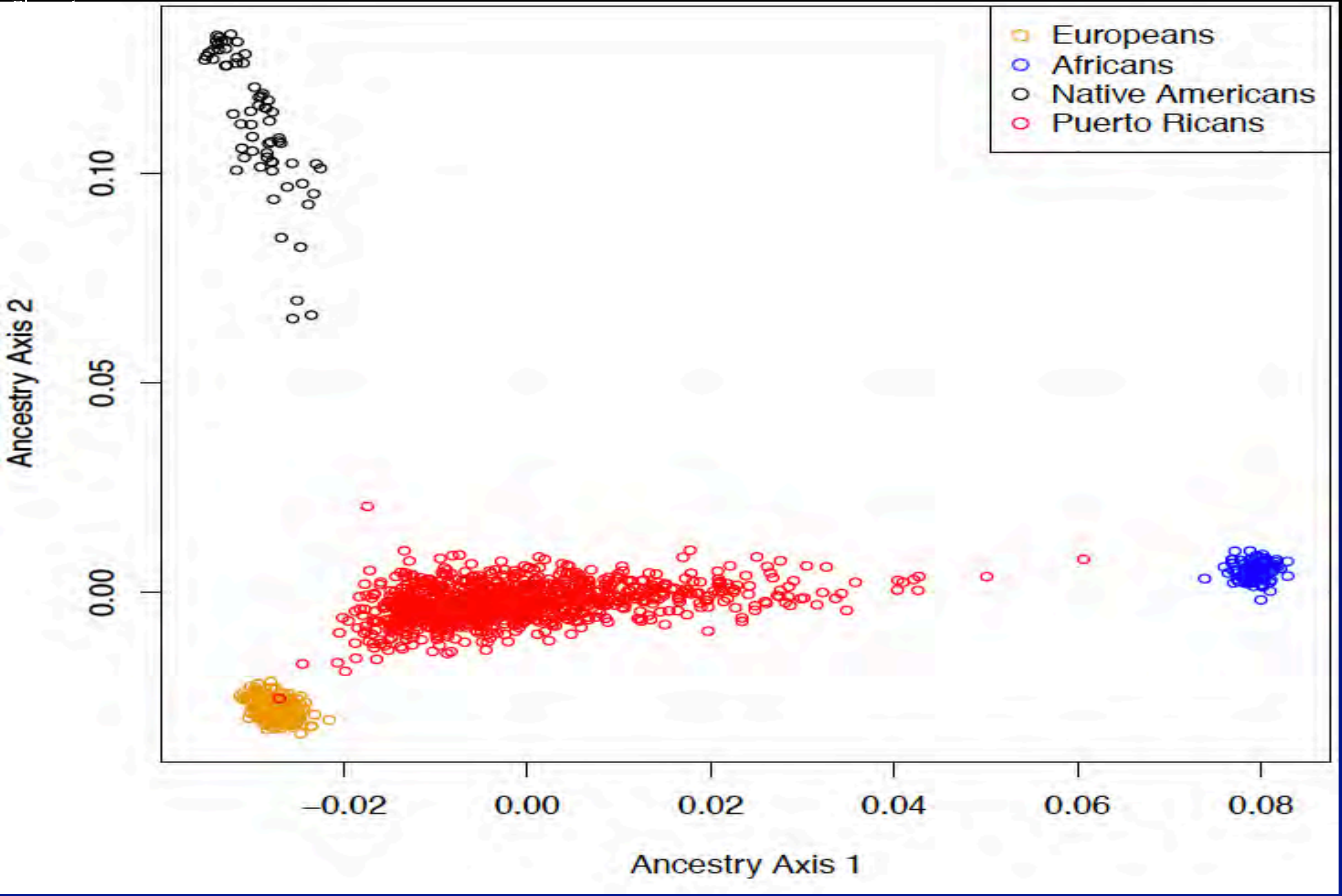
J ALLERGY CLIN IMMUNOL
VOLUME 129, NUMBER 6

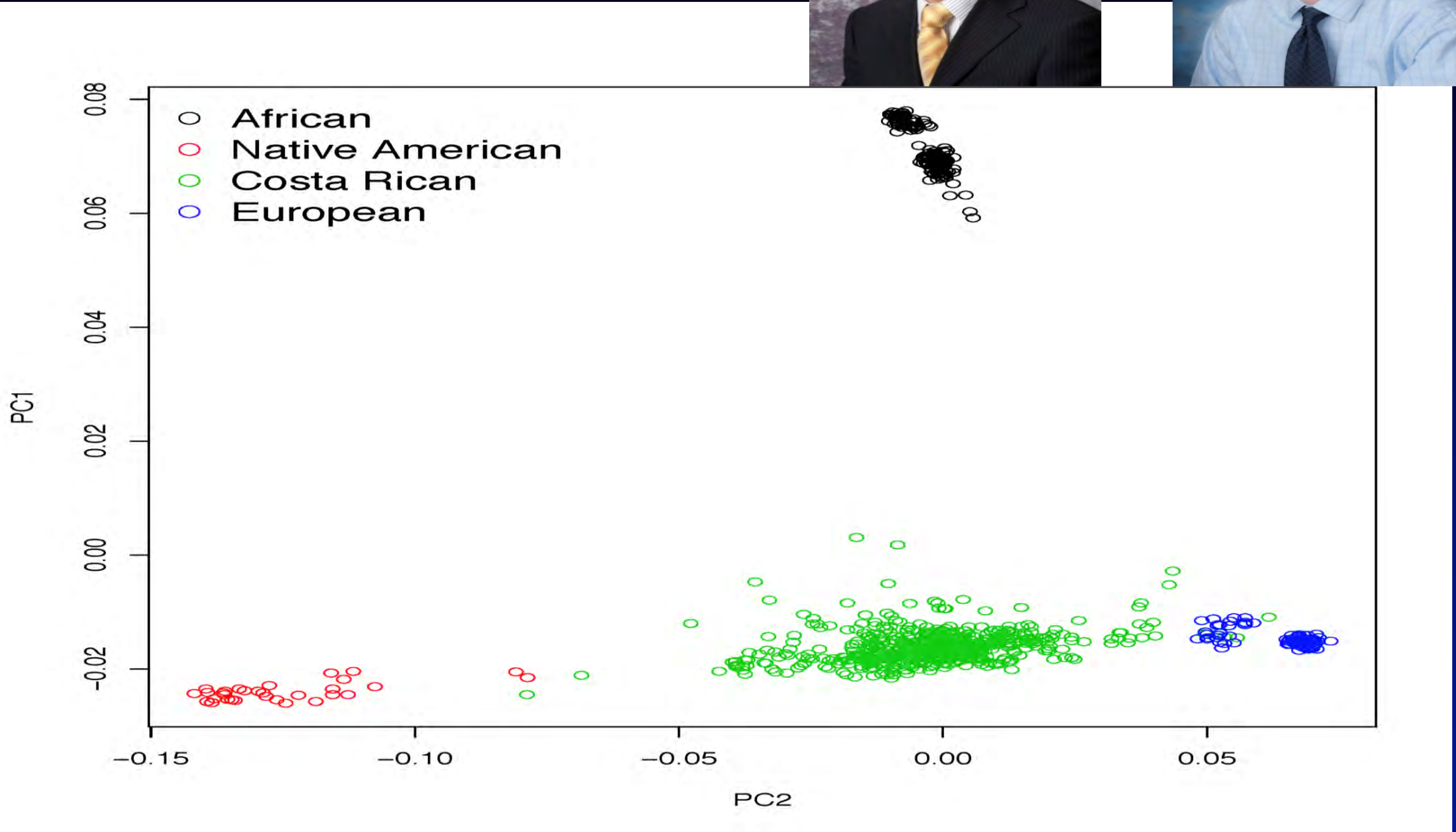

Europeans
Africans
Native Americans
Puerto Ricans
Ancestry Axis 2
0.10
0.05
0.00
−0.02
0.00
0.02
0.04
0.06
0.08
Ancestry Axis 1

African Ancestry and Lung Function in Children with Asthma (Combined Cohort)

	Beta coefficient (95% CI) , P value
Outcomes	**Adjusted***
Pre-BD FEV1 (ml)	-105 (-159 to -51), <0.001
Pre-BD FVC (ml)	-133 (-197 to -69, <0.001
Post-BD FEV1 (ml)	-152 (-210 to -94), <0.001
Post-BD FVC (ml)	-145 (-211 to -79), <0.001

*For age, gender, income, ICS use, study site, height, height squared and body mass index. **Per each 20% increment in African ancestry

NICARAGUA
PANAMA
MAR CARIBE
OCEANO PACIFICO
PROVINCIA DE GUANACASTE
PROVINCIA DE ALAJUELA
PROVINCIA DE HEREDIA
PROVINCIA DE LIMON
PROVINCIA DE SAN JOSE
PROVINCIA DE CARTAGO
PROVINCIA DE PUNTARENAS
CORDILLERA DE GUANACASTE
CORDILLERA CENTRAL
CORDILLERA DE TALAMANCA
PENINSULA DE NICOYA
PENINSULA DE OSA
GOLFO DE PAPAGAYO
LIBERIA
PUNTARENAS
ALAJUELA
HEREDIA
SAN JOSE
CARTAGO
LIMON
La Cruz
S. Cecilia
Los Chiles
Upala
Cuatro Bocas
Santa Rosa
Cañas Dulces
Tierras Morenas
Arenal
Tilarán
Cañas
Líbano
Bagaces
Sardinal
Palmira
Filadelfia
Tempate
Belén
Bolsón
Pto. Humo
Veintisiete de Abril
S. Cruz
Nicoya
Marbella
Mansión
Hojancha
Carmona
Garza
Puerto Coyote
Lepanto
Paquera
Cóbano
Cabuya
Jacó
Parrita
Quepos
Matapalo
Dominical
San Isidro
Buenos Aires
Volcán
Palmar
Boruca
Potrero Grande
Coto Brus
San Vito
Sabalito
Agua Buena
Golfito
Neily
Canoas
La Cuesta
Pto. González
Pto. Jiménez
Rincón
Sierpe
Pto. Cortés
Trinidad
Medias
Pto. Viejo
Tortuguero
Colorado
Cariari
Roxana
Guápiles
Jiménez
Guácimo
Pocora
Siquirres
Pacuarito
Matina
Zent
Moín
San Andrés
Pandora
Cahuita
Pto. Viejo
Bribri
Uatsi
Amubri
Sixaola
Turrialba
Pacayas
Juan Viñas
La Suiza
Tayutic
Moravia
Orosi
El Tejar
S. Cristobal N.
S. María
S. Marcos
S. Pablo
Aserrí
S. Ignacio
Santiago
Colón
Orotina
Atenas
S. Mateo
Esparza
Caldera
Miramar
Chomes
San Ramón
Palmares
Grecia
Naranjo
Sarchí
Poás
Zarcero
Laguna
Buenavista
Quesada
Florencia
Pital
Aguas Zarcas
Río Cuarto
Venado
San Rafael
Caño Ciego
Llanura de los Guatusos
Llanura de San Carlos
Llanura del Tortuguero
V. Orosí 1440
V. Rincón de la Vieja 1806
V. Miravalles 2028
V. Tenorio 1916
V. Arenal 1633
V. Poás 2704
V. Barva 2906
V. Irazú 3432
V. Turrialba 3339
C. Buenavista 3491
C. Chirripó 3819
C. Matama 2750
C. Kamuk 2402
C. Pittier 2869
C. Echandi 3162
Valle de Parrita
Valle del General
Valle de Diquís
Valle de Coto Brus
Valle de Coto Colorado
Valle de la Estrella
Valle de Talamanca
San José Cabecar
Isla del Caño
Pta. Llorona
Pta. Salsipuedes
Cabo Matapalo
Pta. Banco
Pta. Burica
Pta. Uvita
Pta. Catedral
Pta. Judas
Cabo Blanco
Pta. Guiones
Cabo Velas
Pta. Zapotal
Pta. Descartes
Pen. Santa Elena
87°04'
ESCALA 1: 300 000
I. Manuelita
ISLA DEL COCO
C. Iglesias 634
Pta. Turrialba
OCEANO PACIFICO
5°32'
86°00'
85°00'
84°00'
83°00'
11°00'
10°00'
9°00'
8°00'
0 20 40 60 Km.
ESCALA: 1:1 900 000
SIGNOS CONVENCIONALES
LUGARES POBLADOS
Capital de la República
Capital de Provincia
Otras Poblaciones
Límite Provincial
Límite Internacional
ABREVIATURAS
B. Bahía
C. Cerro
I. Isla
N. Norte
Pen. Península
Pta. Punta
Pto. Puerto
R. Río
S. San, Santo, Santa
V. Volcán
Autorizado por el Instituto Geográfico Nacional
Fuente: Mapas Oficiales IGN.
Elaborado por:
Olman Fernandez C. &
Carlos Hidalgo V.
Edición 1996



Chen W, Brehm J et al. Chest 2014; 145(4):704-10.

