African Signatures of Recent Positive Selection in Human FOXI1

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Forkhead-Box (FOX)

- Transcription Factors
- Helix-turn-helix
- Winged domain

FOXI1

- Influences transcription of:
  - Pendrin
  - Vacuolar H+-ATPase proton pump
  - Carbonic Anhydrase II
- Anatomical development:
  - Distal Nephron Epithelium
  - Epididymal Cells
  - Vestibular Aqueduct

Methods

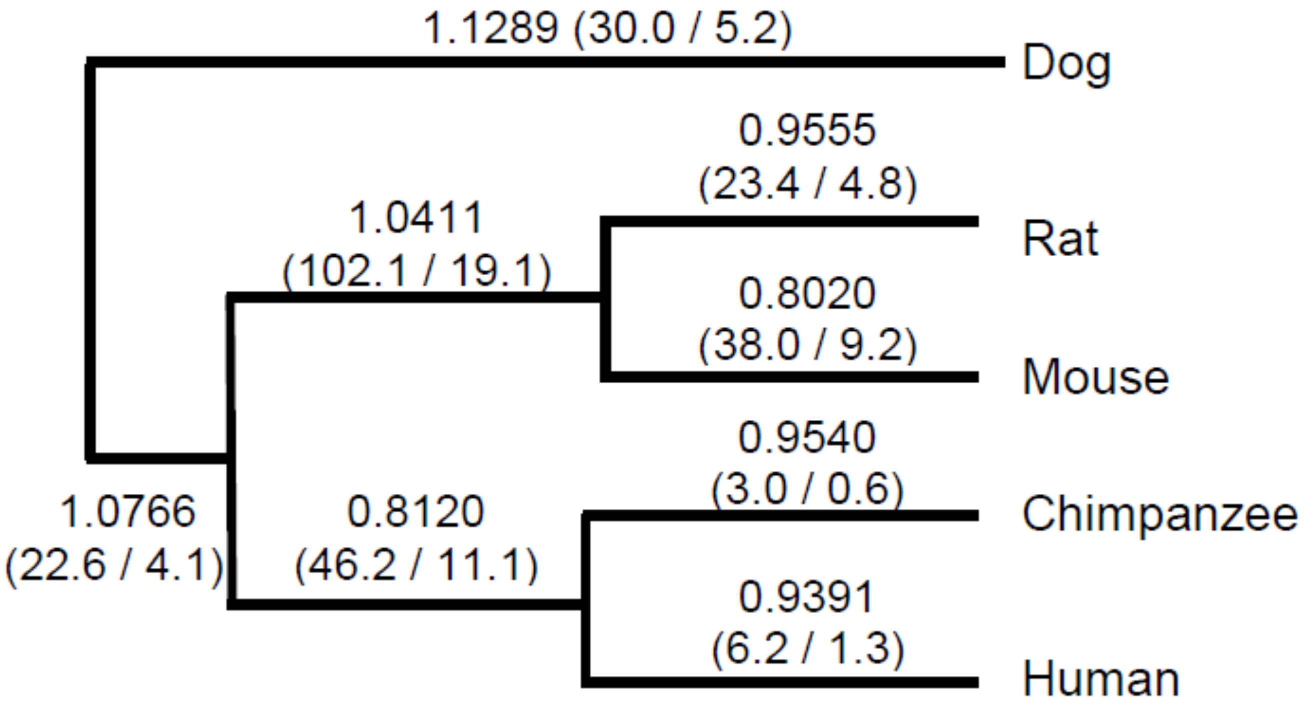
- PCR amplification and sequencing of FOXI1 gene
- HGDP-CEPH
- Detected SNPs
  - Evidence of accelerated evolution ($k=u*f_o$)
    - Low frequency variants
    - High frequency derived alleles
    - Linkage Disequilibrium (Long Range Haplotypes)
- Between species comparison
- Within Human Comparison

Linkage Disequilibrium

- Association of Alleles
- Disrupted by Recombination
- Causes:
  - Nonrandom mating
  - New mutation or union of populations
  - Little to no recombination
    - Inversion,parthenogensis
  - Genetic Drift
  - **Natural Selection**

Results

Figure S1. Phylogeny of the five mammalian species used in PAML analysis.



