

Genetics of Asthma in Latino Americans

Pedro C. Avila, MD
Northwestern University
Chicago, IL

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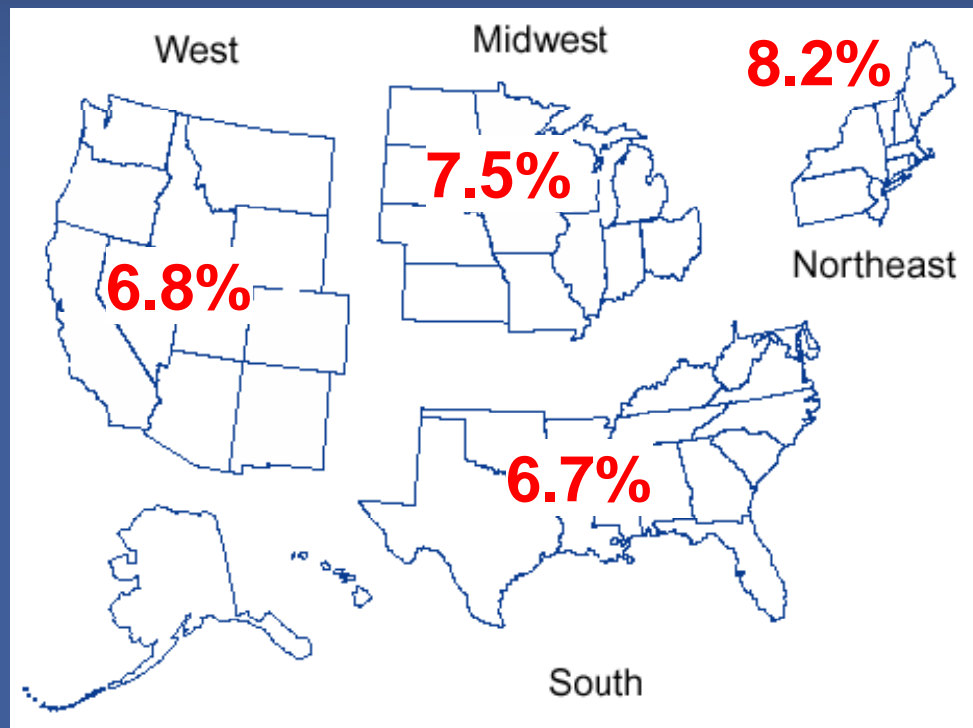
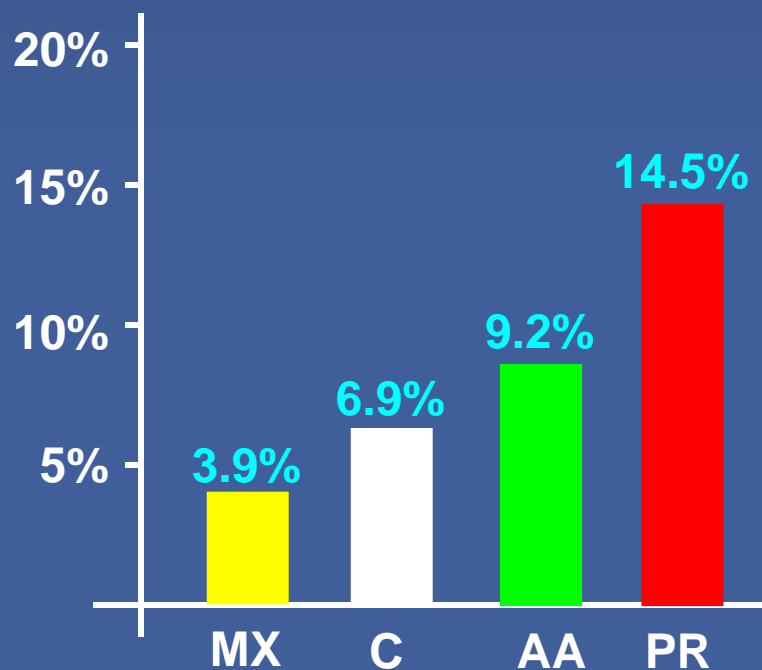
Disclosure of Conflict of Interest Information

I have the following relationships that exist related to this presentation:

Grants: NIH, GSK, Genentech

Membership: ACP, AAP, AAAAI, ACAAI, ATS, ISAAI

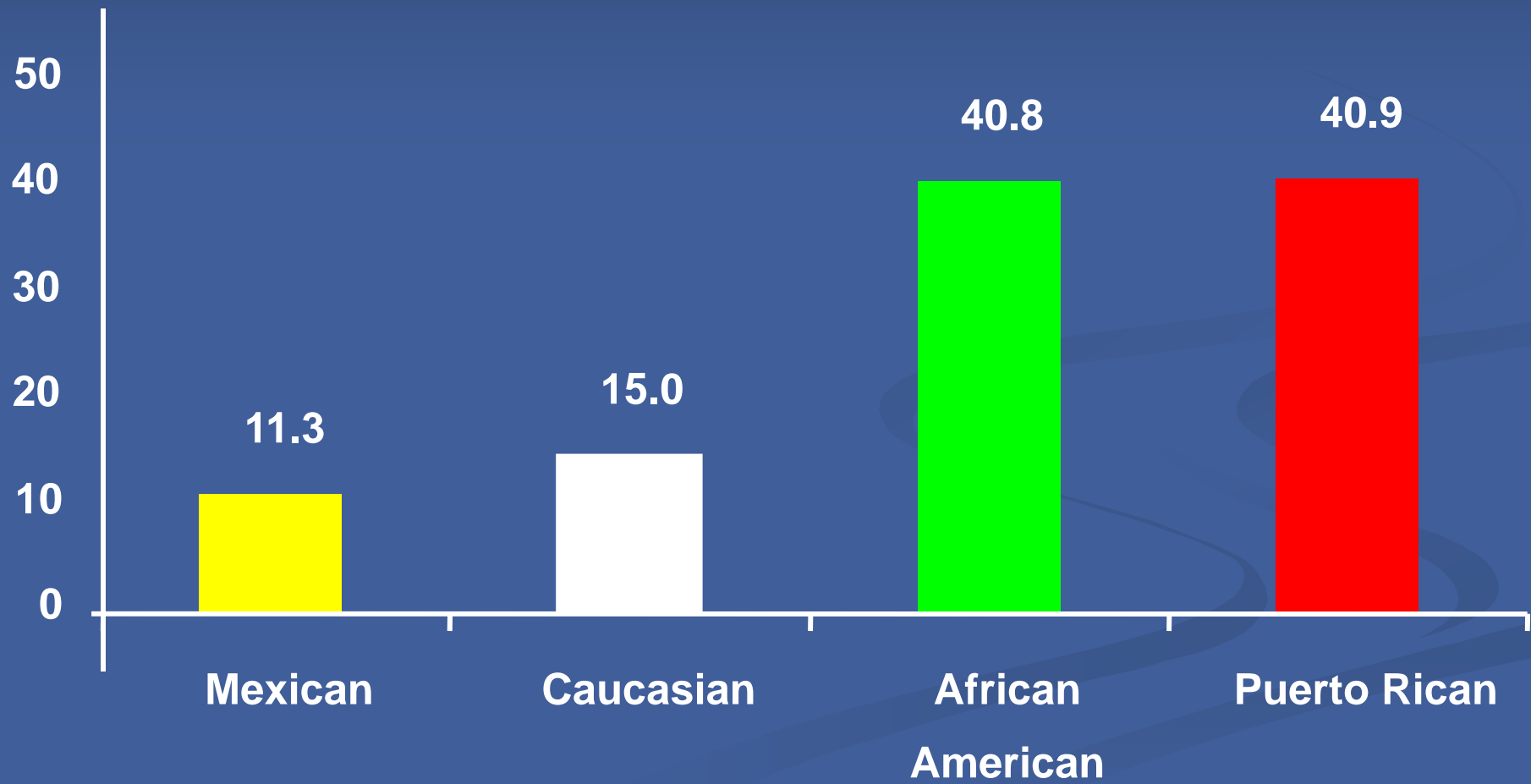
Annual Prevalence of Asthma 2001-03



Moorman JE et al. MMWR 2007; 56(SS08)

U.S. Asthma Mortality 1990-1995

Average Annual Rates per Million



Homa et al. 2000

Asthma

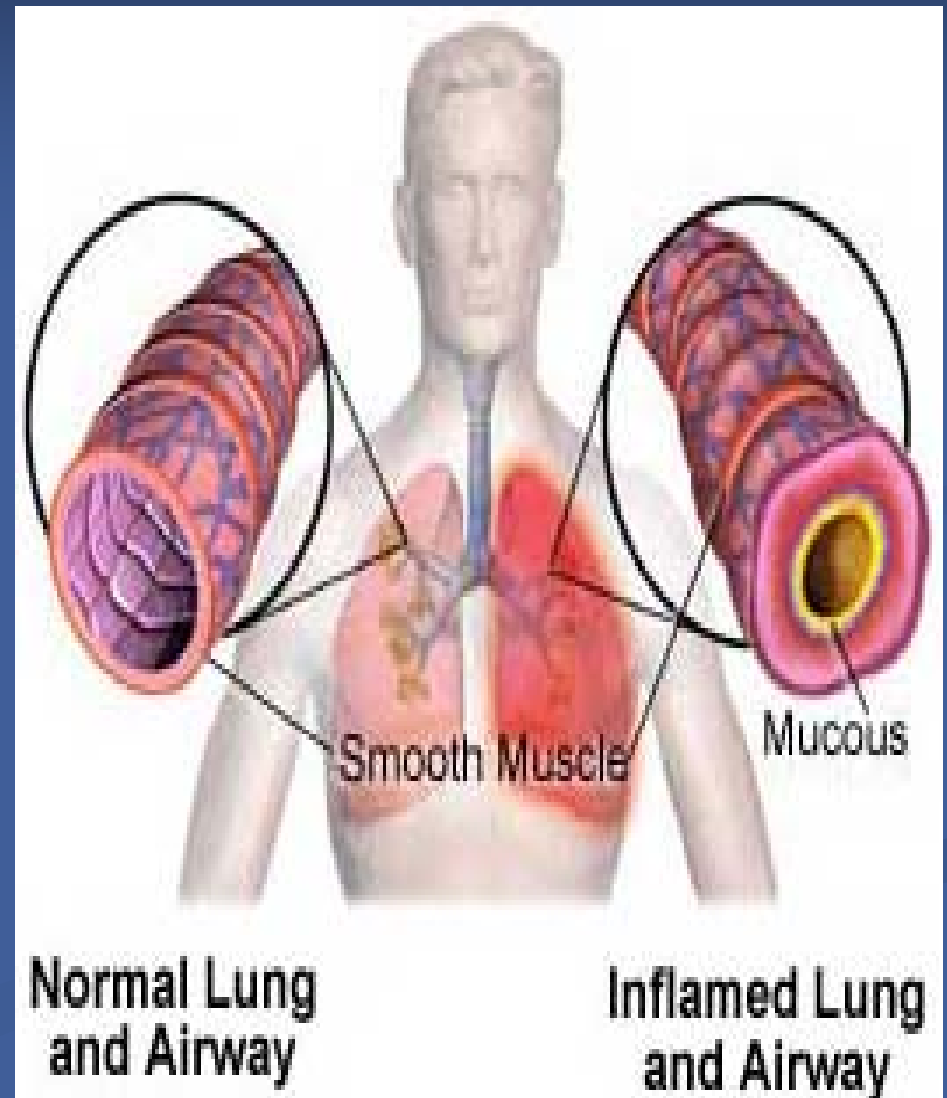
Chronic Inflammation

Reversible airway obstruction

Genetic component (36-79%)

20 million asthmatics in U.S.