Native American Ancestry, Lung Function and COPD in Costa Ricans (n=506)

	Beta coefficient (95% CI) , P value
Outcomes	**Adjusted***
Pre-BD FEV1 (ml)	109 (33.6 to 184), 0.005
Pre-BD FVC (ml)	112 (22.2 to 202), 0.02
Pre-BD FEV1/FVC (%)	0.87 (-0.03 to 1.8), 0.06

*For age, gender, height, education, current smoking, pack-years of smoking and case-control status. **Per each 10% increment in Native American ancestry

Racial ancestry and asthma in Hispanics (GALA and CHS)

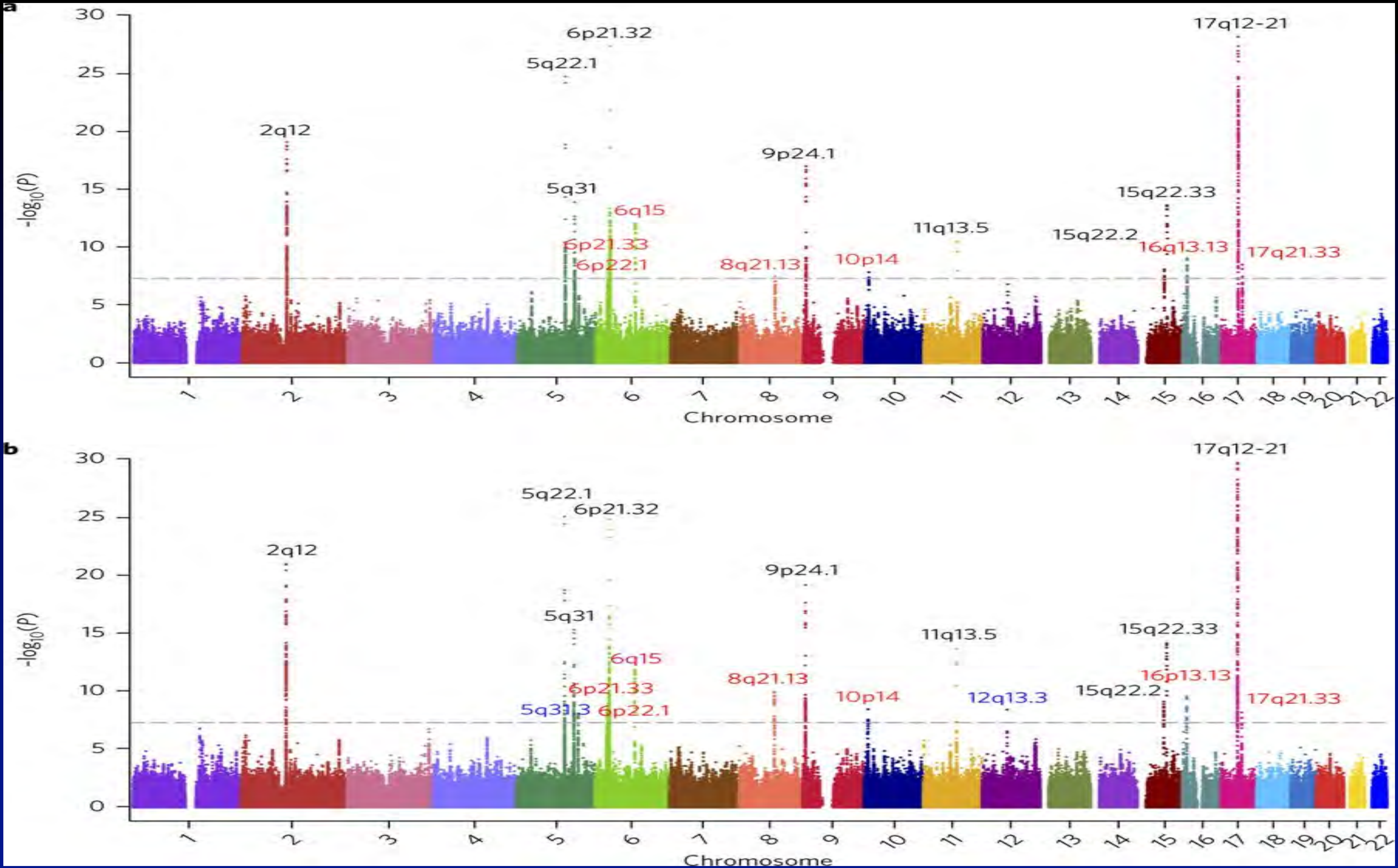
Ancestry	Group	Mean ancestry cases	Mean ancestry controls	OR (95% CI)*	*P* value
Native American	Meta-analysis‡	—	—	0.72 (0.66-0.78)	**1.5×10^{-15}**
African	Meta-analysis‡	—	—	1.40 (1.14-1.72)	**.001**
European	Meta-analysis**	—	—	1.13 (0.89-1.45)	NS

Pino-Yanes M et al. J Allergy Clin Immunol 2015;135(1):228-35

Racial Ancestry and the Hispanic Paradox

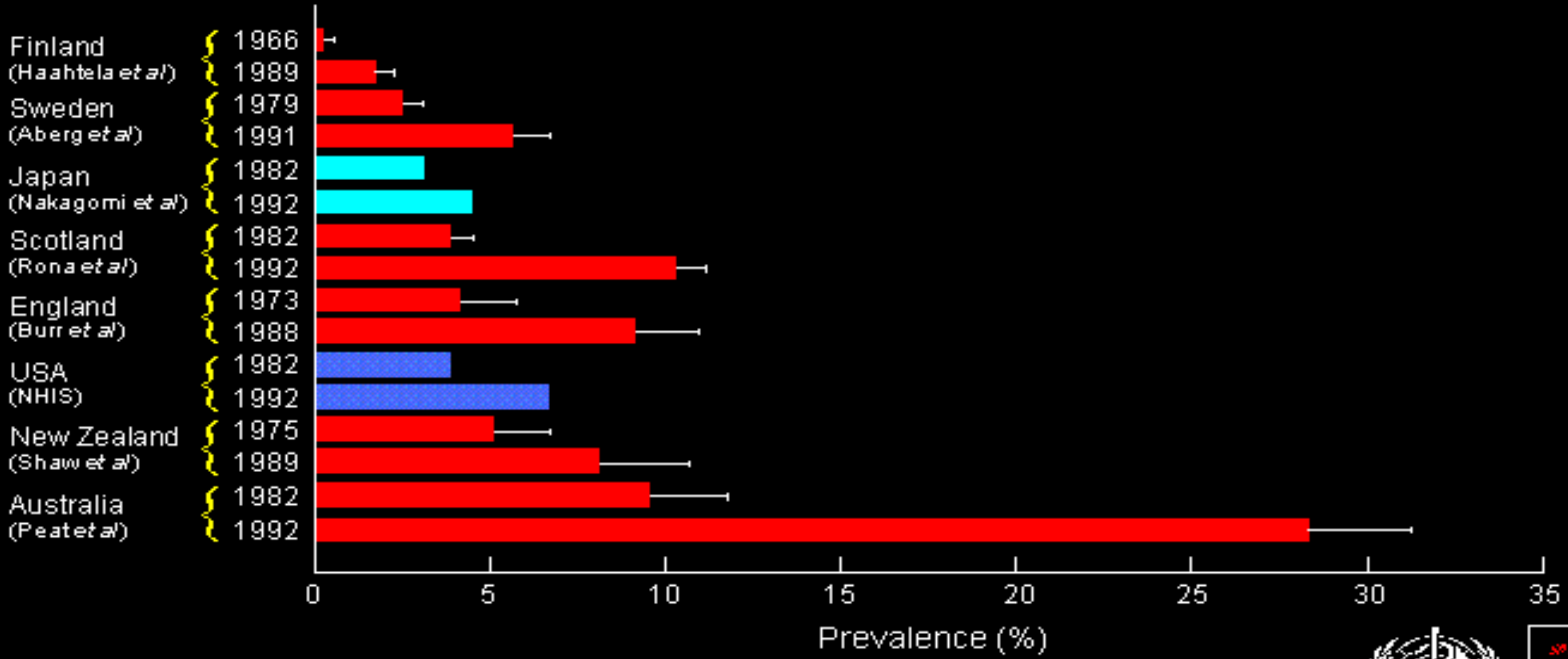
- Our findings (in PR children, CR adults, and NM adults), together with those in African American adults and Hispanics in GALA/CHS, strongly suggest that discrepancies in the burden of obstructive airway diseases (asthma and COPD) between Puerto Ricans and Mexican Americans are at least partly due to differences in underlying racial ancestry
- Although ancestry is a marker of genetic variation, it is also correlated with EL factors

2. Epigenetics



Demenais F et al. Nat Genet 2018 Jan;50(1):42-53.

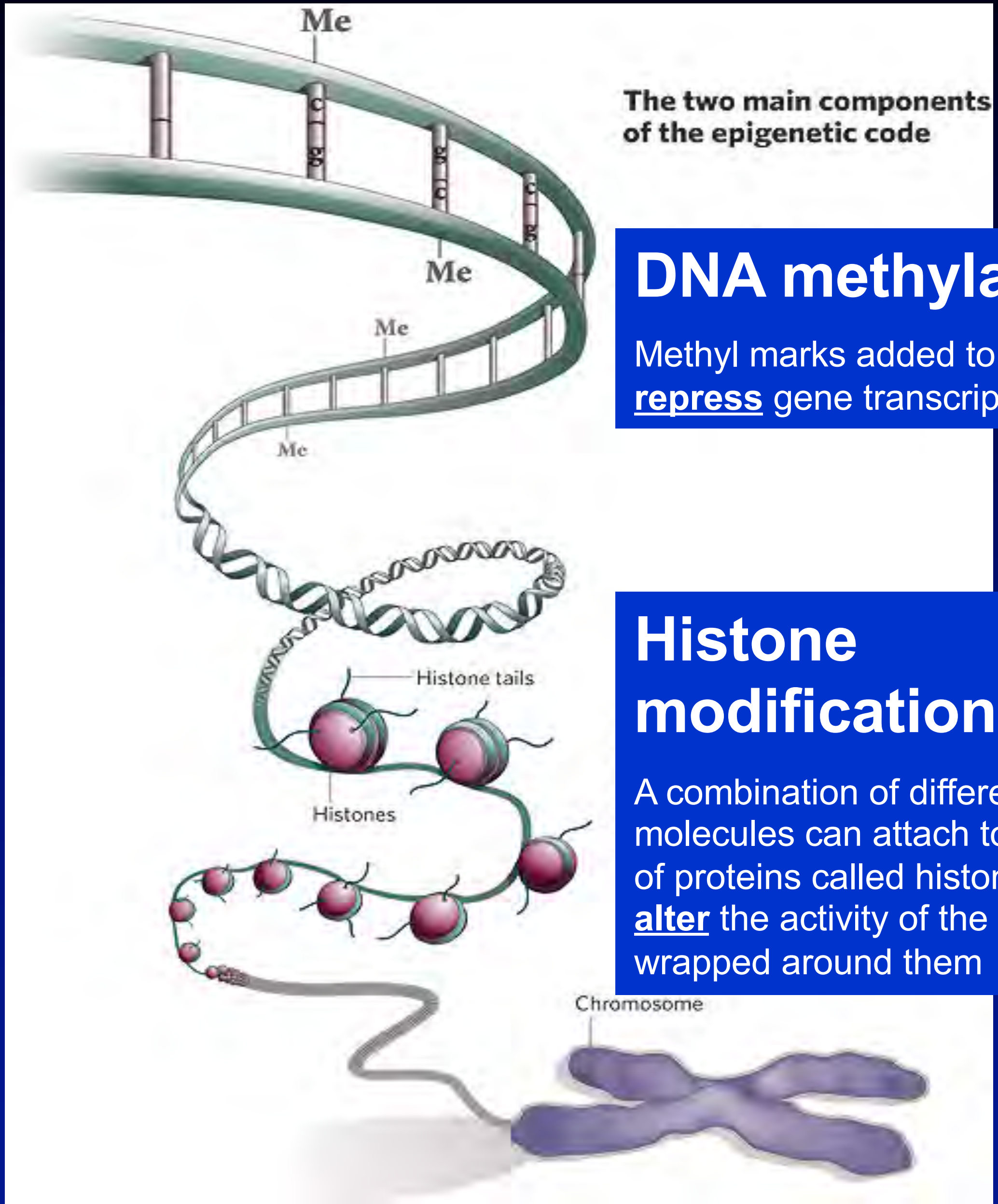
Increased Prevalence of Asthma in Children/Adolescents