Results: Figure S3

- Yellow
  - African
- Blue
  - European
- Green
  - Asian

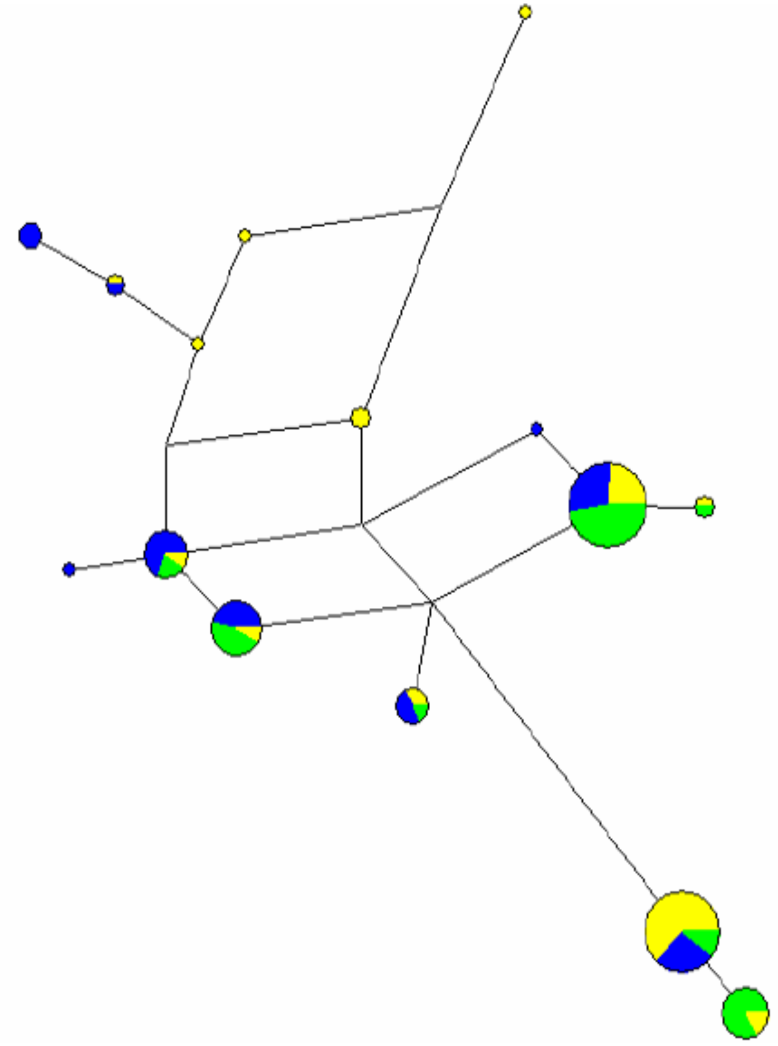


Table 3

Population sequence variation and neutrality test statistics for *FOXI1*

Population	2N[a]	S[b]	π[c]	K[d]	H[e]	Tajima's D	Fu and Li's D*	Fu and Li's D	Fu and Li's F*	Fu and Li's F	Fu's Fs	Fay and Wu's H
European	40	17	0.0012 ± 0.0001	12	0.874 ± 0.026	0.485	0.431	0.433	0.530	0.543	-0.421	1.600
Asian	40	13	0.0010 ± 0.0001	8	0.768 ± 0.045	1.134	0.065	0.030	0.486	0.485	1.969	-1.923
Yoruban	40	16	0.0011 ± 0.0001	12	0.741 ± 0.063	0.487	0.763	0.799	0.793	0.831	-0.664	-2.928
All	120	22	0.0012 ± 0.0001	19	0.837 ± 0.019	0.360	-0.808	-0.863	-0.430	-0.458	-1.417	-0.410