Gao et al 2004; NCEH, 1999



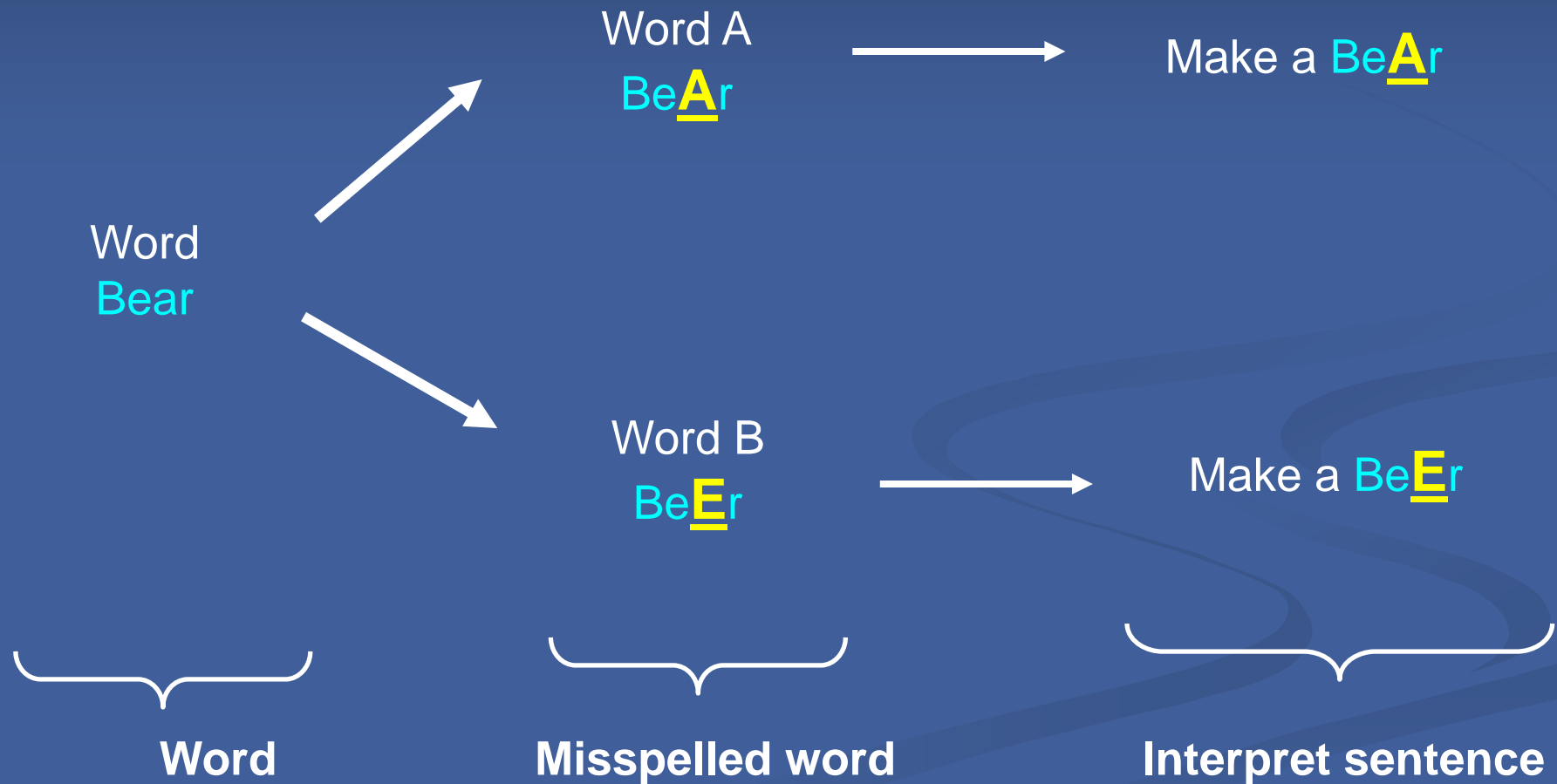
Instructions for English and Biology

English

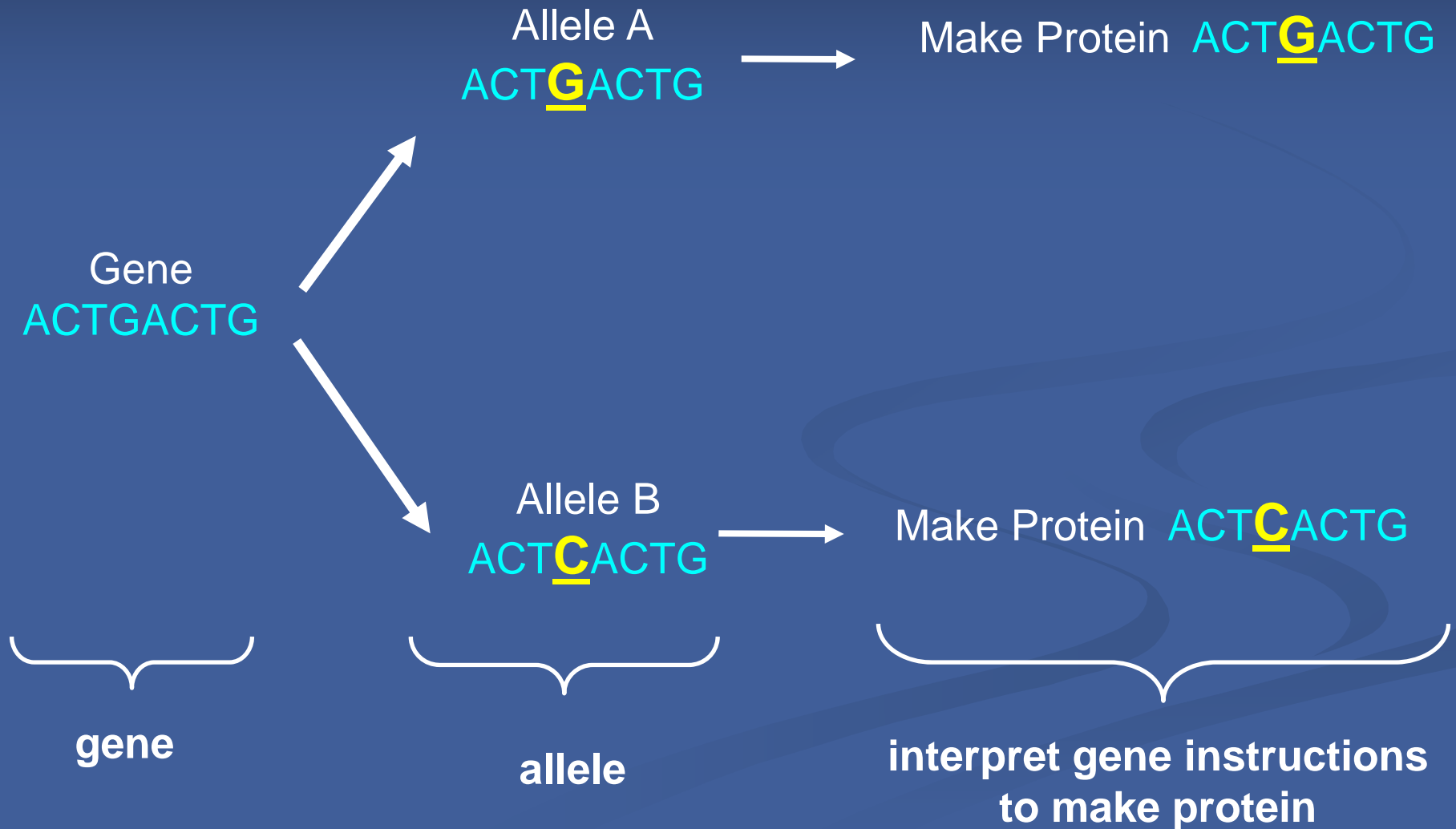
Genetics

- Letter → Base pair
- Word → Gene
- Sentence → Haplotype
- Paragraph → Linkage Disequilibrium
- Chapter → Chromosome

Genetic Variation



Genetic Variation



Genetics of Asthma in Latino Americans

Aim: To determine the genetic factors that can explain why asthma is more severe in Puerto Ricans than in Mexicans.