Epigenetics

- Programming of gene expression that does not depend on the DNA code
- Characteristics of epigenetic programming
  - Modifiable (can be reprogrammed)
  - Active or poised to be activated:
  - *Tissue or cell-specific*

Epigenetic Marks

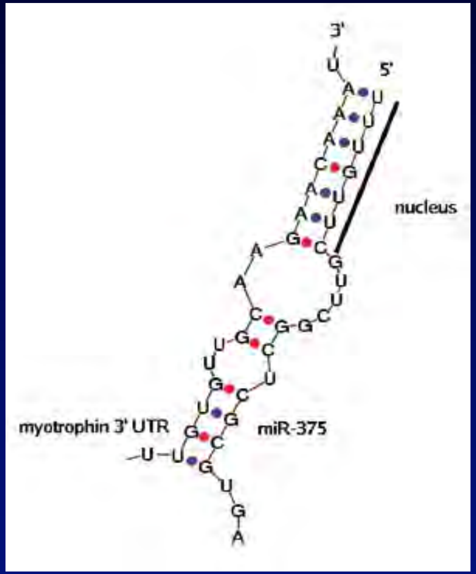


DNA methylation

Methyl marks added to certain DNA bases **repress** gene transcription

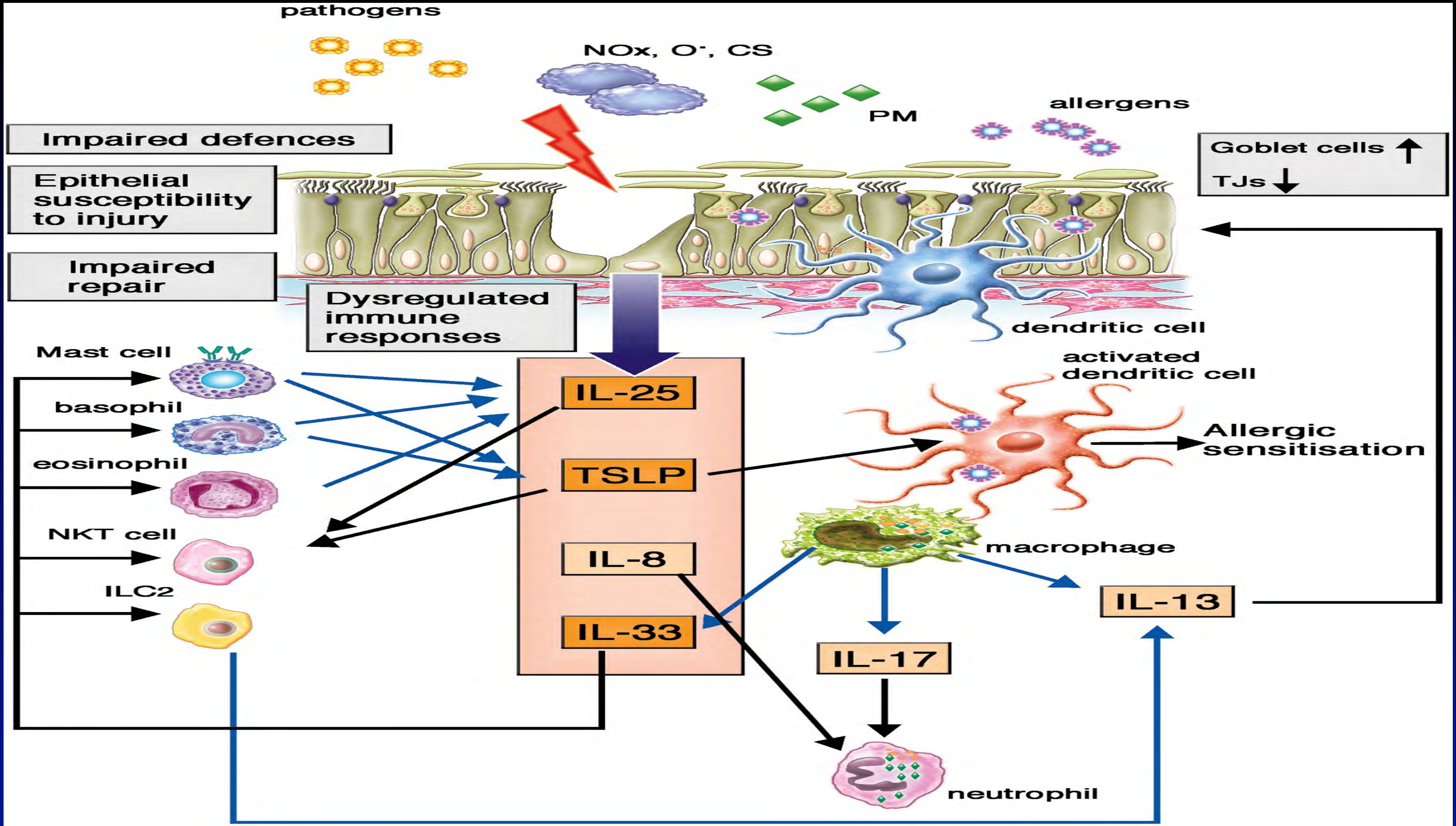
Histone modifications

A combination of different molecules can attach to the 'tails' of proteins called histones. These **alter** the activity of the DNA wrapped around them



MicroRNAs

Small non-coding RNAs that **block translation** of messenger RNAs into proteins

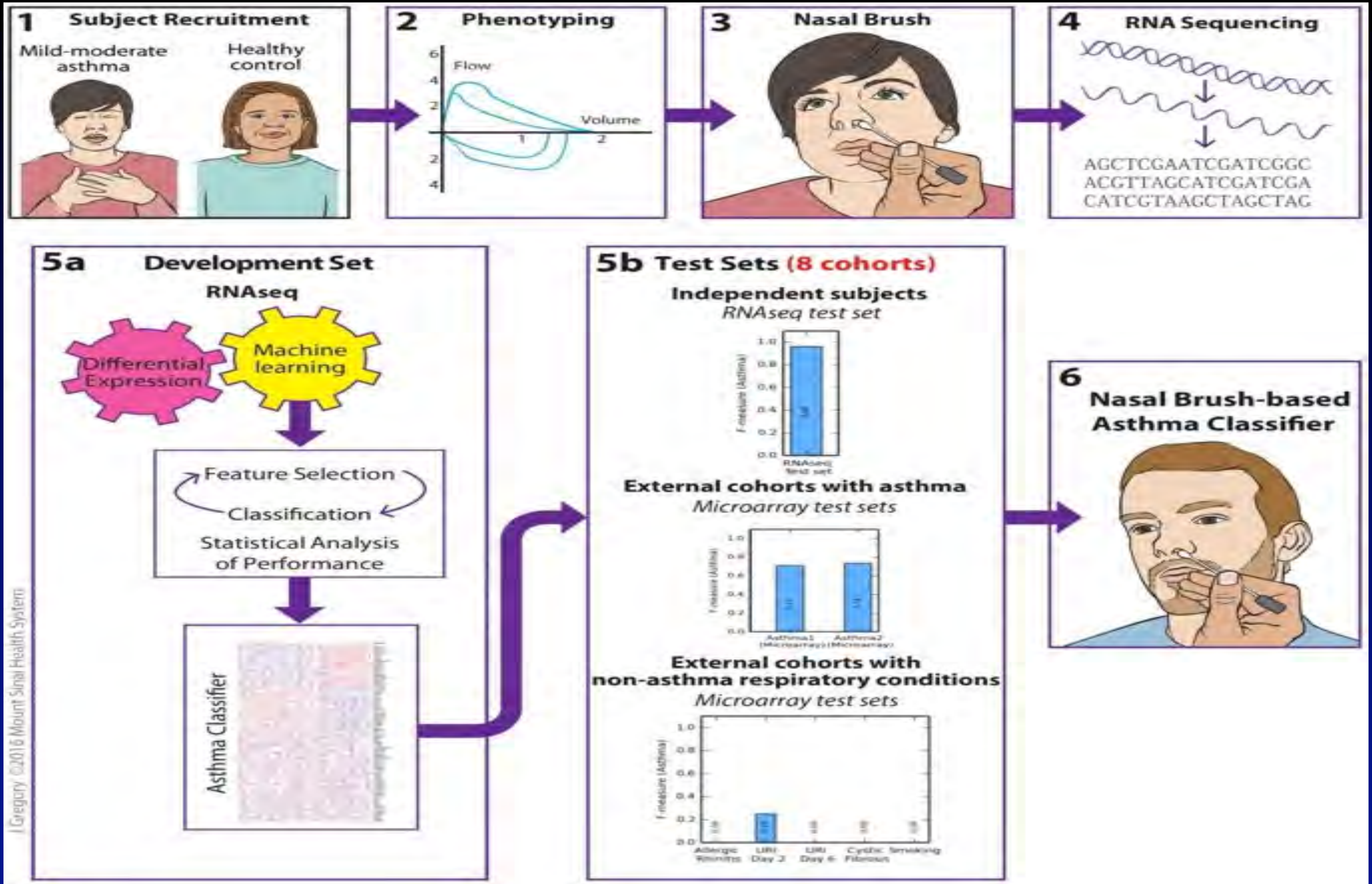


Journal of Allergy and Clinical Immunology 2017; 139, 1736-1751DOI: (10.1016/j.jaci.2017.04.005).

“Asthma genes” and the airway epithelium

- In mice, *ORMDL3* overexpression decreases serum sphingolipid levels and increases inflammation, airway remodeling, and BHR. Pulmonary epithelial expression of *ORMDL3* is sufficient for induction of Alternaria species–induced allergic airways disease
- *IL33*, *IL1RL1*, and *TSLP* have been linked to epithelial activation/damage and type 2 immunity
- *CDHR3* and *PCDH1* appear to play roles in adhesion

Journal of Allergy and Clinical Immunology 2017; 139, 1736-1751.



Pandey G et al. Sci Rep 2018 Jun 11;8(1):8826.