Note: **At P = 0.05, none of the neutrality statistics were significant**

[a] Number of chromosomes

[b] Number of segregating sites

[c] Nucleotide diversity per base pairs

[d] Total number of haplotypes

[e] Haplotype diversity

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- Figure 3

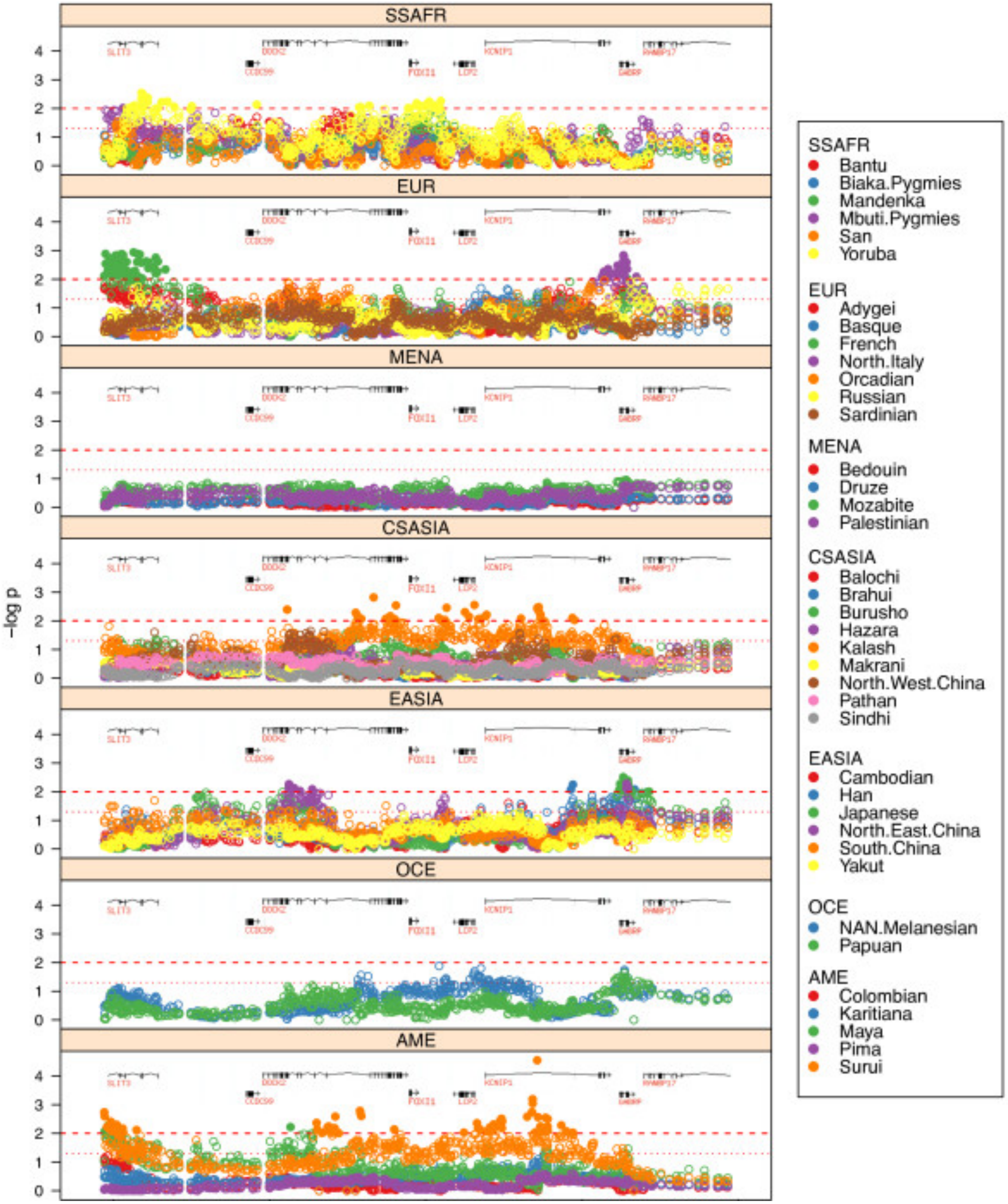

SSAFR
EUR
MENA
CSASIA
EASIA
OCE
AME
-log p
0
1
2
3
4
SLIT3
DOCK2
CCDC99
FOXI1
LCP2
KCNIP1
GABRP
RANBP17
SSAFR
Bantu
Biaka.Pygmies
Mandenka
Mbuti.Pygmies
San
Yoruba
EUR
Adygei
Basque
French
North.Italy
Orcadian
Russian
Sardinian
MENA
Bedouin
Druze
Mozabite
Palestinian
CSASIA
Balochi
Brahui
Burusho
Hazara
Kalash
Makrani
North.West.China
Pathan
Sindhi
EASIA
Cambodian
Han
Japanese
North.East.China
South.China
Yakut
OCE
NAN.Melanesian
Papuan
AME
Colombian
Karitiana
Maya
Pima
Surui