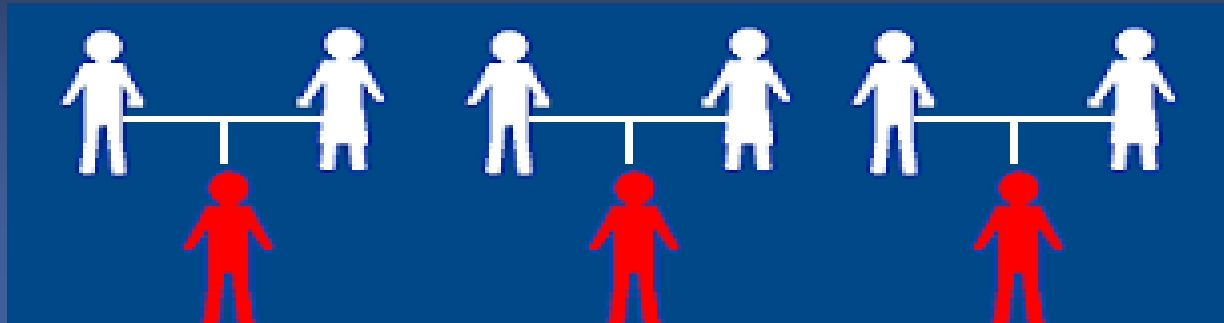
Recruitment:

- Trios: Proband with asthma and both biological parents.
- N = 300 per group
- Transmission Disequilibrium Test (TDT) analysis
- Sites: MX: San Francisco, Mexico City
PR: New York, Puerto Rico
- Period: 1998-2001
- Funding: NIH

Study Visit:

- Questionnaire
- Spirometry and bronchodilator response
- Blood draw (DNA, IgE)

GALA Study



Puerto Ricans

385

Mexicans

301

Combined

686 *

* ~ 2052 individuals

Family-based Analysis

Genetics of Asthma in Latino Americans

TABLE 2. PULMONARY FUNCTION TEST RESULTS

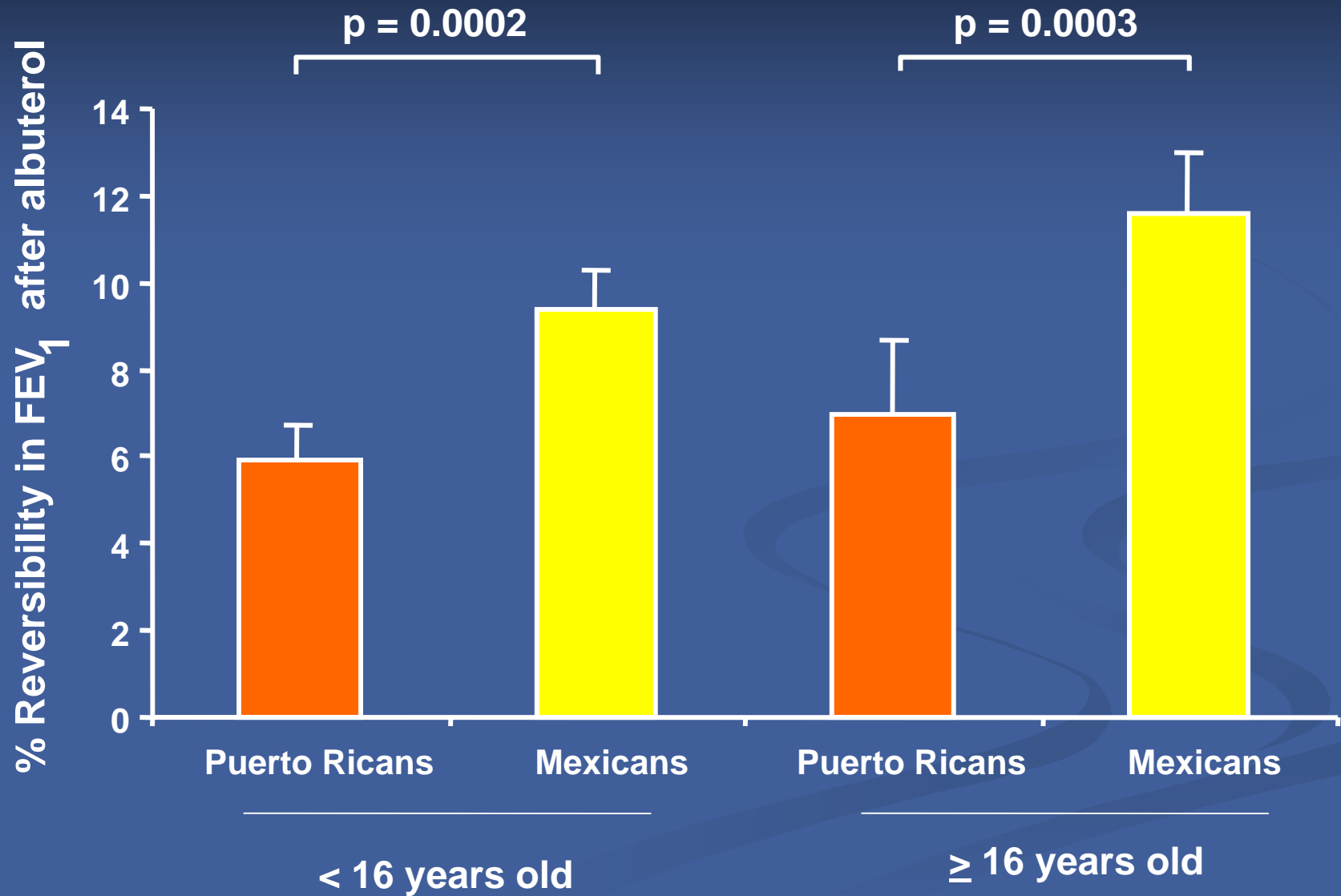
	Comparison by Ethnicity		
	Puerto Ricans (n = 343)	Mexicans (n = 290)	p Value
Baseline spirometry			
FEV ₁ , % predicted	83 (74:93)	90 (77:100)	0.0001
FVC, % predicted	94 (83:105)	97 (86:109)	0.03
FEV ₁ /FVC, % predicted	90 (82:97)	92 (87:99)	0.006
FEF _{25-75%} , % predicted	64 (48:81)	71 (56:88)	0.0004
PEF, % predicted	80 (67:94)	95 (81:107)	< 0.0001
Bronchodilator responsiveness			
FEV ₁ reversibility, %	4.8 (0.5:10)	7.4 (4:12)	< 0.0001
FVC reversibility, %	0.8 (-3.4:5)	2.5 (0.5:7)	< 0.0001
FEV ₁ /FVC reversibility, %	4.3 (0.1:9)	4.3 (1.3:8)	0.92
FEF _{25-75%} reversibility, %	15.9 (2:37)	20.9 (9:36)	0.01
PEF reversibility, %	4.4 (-4.9:15)	5.5 (0.6:13)	0.07

TABLE 4. HEALTH CARE UTILIZATION FOR ASTHMA

Variable	Comparison by Ethnicity		
	Puerto Ricans (n = 365)	Mexicans (n = 294)	p Value
Number of doctor visits in the previous 12 mo	3 (1:6)	2 (1:3)	0.0002
Have ever had ED visit, %	88.0	74.3	< 0.001
Had any ED visits in the previous 12 mo, %	67.1	45.2	< 0.001
Number of lifetime ED visits	10 (2:26)	3 (0:10)	< 0.0001
Have ever hospitalized, %	64.4	41.8	< 0.001
Have ever been in ICU, %	9.9	10.5	0.77