THE LANCET
Respiratory Medicine

DNA methylation in nasal epithelium, atopy, and atopic asthma in children: a genome-wide study

Erick Forno, MD * • Ting Wang, PhD * • Cancan Qi, MsC * • Qi Yan, PhD • Cheng-Jian Xu, PhD • Nadia Boutaoui, PhD • Yueh-Ying Han, PhD • Prof Daniel E Weeks, PhD • Yale Jiang • Franziska Rosser, MD • Judith M Vonk, PhD • Sharon Brouwer, BSc • Edna Acosta-Perez, PhD • Angel Colón-Semidey, MD • María Alvarez, MD • Prof Glorisa Canino, PhD • Prof Gerard H Koppelman, MD † • Wei Chen, PhD † • Prof Juan C Celedón, MD †

Epigenome-wide association study of atopic asthma in Puerto Rican children (n=273)

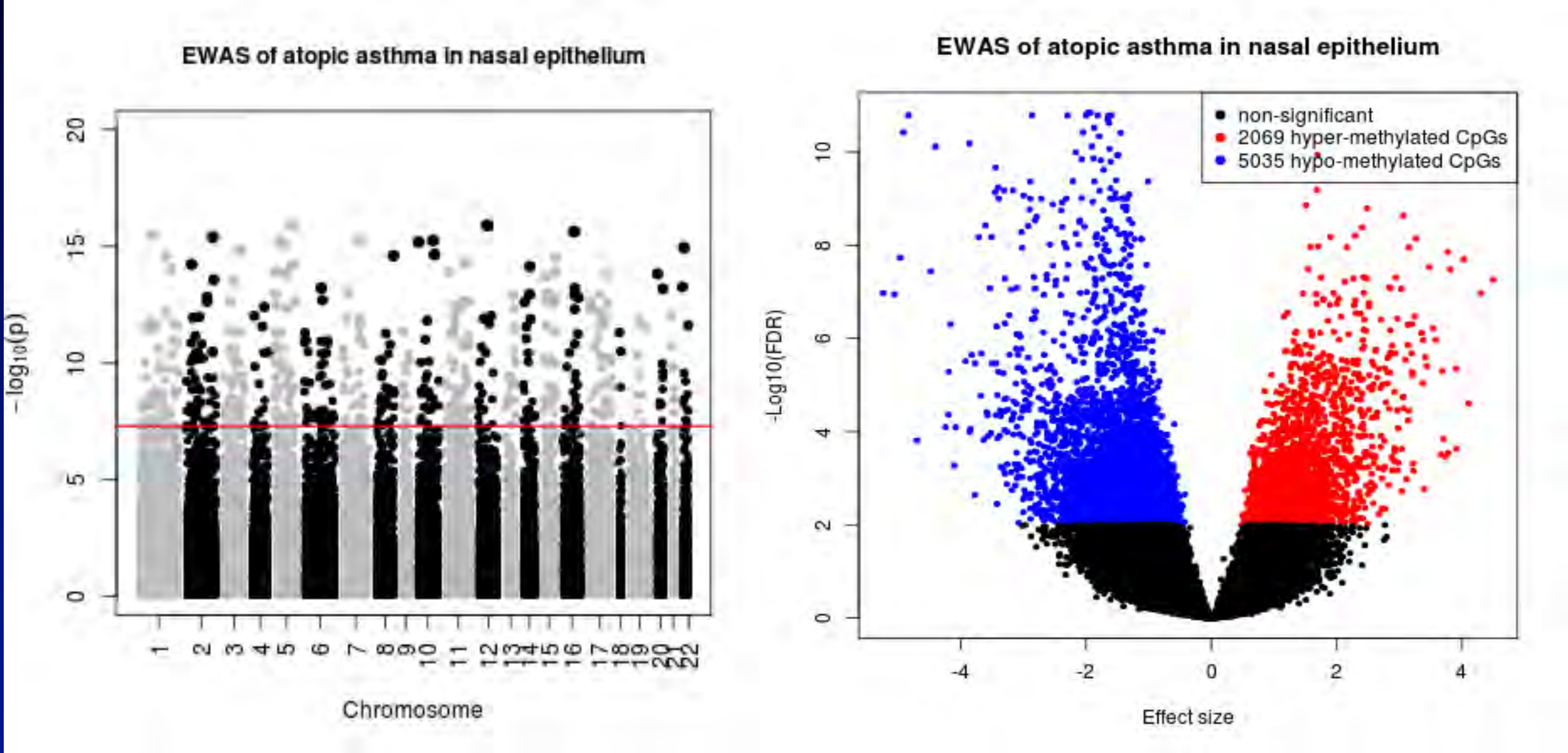


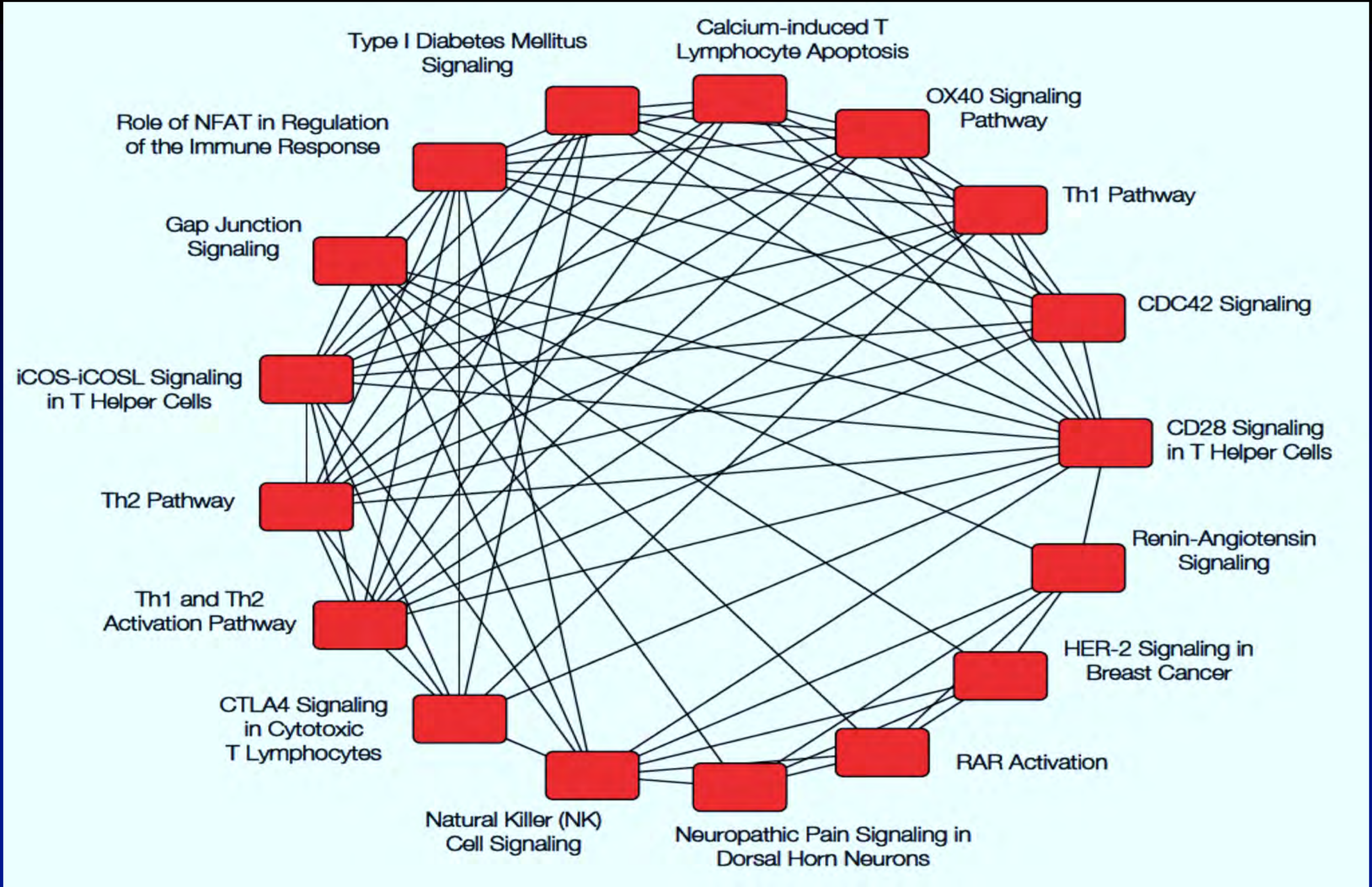
Table 1 –Characteristics of study participants in the discovery and replication cohorts

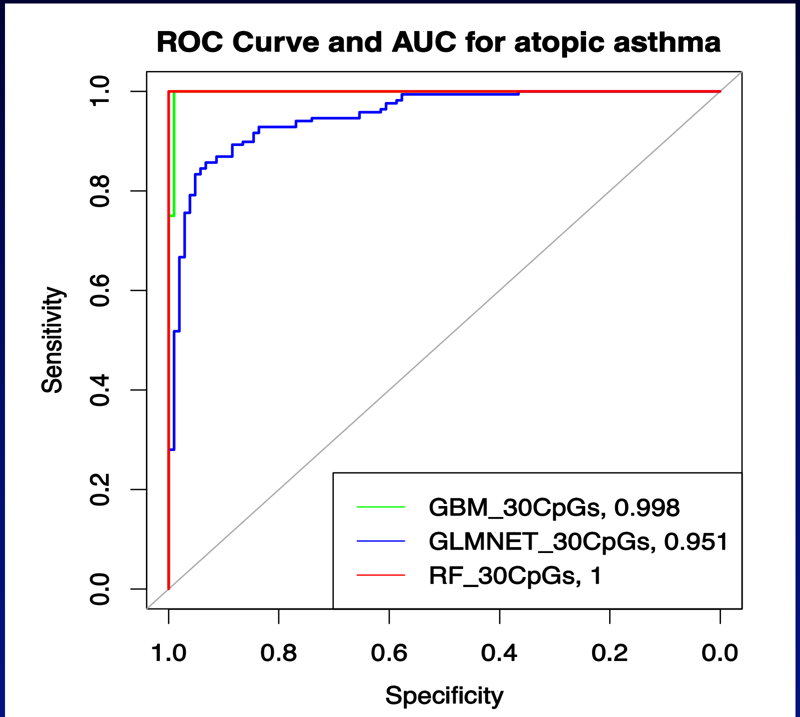
	Puerto Rico (discovery cohort)				Yang et al.		PIAMA	
	Atopy	No atopy	Atopic asthma	Non-atopic controls	Atopic asthma	Non-atopic controls	Atopy	No atopy
N (%)	312 (64·6%)	171 (35·4%)	169 (61·9%)	104 (38·1%)	36 (50%)	36 (50%)	207 (47·9%)	225 (52·1%)
Age (years)	15 (3)	15 (3)	15 (3)	16 (3)	11·1 (0·8)	10·9 (0·9)	16·4 (0·2)	16·3 (0·2)
Female sex, n (%)	140 (44·9%)	93 (54·4%)	66 (39·1%)*	61 (58·7%)	17 (47·2%)	19 (52·8%)	92 (44·4%)	127 (56·4%)
Race/ethnicity								
• Hispanic/Latino	100%				13·9%[a]		0%	
• African American	0				91·7%		0%	
• Non-Hispanic White	0				6·9%		97·1%	
• Other/missing	0				4·2%		2·9%	
Asthma, n (%)	169 (54·2%)*	67 (39·2%)	169 (100%)*	0 (0%)	36 (100%)*	0 (0%)	27 (13·0%)*	6 (2·7%)
Total IgE (IU/mL)	409 [207-816]*	43 [22-93]	386 [214-806]*	42 [21-78]	366 [185-785]	29 [16·5-49·5]	140 [55-140]	20 [10-55]
Number of positive allergen-specific IgEs+	2 [1-3]*	0	2 [1-3]*	0	n/a	0	2 [1-3]*	0

The Puerto Rico cohort (EVA-PR) is a case-control study of asthma. Yang et al. is a case-control study of atopic asthma. PIAMA is a birth cohort, unselected for either atopy or asthma. Numbers represent number of participants (%) for categorical variables and mean (SD) or median [interquartile range] for continuous variables. *P<0·05 for atopy vs. no atopy, or asthma vs. no asthma within each cohort. n/a: not available in public dataset. [a]Does not add up to 100% because participants could report more than one race/ethnicity.

