African ancestry and income are independently associated with risk for dengue hemorrhagic fever

RE Blanton, LK Silva, V Morato, JP Dias, PS Melo, AR Parrado, EA Reis, KA Goddard, MR Nunes, SG Rodrigues, PF Vasconcelos, JM Castro, MG Reis, ML Barreto, MG Teixeira

1-Center for Global Health and Diseases, CWRU, Cleveland, OH

2-Institute for Collective Health, Federal University of Bahia, Brazil

3-Bahia State Health Department, Salvador, Bahia, Brazil

4-Evandro Chagas Institute, Belem, Pará

5-Oswaldo Cruz Foundation, Salvador, Bahia, Brazil

Financial Support: NIH R21 AI056263

Genetics and Host Risk Factors

- Non-neutralizing antibodies
- Age
- Other diseases
- African ancestry
- Genetics
  - HLA
  - Dengue receptor CD209
  - The IFNα response pathway

Results of Havana´s 2001-2 Epidemic

Table 2 Ethnic distribution of DHF and DSS[a] cases.

Ethnic group	Cases (N%)			Havana's population distribution (%)[b]
	DHF	DSS	Total	
White	32 (55.2)	15 (83.3)	47 (61.8)	63.0
Mulatto	15 (25.9)	1 (5.6)	16 (21.1)	20.4
Black	11 (18.9)	2 (11.1)	13 (17.1)	16.4
Total	58	18	76	–

[a] DHF = dengue hemorrhagic fever; DSS = dengue shock syndrome.
[b] 0.2% Asian origin.

González et al. Int J Infect Dis. 2005 Sep;9(5):280-5

Definitions

- Race
  - Based in biology and geography
  - Deterministic and value associated
  - Categorical
- Ethnicity
  - Recognizes the contribution of environment and culture
  - Categorical
- Ancestry
  - Quantifiable and genetically based
  - Captures environmental influences
  - Continuous

Ethnicity vs Ancestry

One in a million!
(2006)

One in a million!
(2006)

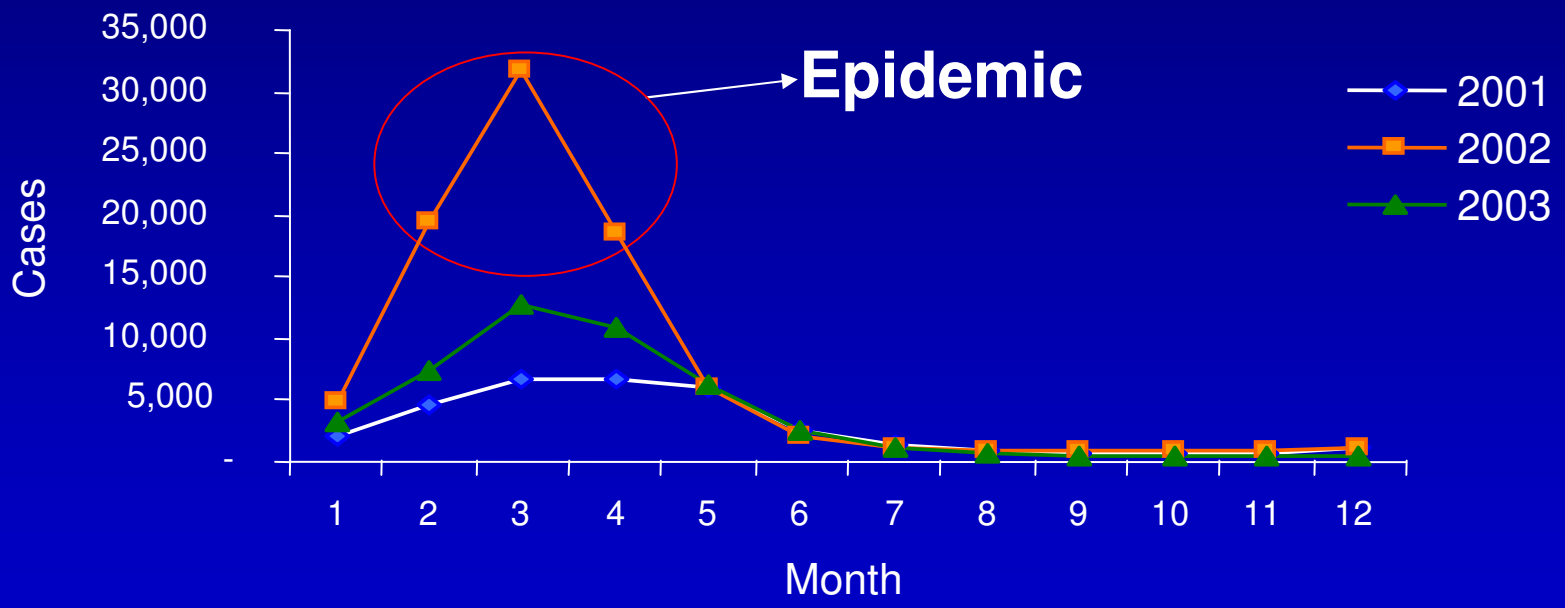
One in a million!
(2006)