Burchard et al. AJRCCM 2004

Puerto Ricans Have Lower Response to Albuterol

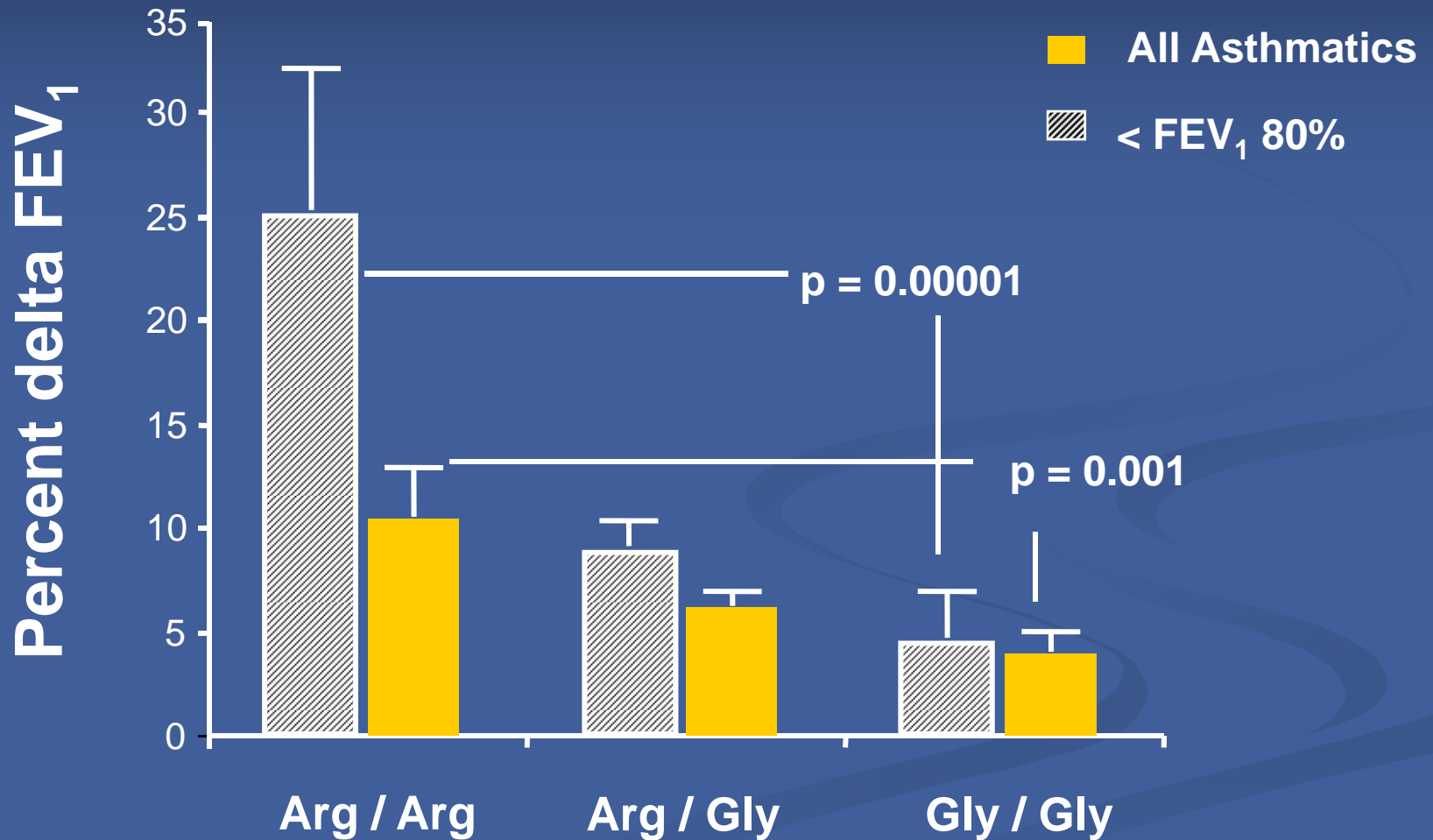


β_2 -Adrenergic Receptor Protein

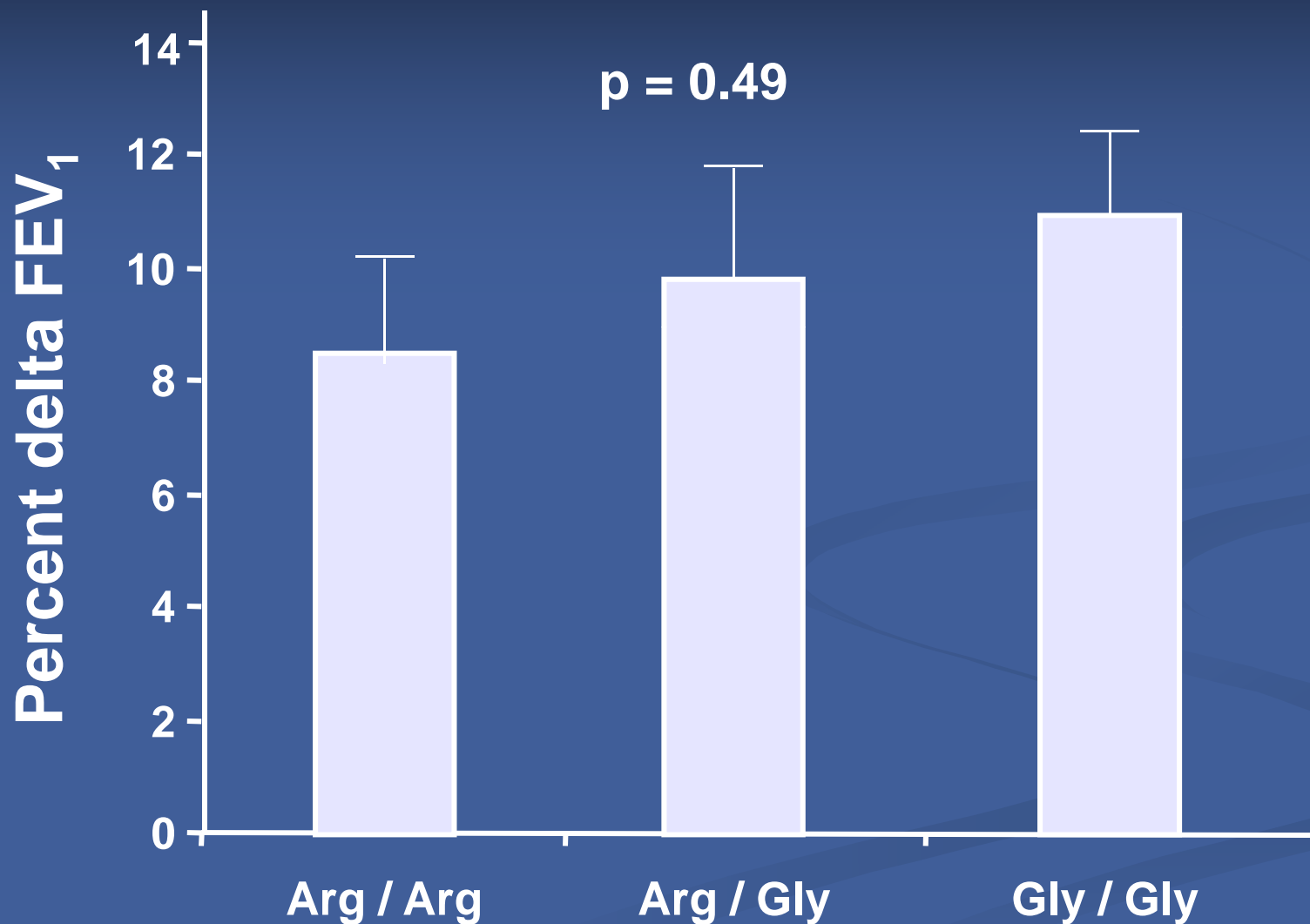


Reihnsaus E et al. *Am J Respir Cell Mol Biol.* 1993;8:334-339.

Bronchodilator Drug Responsiveness and Arg16Gly Genotypes Among Puerto Rican Asthmatics



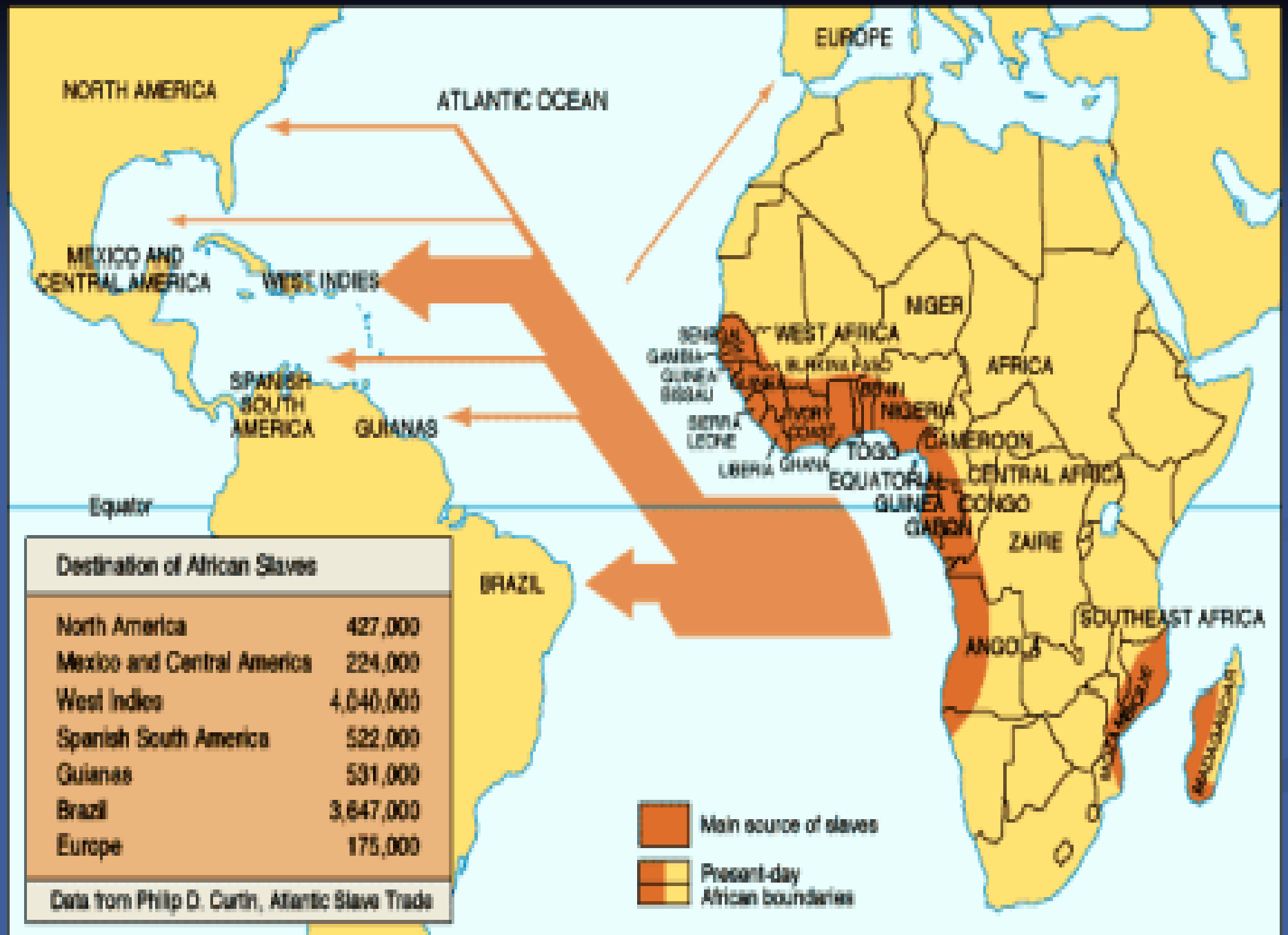
b₂AR genotype is NOT associated with drug response in Mexicans



Genetics of Asthma in Latino Americans

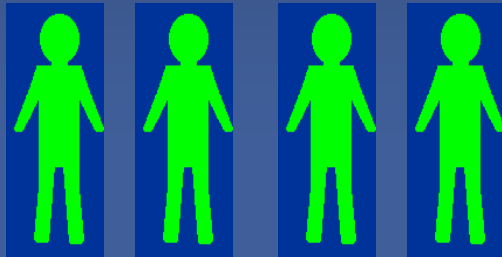
RACE: a group of persons related by common descent or heredity. The group has been partially isolated reproductively from other populations, resulting in a greater degree of **physical and genetic similarity** with one another than with other humans.

ETHNICITY: An ethnic group is a group of humans whose members identify with each other through a **common heritage** (cultural, linguistic, religious, and behavioral traits) that is real or assumed.