Forno E et al. Lancet Respiratory Medicine 2019 Apr; 7(4):336-346.

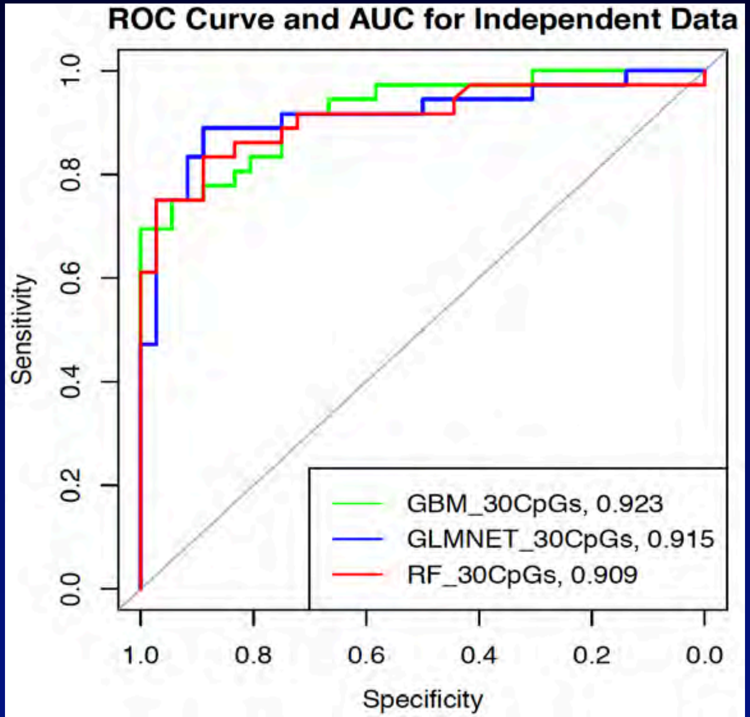
Methylation Δ (%)[a]	P-value	FDR P-value	Methylation Δ (%)[a]	P-value	Methylation Δ (%)[a]	P-value	Combined P-value[b]
-23·8%	$9{\cdot}59\times10^{-28}$	$2{\cdot}18\times10^{-22}$	-22·4%	$1{\cdot}15\times10^{-12}$	-7·4%	$6{\cdot}01\times10^{-18}$	$1{\cdot}05\times10^{-47}$
-16·0%	$9{\cdot}56\times10^{-26}$	$8{\cdot}53\times10^{-21}$	-15·4%	$3{\cdot}61\times10^{-10}$	-4·4%	$2{\cdot}72\times10^{-14}$	$4{\cdot}20\times10^{-40}$
-10·3%	$1{\cdot}62\times10^{-25}$	$8{\cdot}53\times10^{-21}$	-8·0%	$1{\cdot}21\times10^{-07}$	-3·8%	$1{\cdot}21\times10^{-13}$	$5{\cdot}39\times10^{-37}$
-15·8%	$1{\cdot}63\times10^{-25}$	$8{\cdot}53\times10^{-21}$	-12·7%	$2{\cdot}97\times10^{-07}$	-8·1%	$2{\cdot}16\times10^{-09}$	$1{\cdot}85\times10^{-32}$
-19·2%	$2{\cdot}33\times10^{-25}$	$8{\cdot}53\times10^{-21}$	-23·3%	$3{\cdot}77\times10^{-10}$	-6·9%	$9{\cdot}23\times10^{-12}$	$1{\cdot}32\times10^{-37}$
-18·3%	$2{\cdot}74\times10^{-25}$	$8{\cdot}53\times10^{-21}$	-20·4%	$1{\cdot}40\times10^{-09}$	-5·2%	$4{\cdot}52\times10^{-07}$	$1{\cdot}82\times10^{-32}$
-23·1%	$2{\cdot}78\times10^{-25}$	$8{\cdot}53\times10^{-21}$	-23·6%	$2{\cdot}68\times10^{-13}$	-7·6%	$2{\cdot}23\times10^{-14}$	$2{\cdot}95\times10^{-43}$
-27·1%	$3{\cdot}00\times10^{-25}$	$8{\cdot}53\times10^{-21}$	-20·8%	$1{\cdot}41\times10^{-08}$	-11·7%	$2{\cdot}37\times10^{-11}$	$1{\cdot}15\times10^{-35}$
-18·8%	$3{\cdot}41\times10^{-25}$	$8{\cdot}63\times10^{-21}$	-16·0%	$4{\cdot}80\times10^{-11}$	-5·3%	$4{\cdot}62\times10^{-17}$	$1{\cdot}13\times10^{-43}$
-24·1%	$5{\cdot}41\times10^{-24}$	$1{\cdot}23\times10^{-19}$	-25·9%	$8{\cdot}61\times10^{-11}$	-5·8%	$4{\cdot}44\times10^{-07}$	$1{\cdot}59\times10^{-32}$
-22·6%	$1{\cdot}06\times10^{-23}$	$2{\cdot}20\times10^{-19}$	-21·2%	$4{\cdot}65\times10^{-08}$	-5·9%	$1{\cdot}04\times10^{-10}$	$3{\cdot}74\times10^{-33}$
-15·4%	$3{\cdot}12\times10^{-23}$	$5{\cdot}93\times10^{-19}$	-9·0%	$3{\cdot}08\times10^{-06}$	-6·0%	$2{\cdot}87\times10^{-09}$	$1{\cdot}49\times10^{-29}$
-19·0%	$3{\cdot}84\times10^{-23}$	$6{\cdot}73\times10^{-19}$	-14·4%	$4{\cdot}29\times10^{-05}$	-7·2%	$3{\cdot}51\times10^{-04}$	$1{\cdot}88\times10^{-23}$
-12·3%	$4{\cdot}75\times10^{-23}$	$7{\cdot}72\times10^{-19}$	-7·1%	$5{\cdot}65\times10^{-04}$	-4·6%	$1{\cdot}14\times10^{-09}$	$1{\cdot}25\times10^{-27}$
-15·0%	$1{\cdot}58\times10^{-22}$	$2{\cdot}40\times10^{-18}$	-6·5%	$1{\cdot}48\times10^{-04}$	-2·4%	$2{\cdot}25\times10^{-04}$	$1{\cdot}38\times10^{-22}$
-15·9%	$1{\cdot}81\times10^{-22}$	$2{\cdot}58\times10^{-18}$	-16·3%	$1{\cdot}91\times10^{-10}$	-4·2%	$1{\cdot}74\times10^{-09}$	$3{\cdot}03\times10^{-33}$
-11·3%	$2{\cdot}40\times10^{-22}$	$3{\cdot}21\times10^{-18}$	-7·6%	$2{\cdot}52\times10^{-04}$	-2·6%	$2{\cdot}91\times10^{-07}$	$4{\cdot}92\times10^{-25}$
-16·9%	$2{\cdot}91\times10^{-22}$	$3{\cdot}68\times10^{-18}$	-15·2%	$2{\cdot}76\times10^{-07}$	-4·2%	$3{\cdot}20\times10^{-11}$	$1{\cdot}05\times10^{-31}$
-8·0%	$3{\cdot}19\times10^{-22}$	$3{\cdot}83\times10^{-18}$	-12·0%	$4{\cdot}30\times10^{-08}$	-1·6%	0·036	$1{\cdot}12\times10^{-23}$
-13·8%	$3{\cdot}65\times10^{-22}$	$4{\cdot}16\times10^{-18}$	-9·1%	$6{\cdot}30\times10^{-07}$	-5·6%	$9{\cdot}20\times10^{-07}$	$5{\cdot}77\times10^{-27}$


Type I Diabetes Mellitus Signaling
Calcium-induced T Lymphocyte Apoptosis
OX40 Signaling Pathway
Role of NFAT in Regulation of the Immune Response
Th1 Pathway
Gap Junction Signaling
CDC42 Signaling
iCOS-iCOSL Signaling in T Helper Cells
CD28 Signaling in T Helper Cells
Th2 Pathway
Renin-Angiotensin Signaling
Th1 and Th2 Activation Pathway
HER-2 Signaling in Breast Cancer
CTLA4 Signaling in Cytotoxic T Lymphocytes
RAR Activation
Natural Killer (NK) Cell Signaling
Neuropathic Pain Signaling in Dorsal Horn Neurons



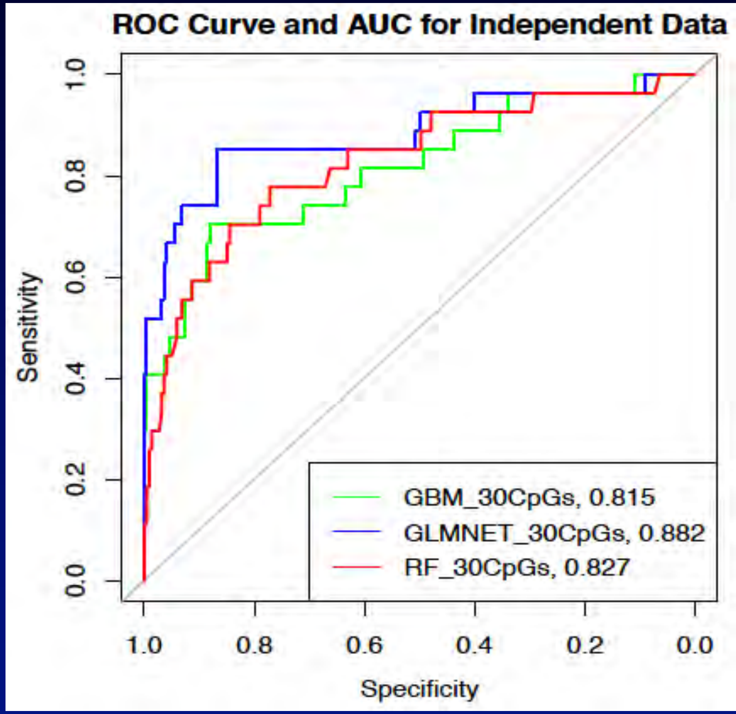
Accuracy = 88%

Yang et al.



Accuracy = 82%

PIAMA



Accuracy = 87%

The Nasal Methylome and Atopic Asthma

- 28 of the 30 top findings in Puerto Ricans were replicated in two cohorts of African American and Dutch children
- Most of the methylation signals affected gene expression (resulting in either down-regulation or up-regulation)
- The top CpG (methylation) sites were located in genes regulating airway epithelial barrier and function (i.e. *CDHR3* and *CDH26)* and immune responses
- The set of predictive markers of asthma in Puerto Ricans performed well in both African American children (Yang et al) and in Dutch children in the PIAMA Study

Forno E et al. Lancet Respiratory Medicine 2019 Apr; 7(4):336-346.