Pedro Henrique Rodrigues (branco) e Nathan Henrique Rodrigues (negro), com o pai, Carlos Henrique da Fonseca / FOTO: Marcelo Theobald

Gêmeos nem tão raros
no Brasil (O Globo 2006)

Ethnicity: What you make it

Dengue in Bahia 2001-2003



P. Melo Master's Thesis, source SESAB

Study Design-Salvador (2004)

- Population
  - DHF cases identified: **82**
  - DHF cases validated: **60**
  - DHF Cases Collected: **55**
  - DF controls: **289**
  - Asymptomatic controls: **286**
- Demographic survey
- Dengue serology (+) for 90%
- Illumina Microbead Array Genotyping
  - 78% polymorphic
  - Error rates <0.1%

Candidate Gene Categories

- 768 SNP markers
- 71 genes
  - viral sensing/receptors (e.g. CD209, TLRs)
  - control of IFNα induction (e.g. NFKB1, MYD88, EIF2AK2)
  - IFNα production (e.g. IFNA 1-21)
  - IFNα suppression (e.g. DNAJC3)
  - IFNα signaling (e.g. IFNARs, JAKs, STATs, MAPK1)
  - effector molecules (e.g. OASs, RNASEL, MX1, ADAR)
  - effector suppression (e.g. SOCSs)
  - published associations (e.g. IL18, RANTES-CCL5, VDR)
  - Ancestry informative Markers (AIMs) (e.g. Duffy)

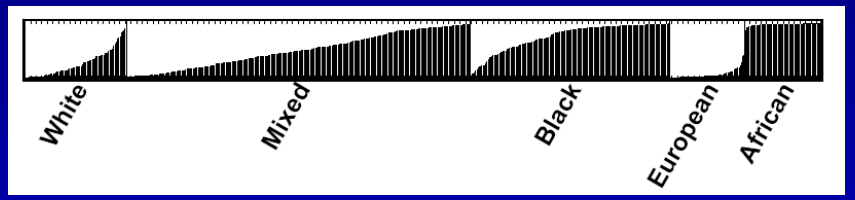
DHF Distribution: Salvador 2002

	DHF	Salvador
White	24	7
Mixed	62	50
Black	14	43

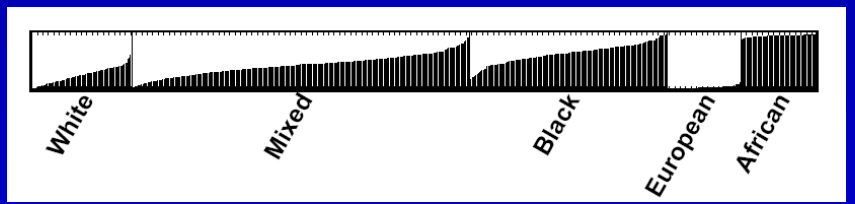
Distribution of African Ancestry

- Significant admixture within self-defined ethinic groups
- Significantly more African ancestry in Blacks and Mixed groups

AIMs (29)