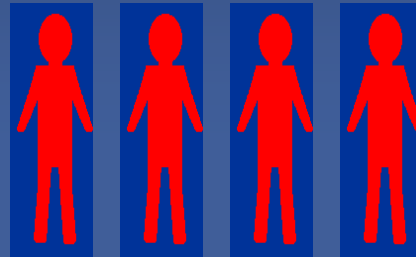


Ancestry of Latinos & African Americans

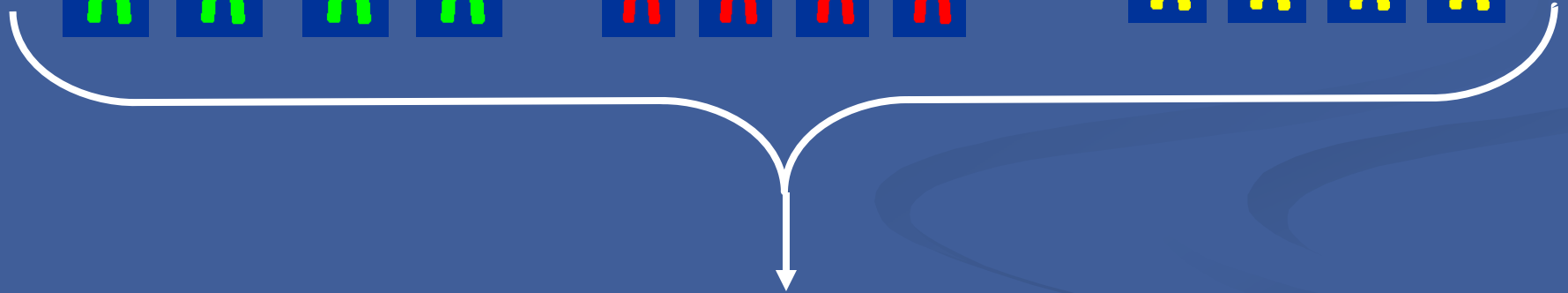
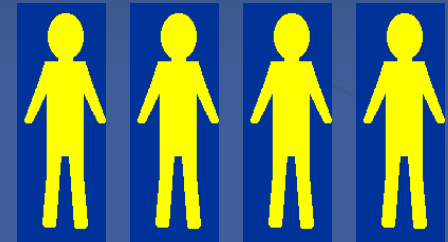
African



Native American

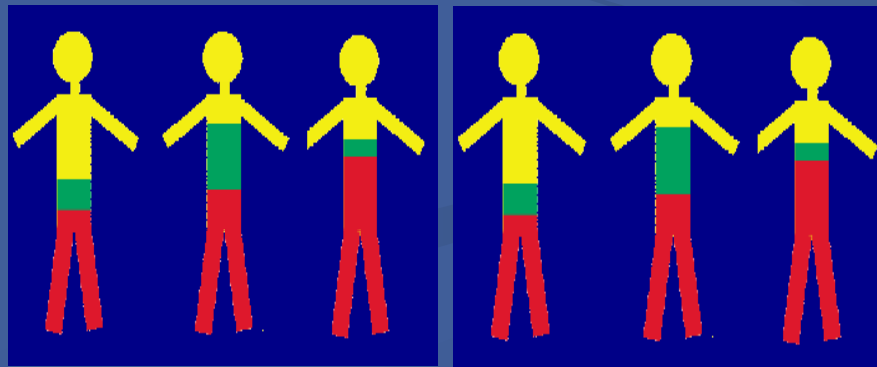


European



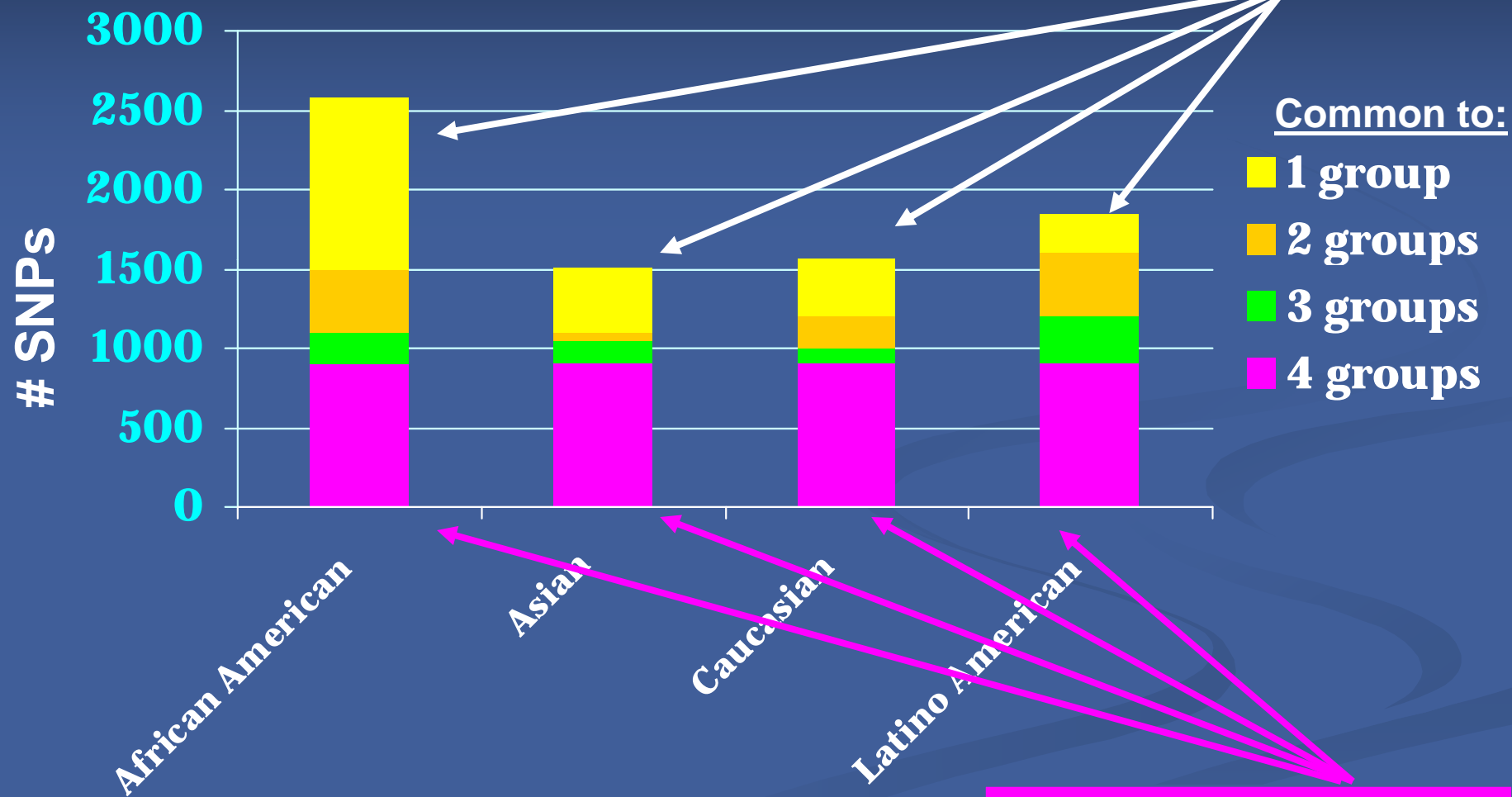
"Mestizos"

=



3,899 SNPs in 313 genes in 4 U.S. groups

12% of SNPs are racially specific

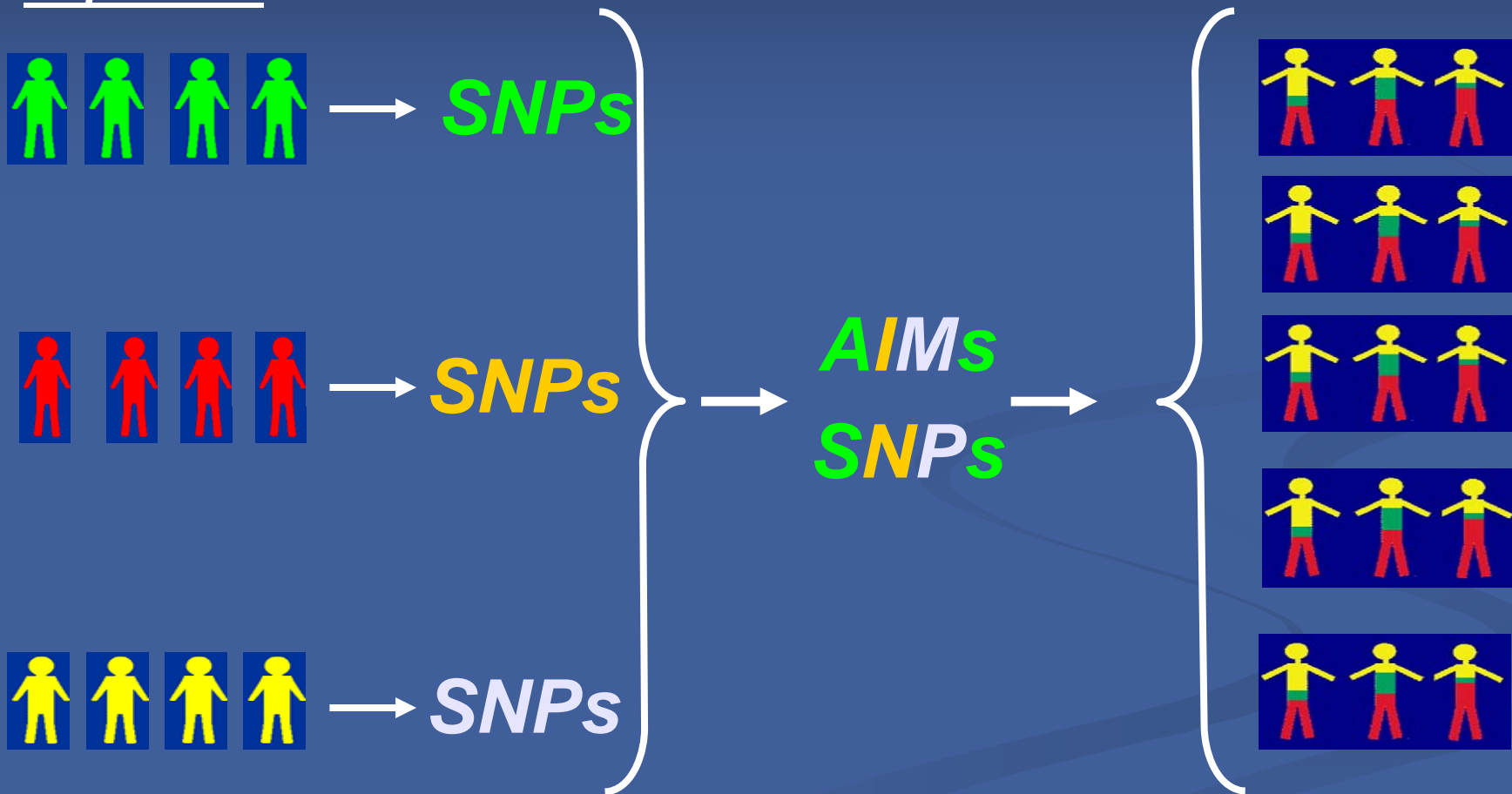


25% of SNPs are Pan Racial

Ancestry Informative Genetic Markers (AIMs)