3. Psychosocial stress and exposure to violence

ADCYAP1R1 and Asthma in Puerto Rican Children

Wei Chen[1], Nadia Boutaoui[1], John M. Brehm[1], Yueh-Ying Han[1], Cassandra Schmitz[1], Alex Cressley[1], Edna Acosta-Pérez[2], María Alvarez[2], Angel Colón-Semidey[2], Andrea A. Baccarelli[3], Daniel E. Weeks[4], Jay K. Kolls[5], Glorisa Canino[2], and Juan C. Celedón[1]

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Psychosocial Stress and Asthma in Puerto Rican Children

- Puerto Ricans are often exposed to high levels of stress and violence
  - -Martinez-Taboas A et al. J Trauma Stress 2006; 19:439-48.
  - -Vermeiren R et al. Pediatrics 2003; 111:535-40.
- Childhood abuse and parental psychosocial stress are associated with asthma morbidity in PR children
  - Cohen R et al. Am J Respir Crit Care Med 2008;178(5):453-9.
  - Lange N et al. J Allergy Clin Immunol 2011; 127(3):734-40.
- Unclear mechanisms

ADCYAP1R1 and Asthma in Puerto Rican Children

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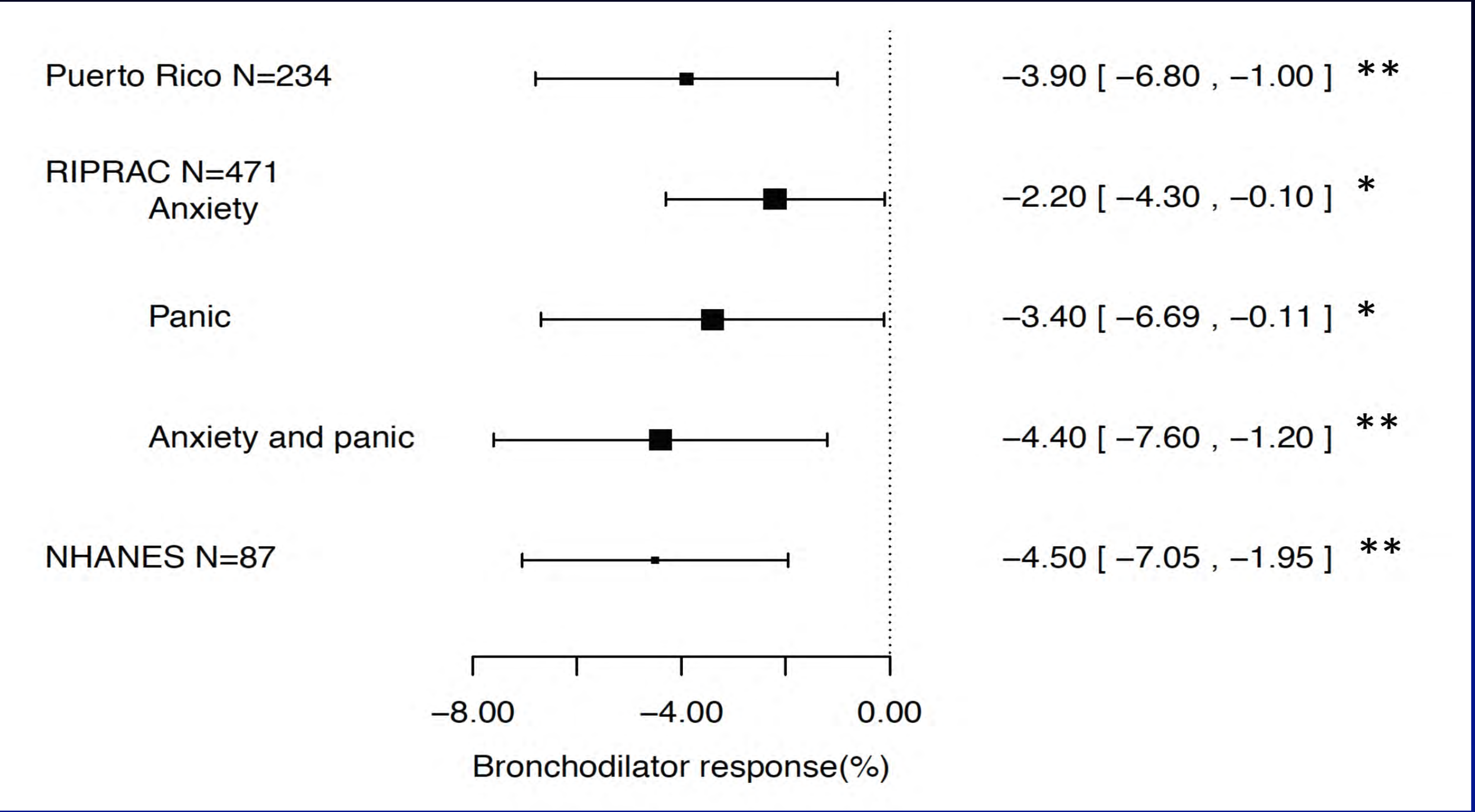
- Genetic and epigenetic variation in *ADCYAP1R1* is associated with childhood asthma in Puerto Ricans
- This is the first study to provide a potential genetic/epigenetic mechanism for an association between psychosocial stress and childhood asthma
- Longitudinal studies are needed in Puerto Ricans and other populations often exposed to stress and violence

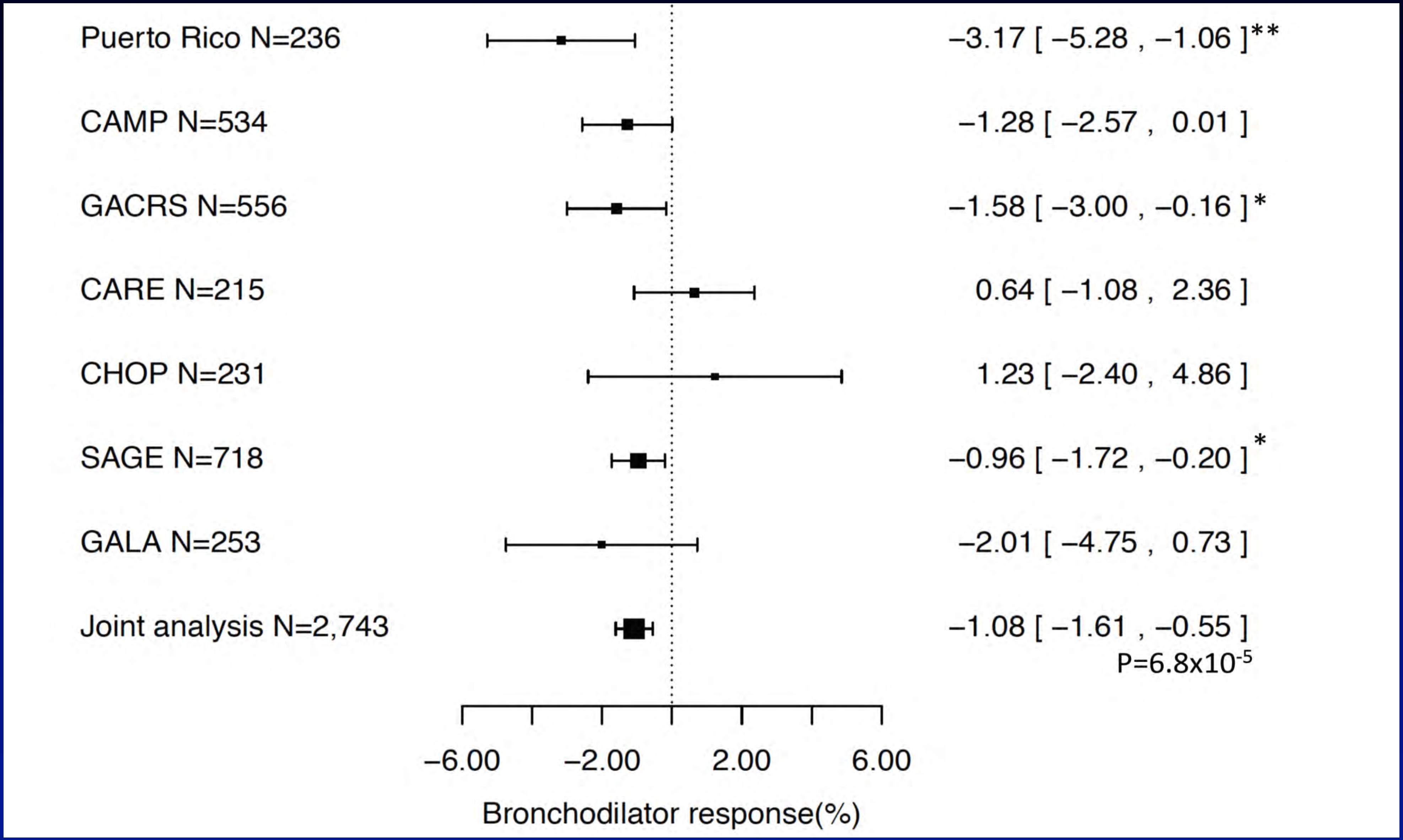
Stress and bronchodilator response

- Puerto Ricans have lower response to short-acting bronchodilators (BDR) than members of other ethnic groups
  - This has been partly attributed to ethnic-specific variation in the frequency of SNPs in *ADRB2*
- Chronic stress (alone or accompanied by acute stress) has been associated with reduced expression of *ADRB2* in leukocytes of subjects with asthma
  - Miller GE, Chen E. *Proc Natl Acad Sci U S A* 2006;103:5496-5501.
- We hypothesized that stress causes reduced BDR in Puerto Rican children