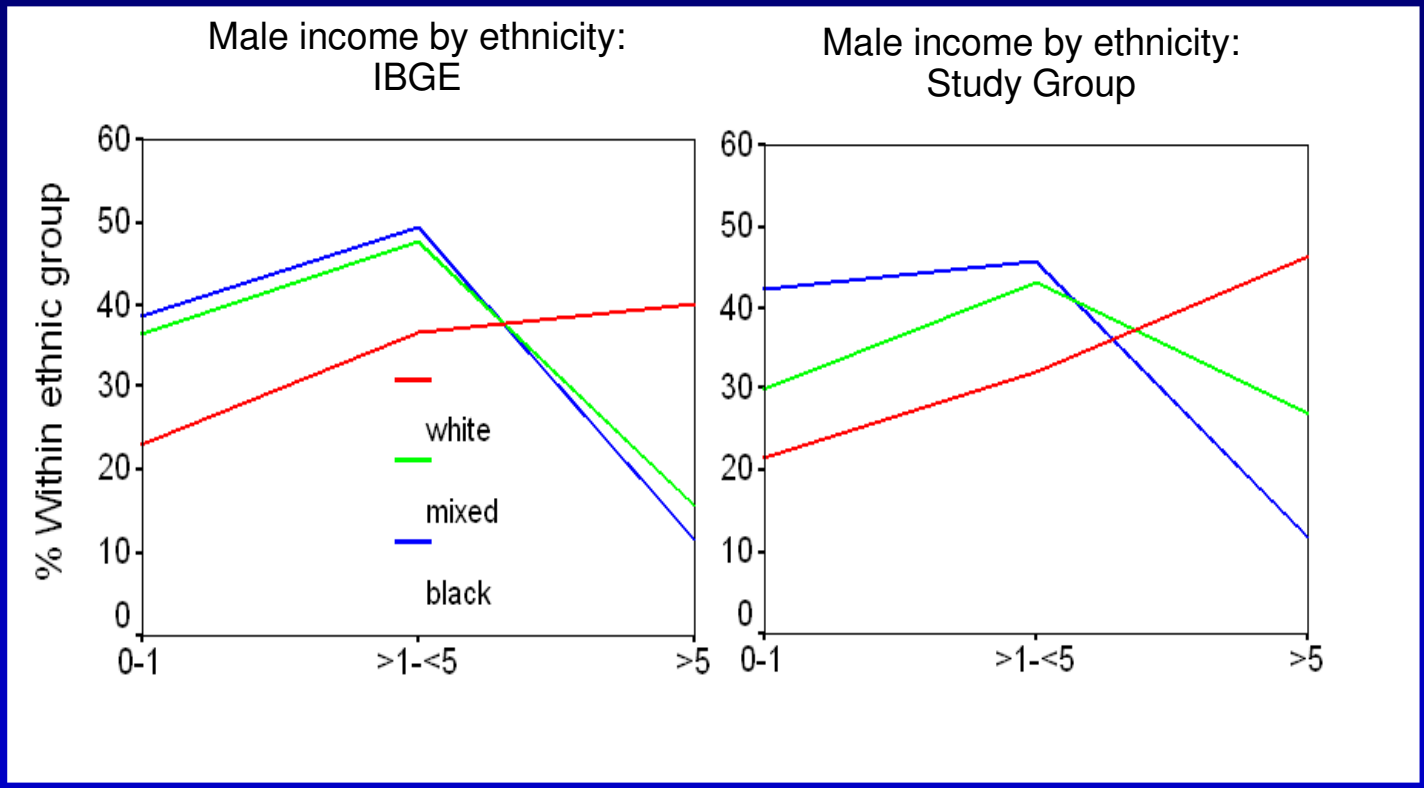


Unlinked (308)