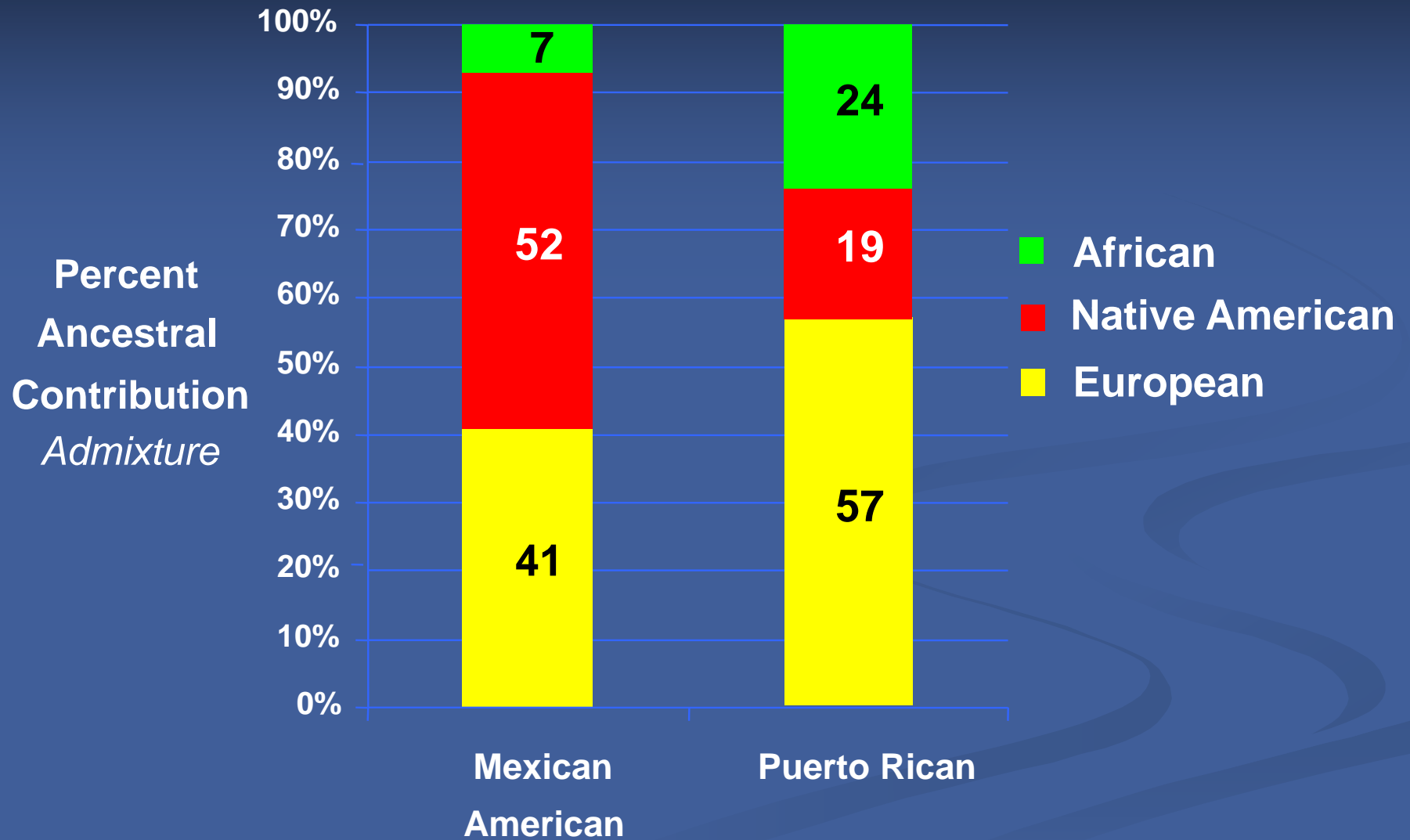
Ancestral
Population

Contemporary
Population

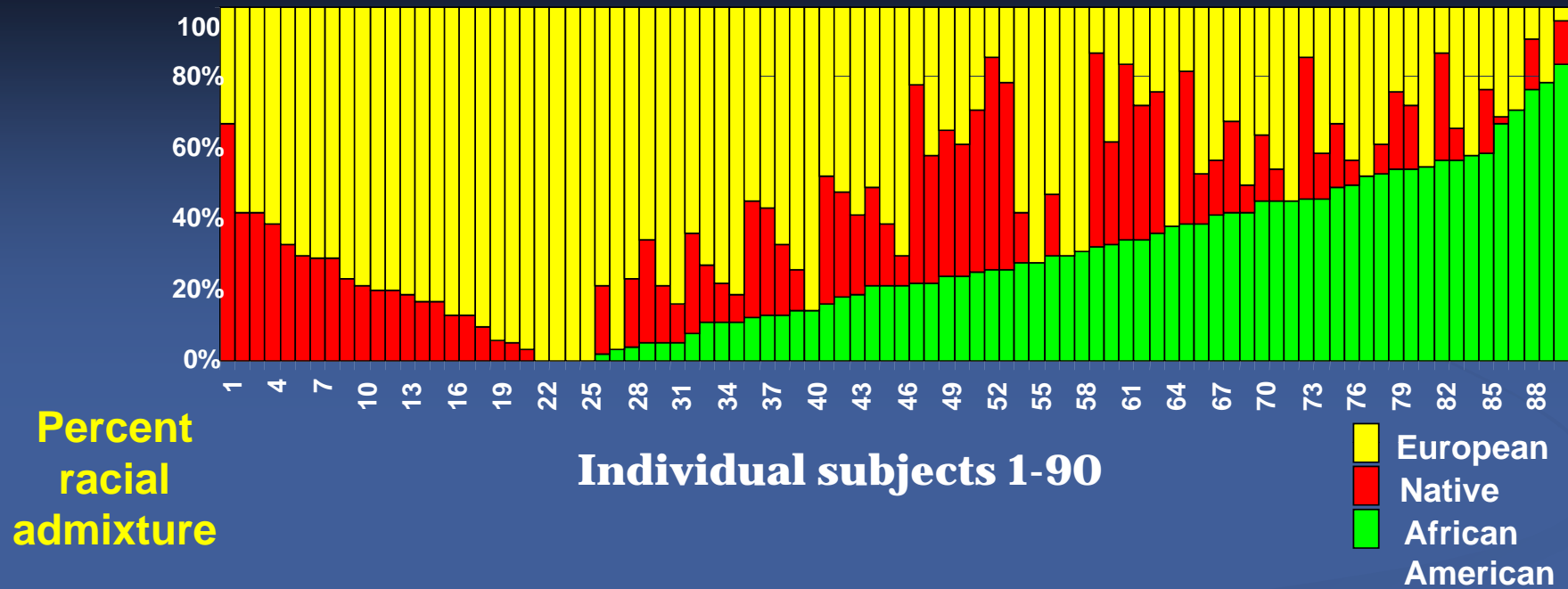


SNPs = Single Nucleotide Polymorphisms

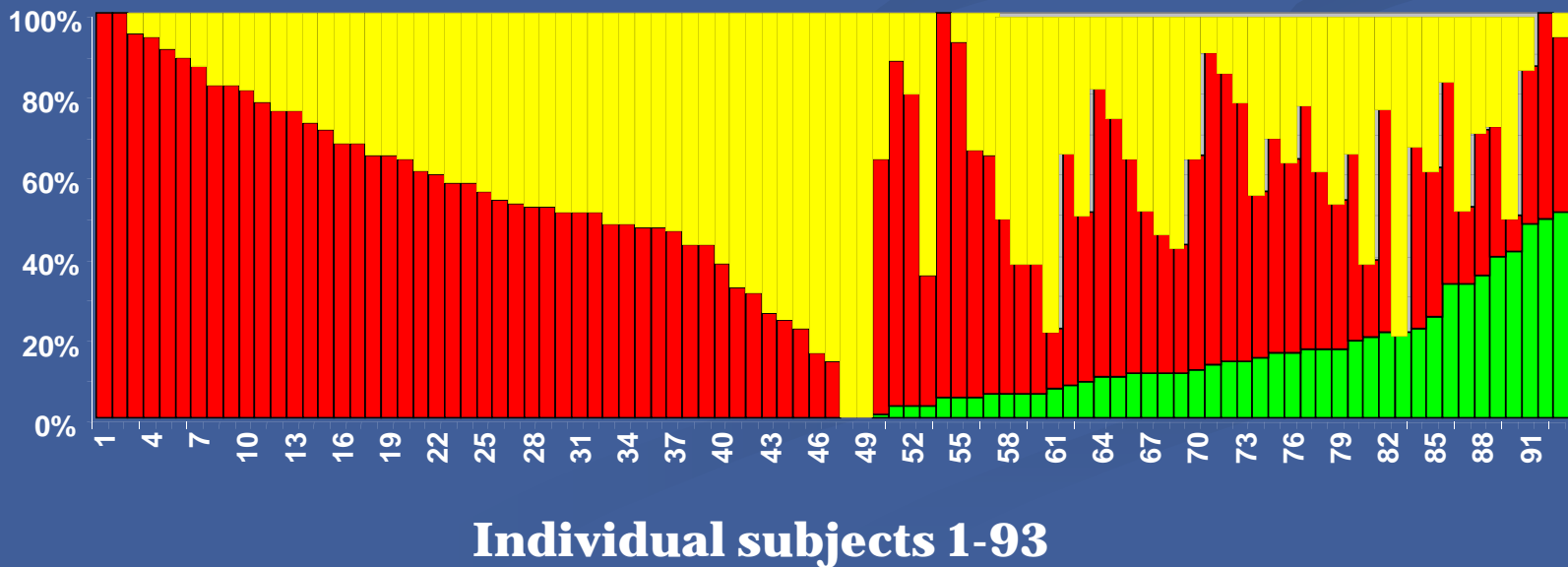
Genetic Origins of Latino Ethnic Groups