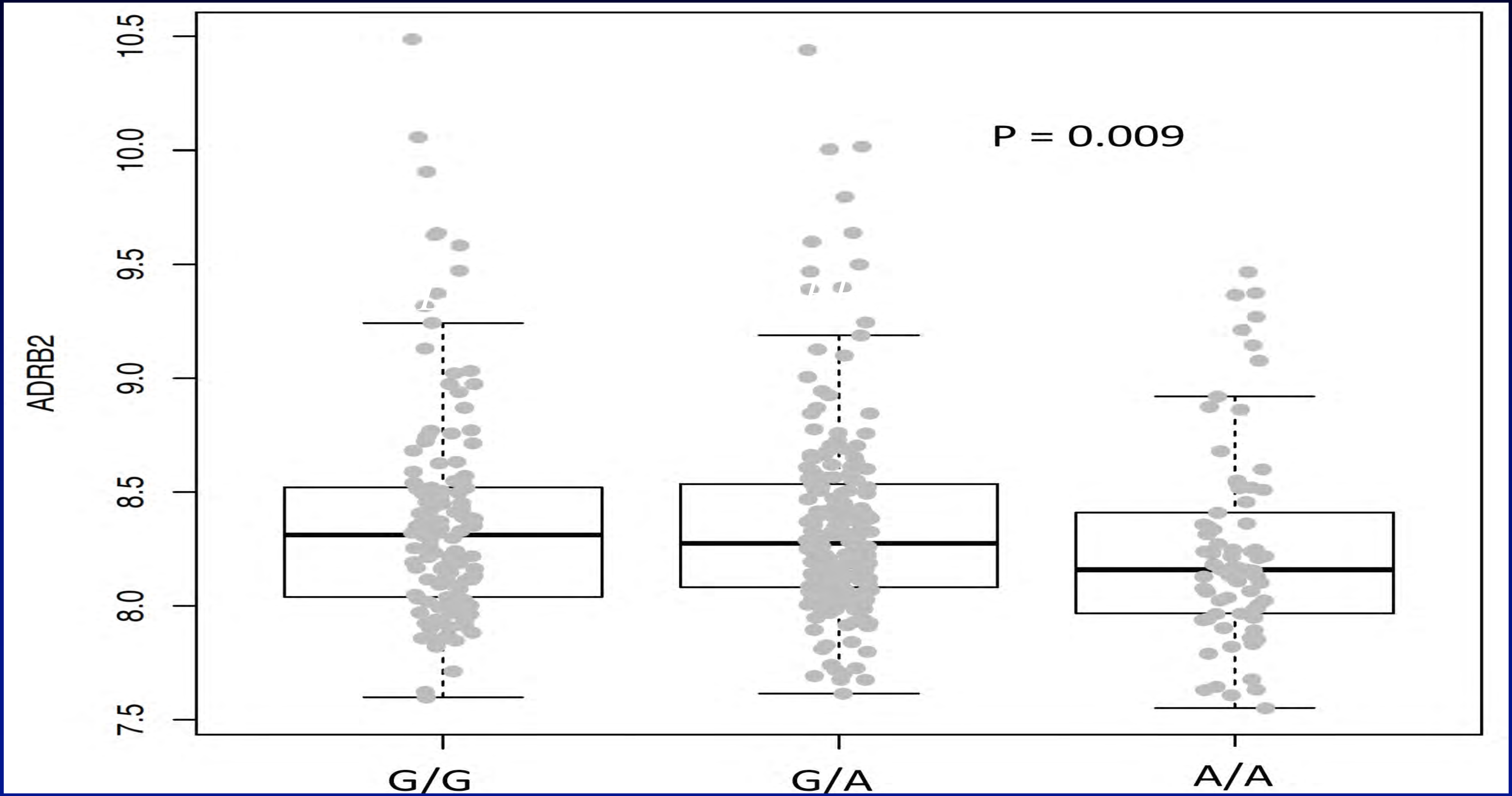
Stress and bronchodilator response

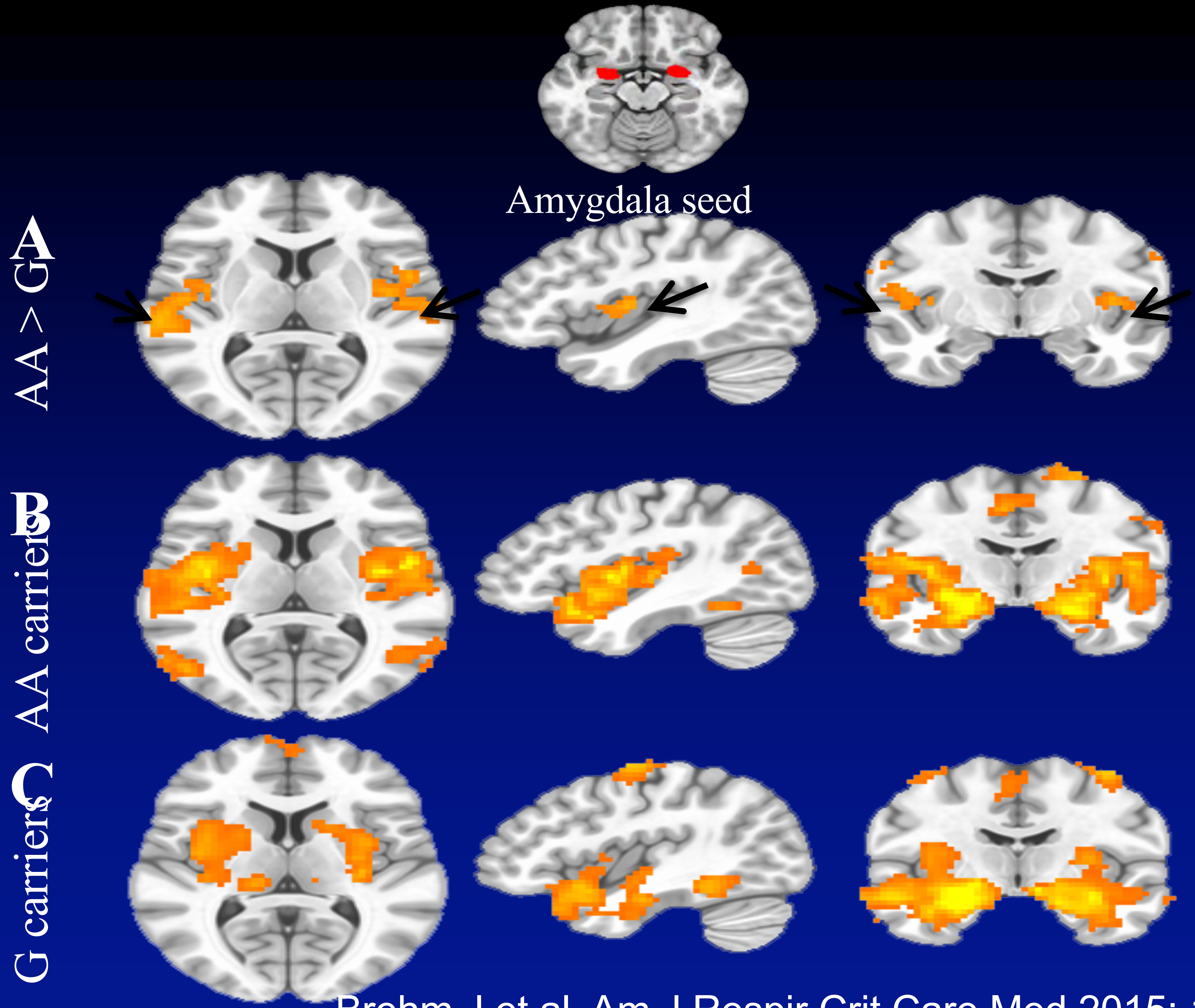


ADCYAP1R1 and BDR



ADCYAP1R1 and *ADRB2* expression





Brehm J et al. Am J Respir Crit Care Med 2015; 192:47-56.

ADCYAP1R1 and BDR

- Both stress and an *ADCYAP1R1* SNP are associated with reduced BDR in children with or at risk for asthma
  - This SNP is also associated with reduced expression of *ADRB2* in CD4+ T lymphocytes of subjects with asthma
- Our findings are consistent with a negative effect of SNP rs34548976 on BDR through neuro-hormonal mechanisms (e.g persistently high catecholamine levels) leading to down-regulation of *ADRB2* in highly stressed children
- Our results provide potential mechanisms for stress-induced morbidity in other cardiopulmonary diseases

Brehm J et al. Am J Respir Crit Care Med 2015; 192(1):47-56.

PTSD and incident asthma in WTC rescue and recovery workers

- PTSD has been linked to asthma in cross-sectional studies
- We examined the relation between probable PTSD at baseline and incident (new onset) asthma at follow up (~4.5 years later) in a cohort of 3,757 WTC rescue/recovery workers who had never smoked and had never been diagnosed with asthma

PTSD Symptoms and Incident Asthma among WTC Rescue/Recovery Workers

Variable	**Never smokers, never diagnosed with asthma (at baseline) (n=3,757)**	
Odds Ratio, 95% confidence interval, P value		
Probable PTSD (PTSD CL >=44 points)	**Unadjusted**	
No	1.0	1.0
Yes	2.64 (2.07 to 3.37), <0.001	2.41 (1.85. to 3.13), <0.001
Model adjusted for age, gender, race/ethnicity, WTC occupational exposure, educational level, body mass index, weight gain from baseline, and bronchodilator response at baseline		

De la Hoz R, Jeon Y, Wisnivesky J, Celedón JC. Am J Respir Crit Care Med 2016 Dec 1;194(11):1383-1391.

PTSD and incident asthma in WTC workers

- In a cohort of adult workers exposed to a severe traumatic event (9/11), probable PTSD is significantly associated with BDR at baseline, as well as with incident asthma
- Our findings support a growing body of evidence implicating psychosocial stress in the pathogenesis of asthma and morbidity from asthma

De la Hoz R, Jeon Y, Wisnivesky J, Celedón JC. Am J Respir Crit Care Med 2016 Dec 1;194(11):1383-1391.

Multivariable analysis of severity of victimization and current asthma, by gender, among 24,612 high school students in the U.S.

	All participants	Male	Female
Severity of victimization	**Odds ratio, 95% confidence interval**		
Any victimization	1.43 (1.29, 1.58)*	1.40 (1.23, 1.60)*	1.44 (1.24, 1.68)*
None	1.0	1.0	1.0
One type	1.27 (1.12, 1.44)*	1.27 (1.08, 1.48)*	1.26 (1.07, 1.51)*
Two types	1.68 (1.40, 2.02)*	1.63 (1.28, 2.08)*	1.70 (1.26, 2.31)*
More than three types	2.44 (1.94, 3.07)*	2.20 (1.60, 3.03)*	2.85 (1.89, 4.29)*

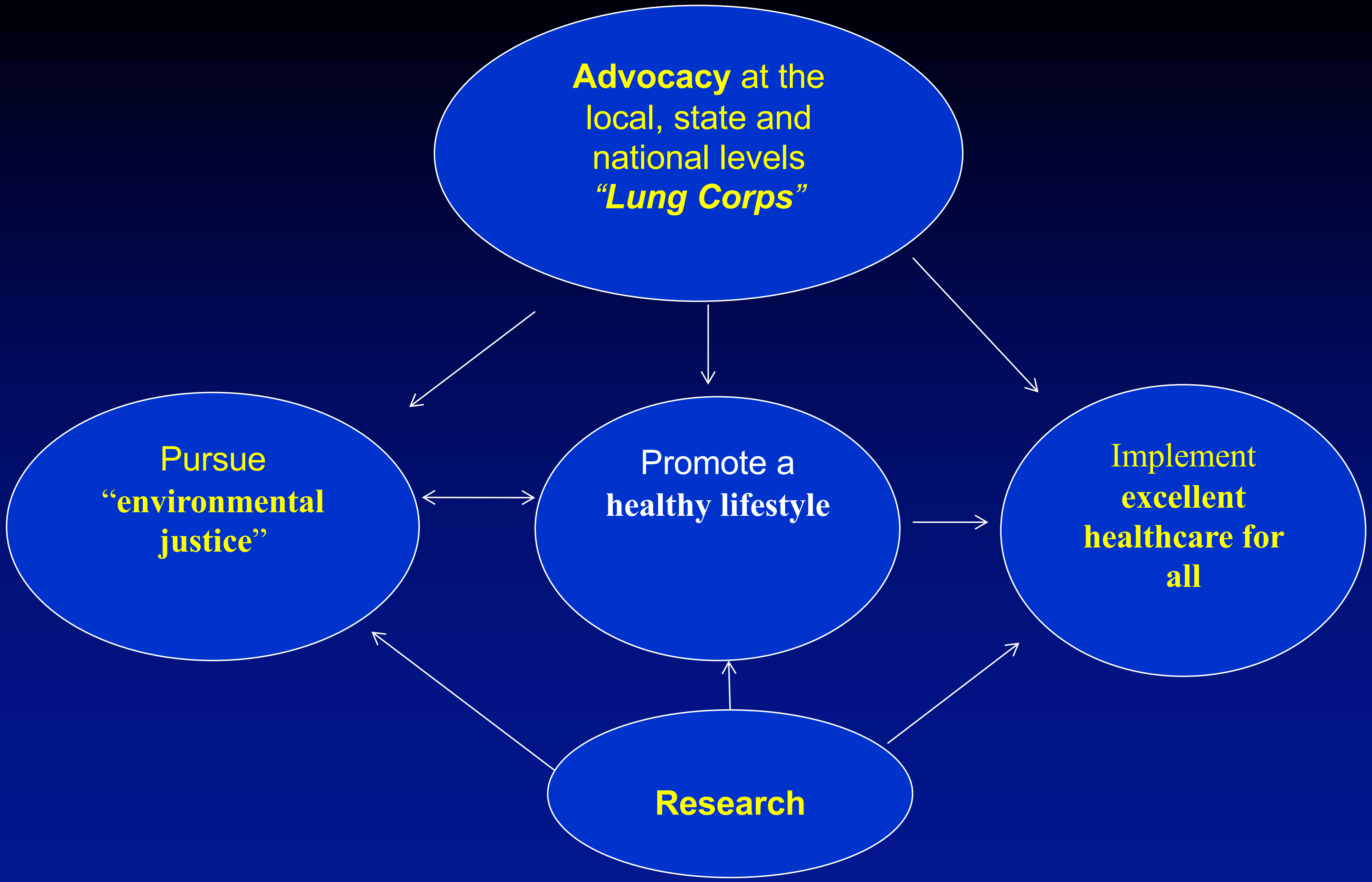
Five types of victimization included are: feared to attend school in the past month, threatened or injured by a weapon at school in the past year, physically abused by dating partner in the past year, ever coerced into sex, and ever bullied at school. *P <0.01

Models included age, sex (all participants), race/ethnicity, BMI, average hour of sleep, consumption of fruit or vegetable, and soda/pop, smoking, and used marijuana or illegal drugs.

Han Y et al. Pediatric Pulmonology 2019 January 6 [Epub ahead of print].

Future directions

- Study of exposure to violence or chronic stress, nasal epigenomics, and asthma and treatment response in Puerto Rican children
- Study of nasal transcriptomics and asthma and treatment response in Puerto Rican children
- Birth cohort study of prenatal stress, epigenetics and childhood asthma
- Study of nasal epigenomics and transcriptomics and asthma morbidity among adults in HCHS/SOL
- Clinical trials of stress reduction, depression treatment, and weight loss on asthma morbidity



Celedón JC et al. Annals Am Thorac Soc 2014; 11(4):473-9.