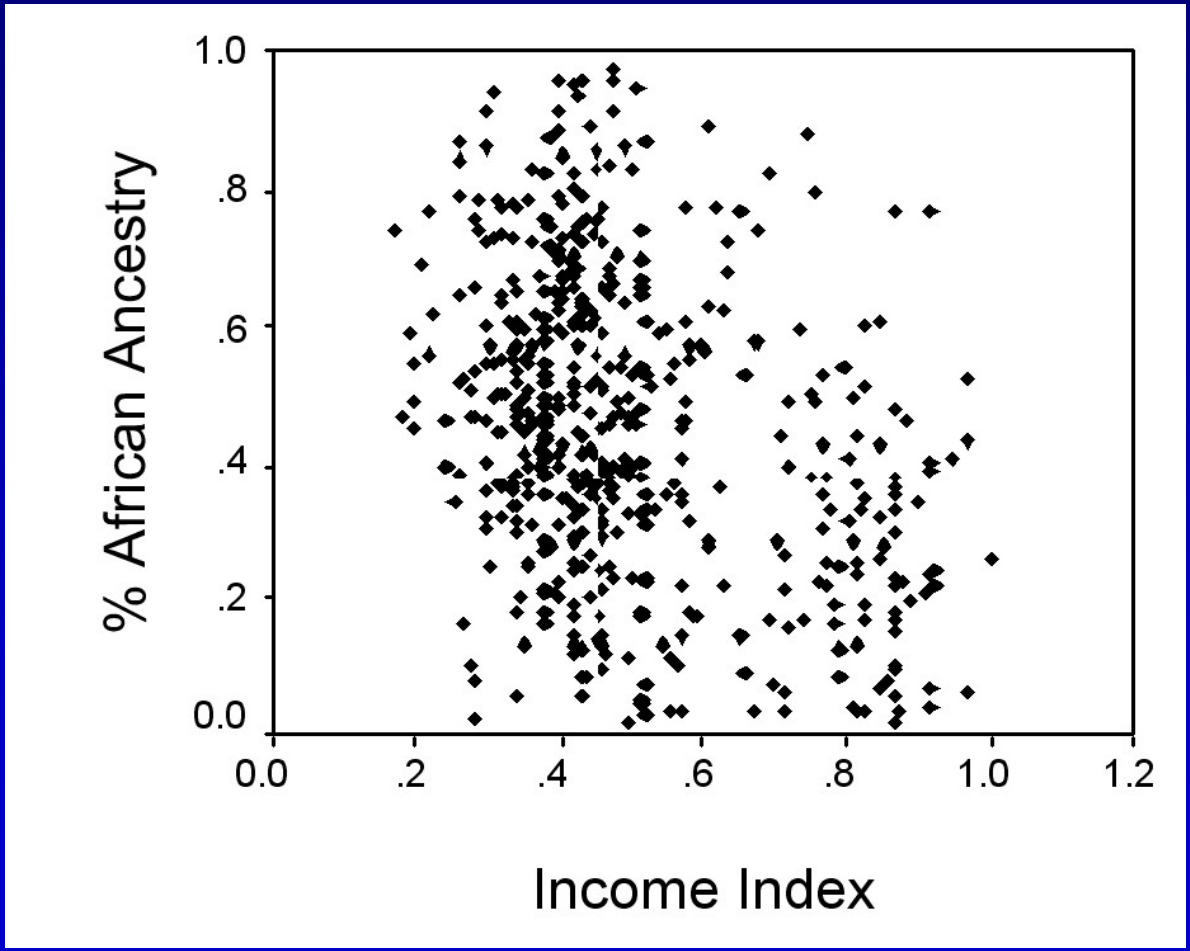
Estimates used the program Structure – Pritchard 2000

Reported Incomes by Ethnicity: Salvador



Income in Minimum Monthly Salaries
(US$97.03 in 2004)

Distribution of Income by African Ancestry



Association of African Ancestry and DHF

- χ^2 – ancestry, income
- Logistic regression
- African ancestry and lower income are independently protective

Variables	DHF vs DF		
	p	OR	CI
Sex	0.94	0.98	0.50 - 1.90
Age	0.18	0.99	0.96 - 1.01
%African Ancestry	0.02	0.13	0.02 - 0.69
Income Index	0.01	9.71	1.70 - 55.62

Income and DHF

- Chinese-Malays/Indians (Singapore)
- Indians-Africans (Trinidad)
- Whites-Blacks (Cuba, Brazil)
- Risk of diagnosis
- Risk of infection (Vasconcelos *Rev Saúde Pública* 1998)

Acknowledgements

ISC-UFBA

M. Glória Teixeira
Vanesa Morato
Maurício Barreto

Div. Genetic Epidemiology

Katrina Goddard
Antonio Parrado

Funding

NIH R21 AI056263

FIOCRUZ

Dr. Mitermayer G. dos Reis
Luciano K. Silva
Paulo Melo
Eliana Reis

SESAB

Jesuína Costa
Juarez Dias
Maria Figueiredo

LACEN

Dr. João Rodrigues
Isolina A. Ciuffo