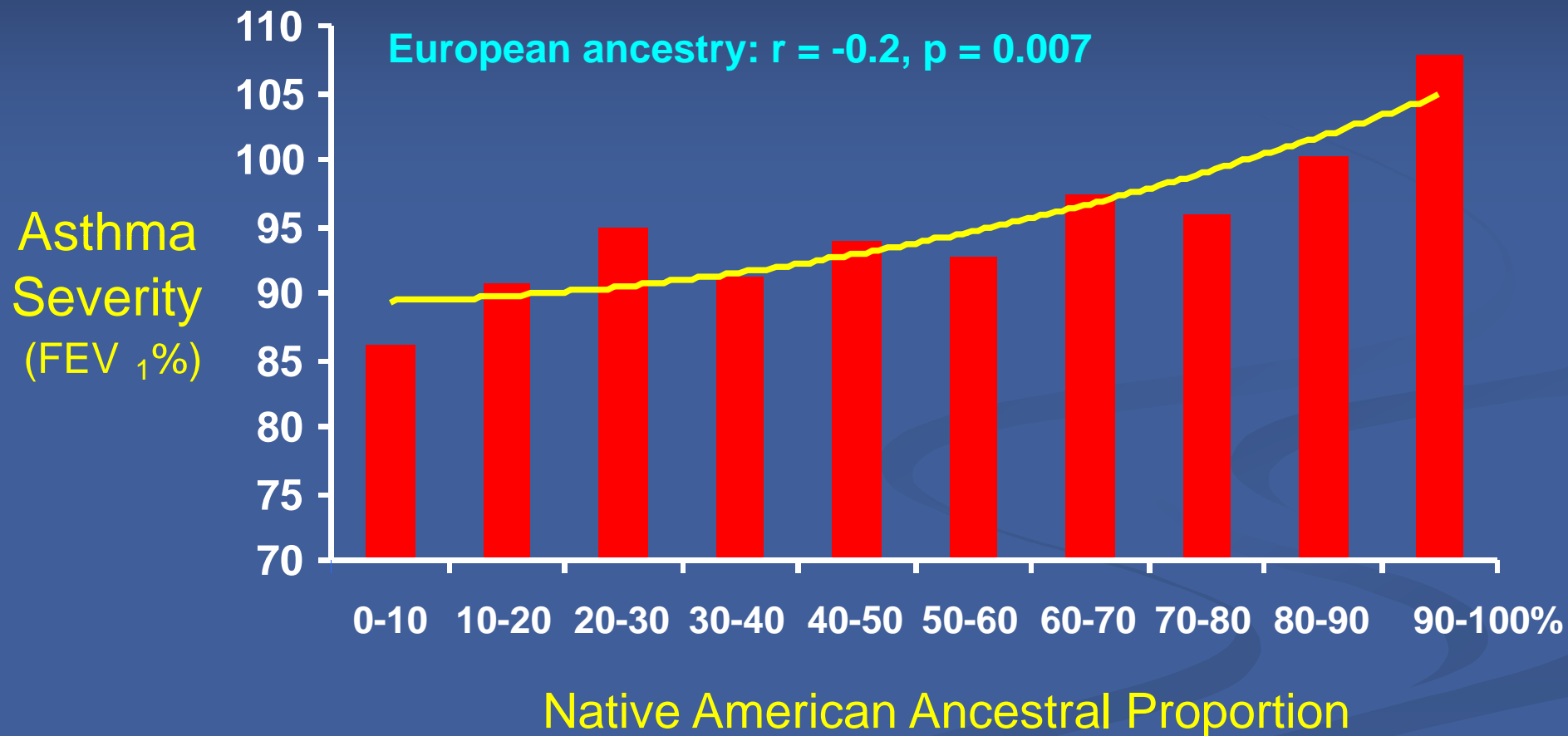
Puerto Rican Volunteers



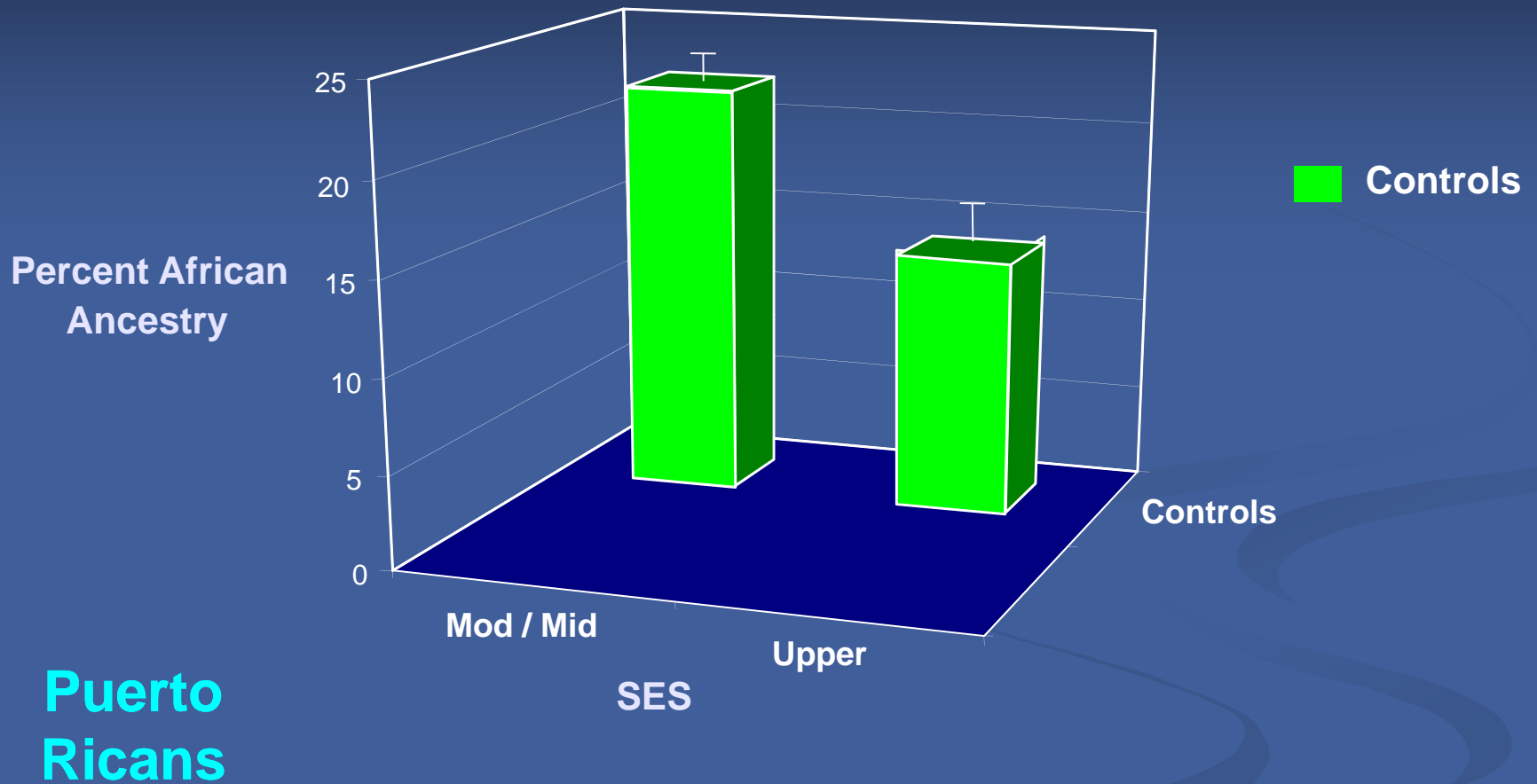
Mexican Volunteers



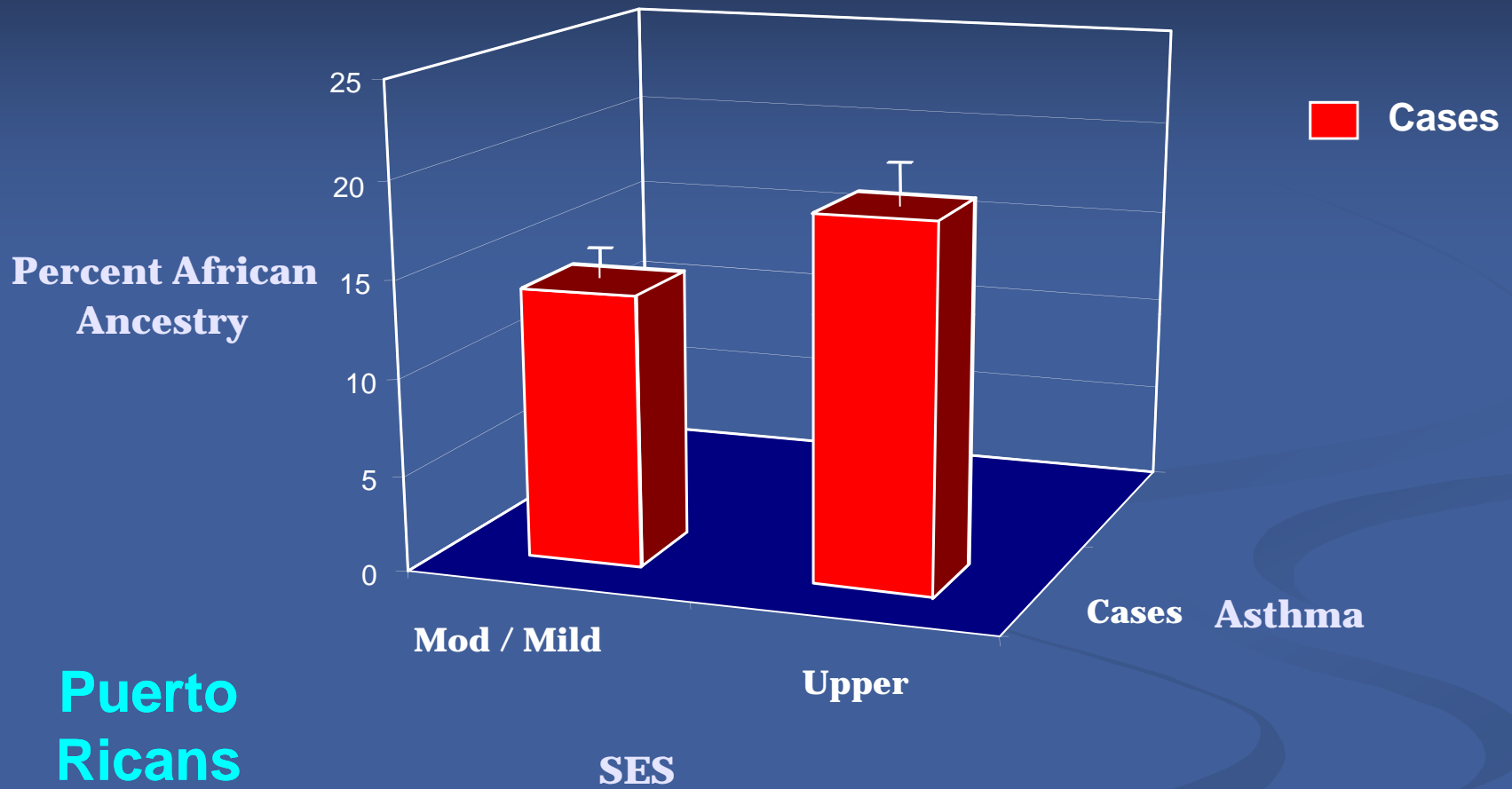
European ancestry confers a risk in Mexican American asthmatics