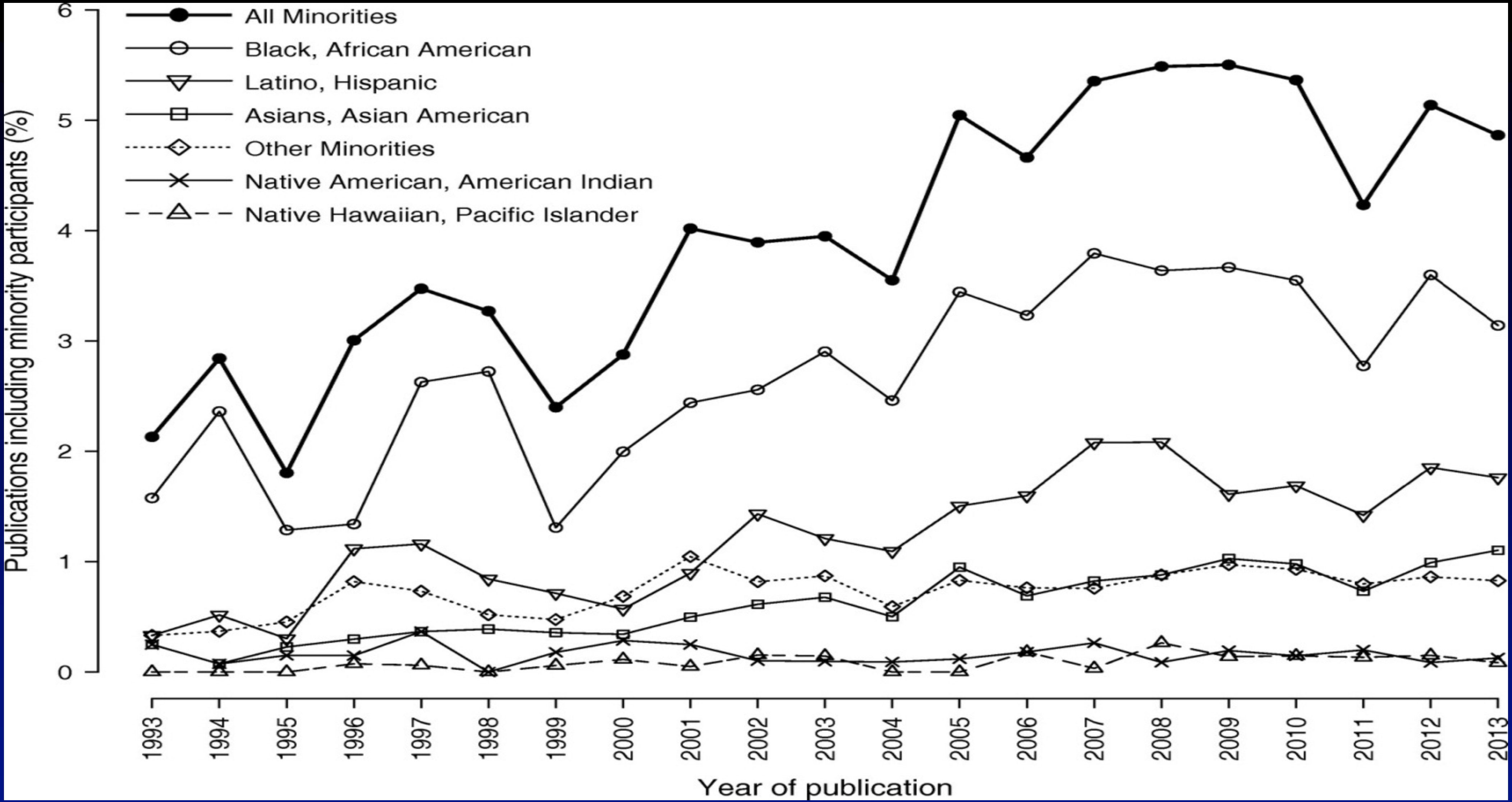
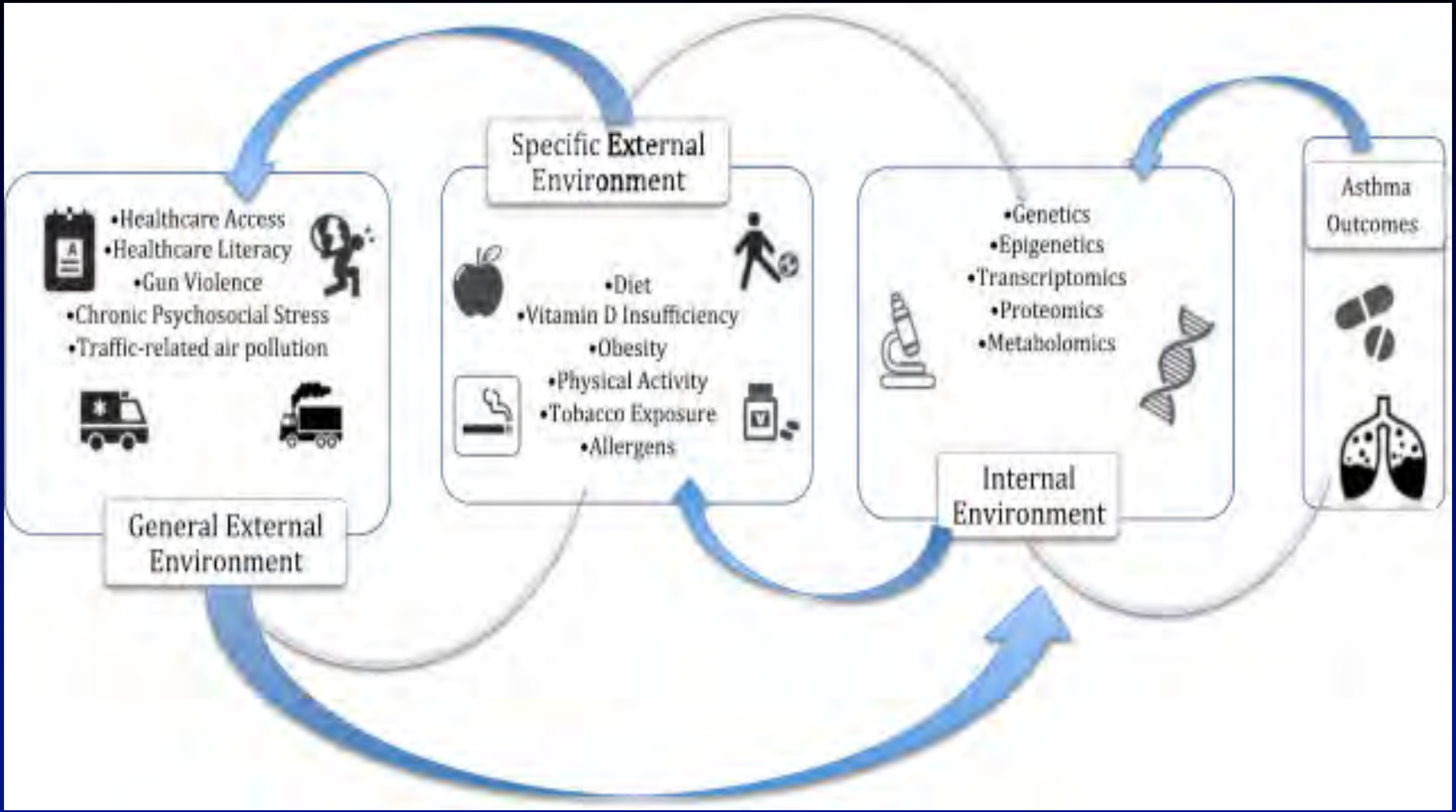


Figure 2. Race-/ethnicity-specific proportions reported for NIH–funded pulmonary publications in PubMed, 1993–2013.

Published in: Esteban G. Burchard; Sam Oh; Marilyn Foreman; Juan C. Celedón. *Am J Respir Crit Care Med* 191, 514-521.



Szentpetery S,…, Celedón JC. J Allergy Clin Immunol 2016; 138:1556-1558.

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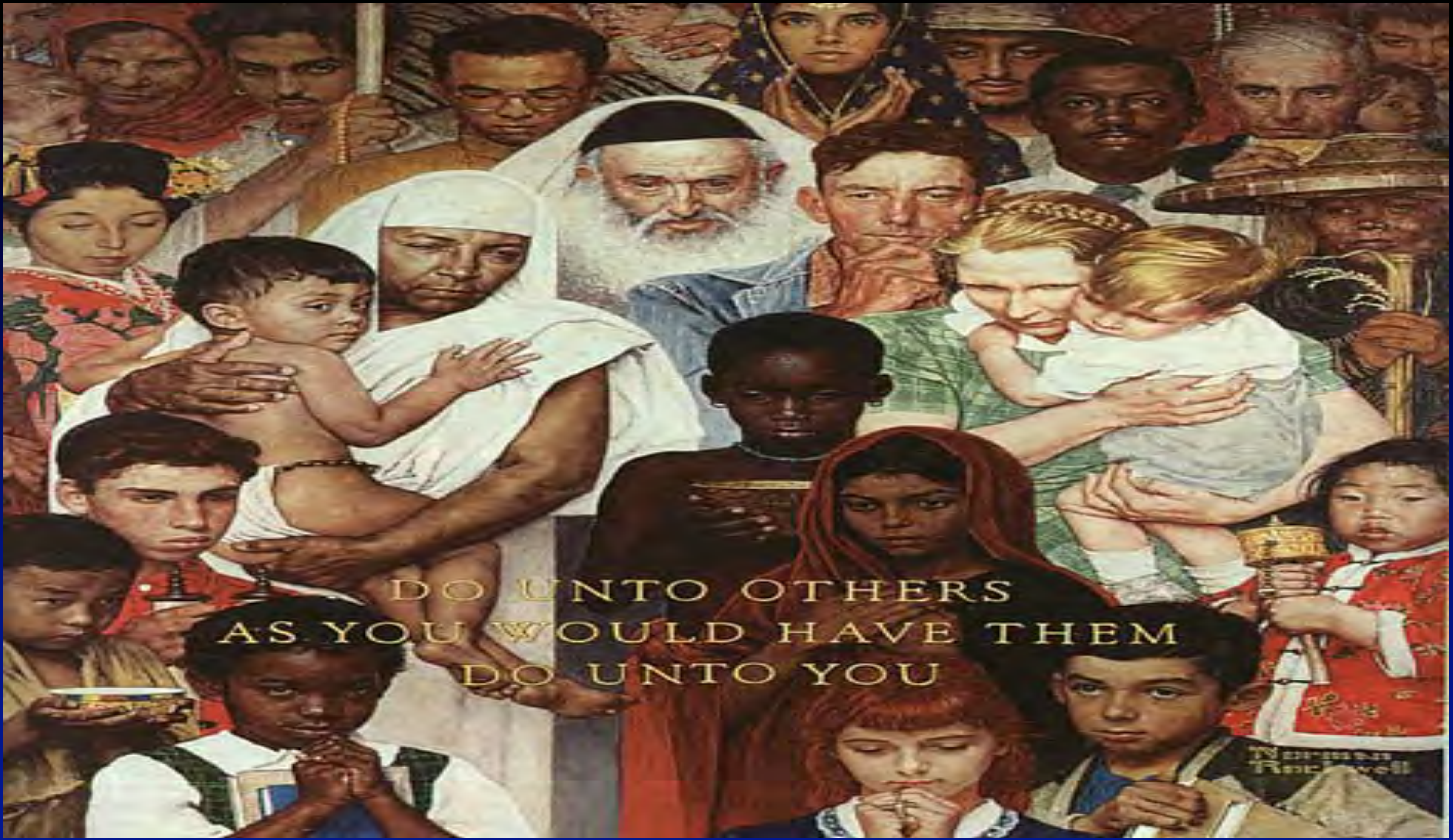
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