Ancestry-SES Interaction & Asthma Risk

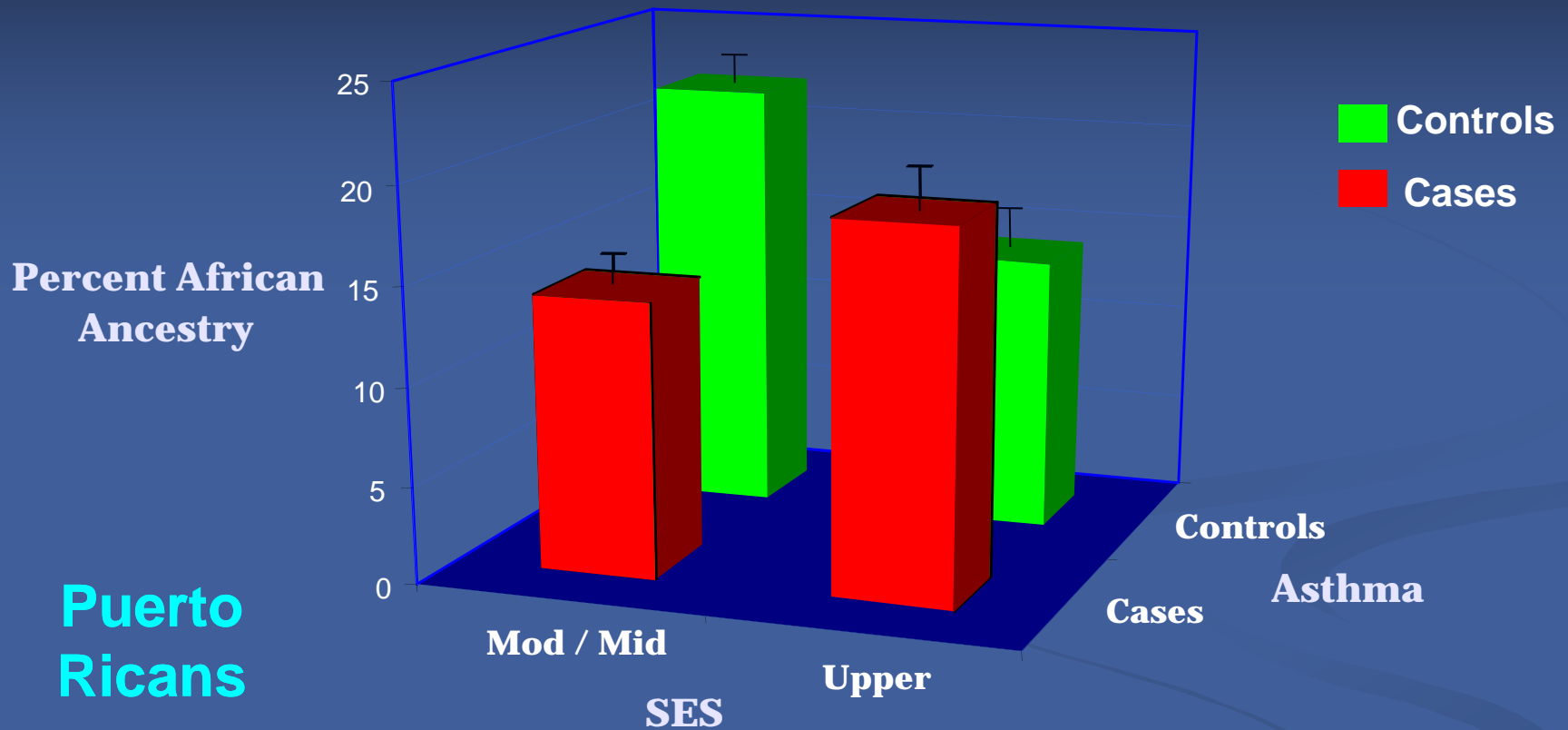


Ancestry-SES Interaction & Asthma Risk



Choudhry et. al. AJRCCM 2006

Ancestry-SES Interaction & Asthma Risk



Lower SES: asthmatics had less African ancestry than healthy controls

Upper SES: asthmatics had more African ancestry than healthy controls

Genetics of Asthma in Latino Americans-II

Aim: To determine the genetic and environmental factors that can explain why asthma prevalence and severity vary widely in Hispanics.

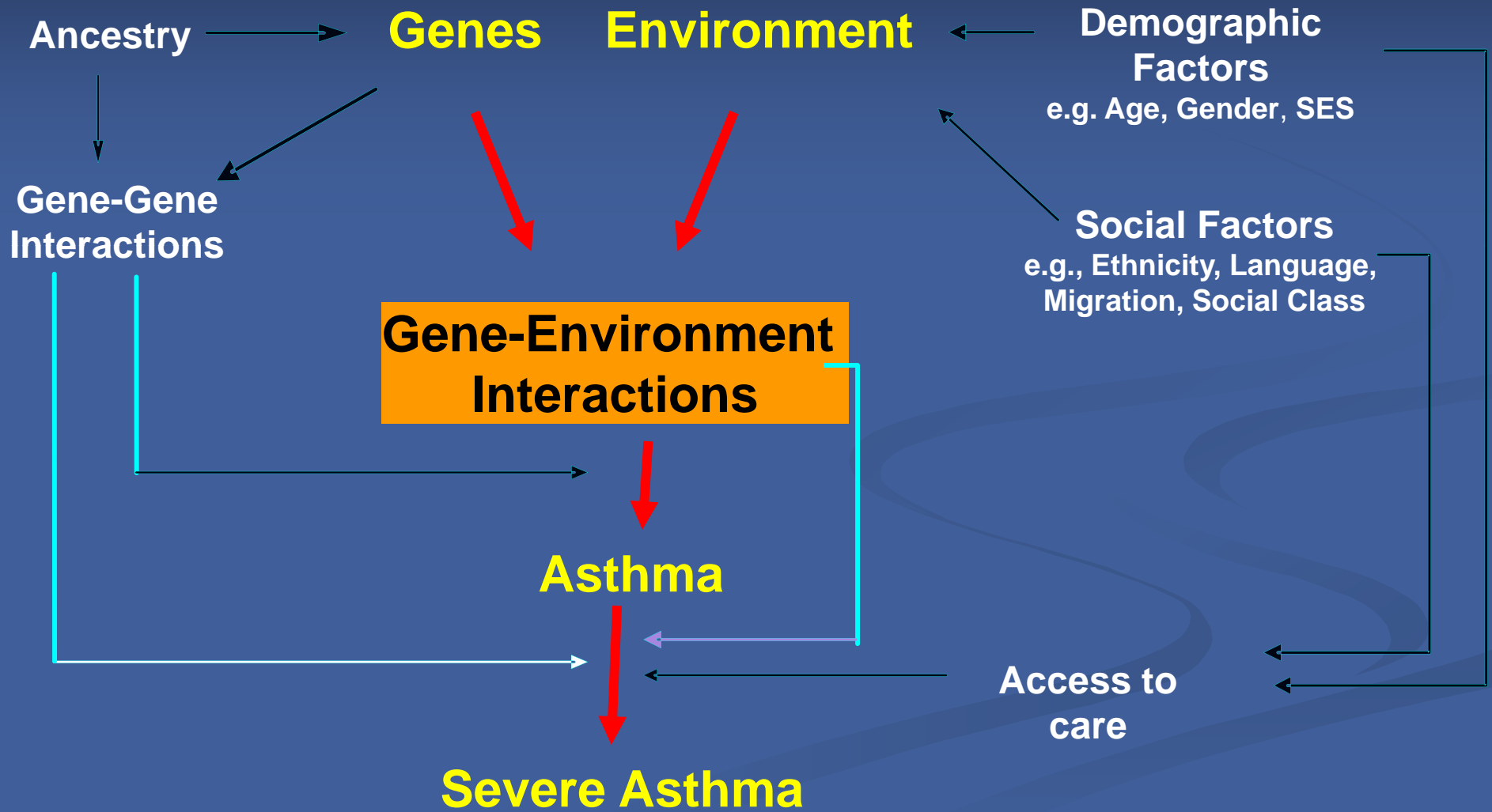
Recruitment:

- Case-Control study
- N = 2000 per group (asthma and control)
- 800 subjects per area:
 - San Francisco, Chicago, Puerto Rico, New York, Houston
- Period: 2009-2011
- Funding: NIH

Study Visit:

- Questionnaire
- Spirometry and bronchodilator response
- Blood draw (DNA, IgE)
- Allergy skin testing
- Methacholine

Causal Model of Asthma



GALA Team

UCSF:

Lung Biology Center

Esteban Burchard

Shweta Choudhry

Elad Ziv

Harriet Corvol

A. De Giacomo

Celeste Eng

Max Seibold

Dean Sheppard

Neil Risch

UCSF, San Francisco

Homer Boushey

Pui Yan Kwok

Shannon Thyne

Oakland

Michael LeNoir

G. Watson

Kelley Meade

Kenny Beckman

Mexico

Rocio Chapela

Moises Selman

Jorge Salas

Penn State Univ.

Mark Shriver

Stanford

Hua Tang

Chicago

Pedro Avila

Rajesh Kumar

Boston

Jeffrey Drazen

Ed Silverman

Scott Weiss

Puerto Rico

William Rodriguez

Jesus Casal

Sylvette Nazario

Alfonso Torres

Jose Rodriguez-

Santana

New York

Jean Ford

Joanne Fagan

Luisa Borrell

UCSF Sandler Center for Basic Research in Asthma

American Lung Association of California

Robert Wood Johnson Foundation

NIH/NHLBI