Figure 2

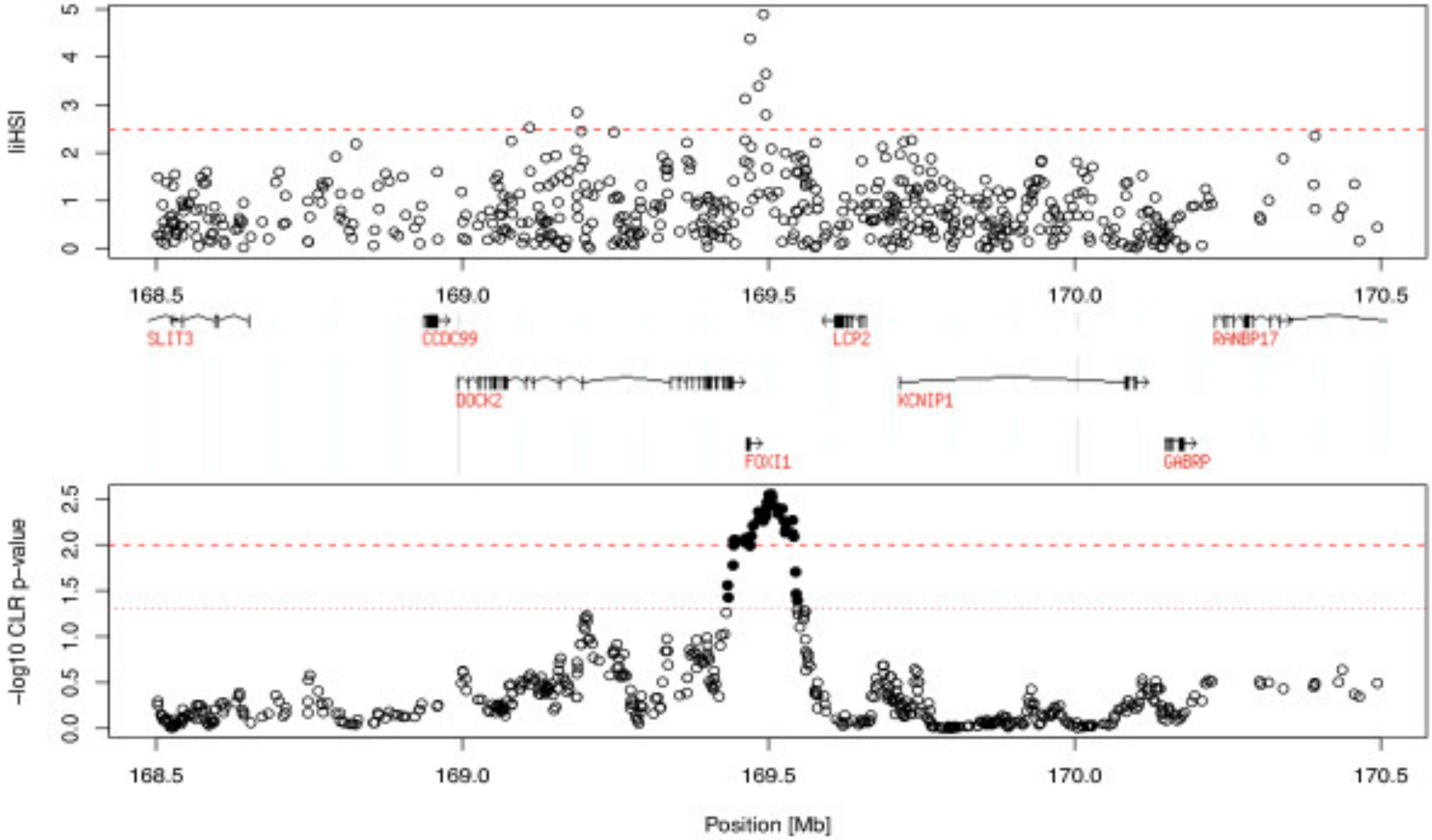
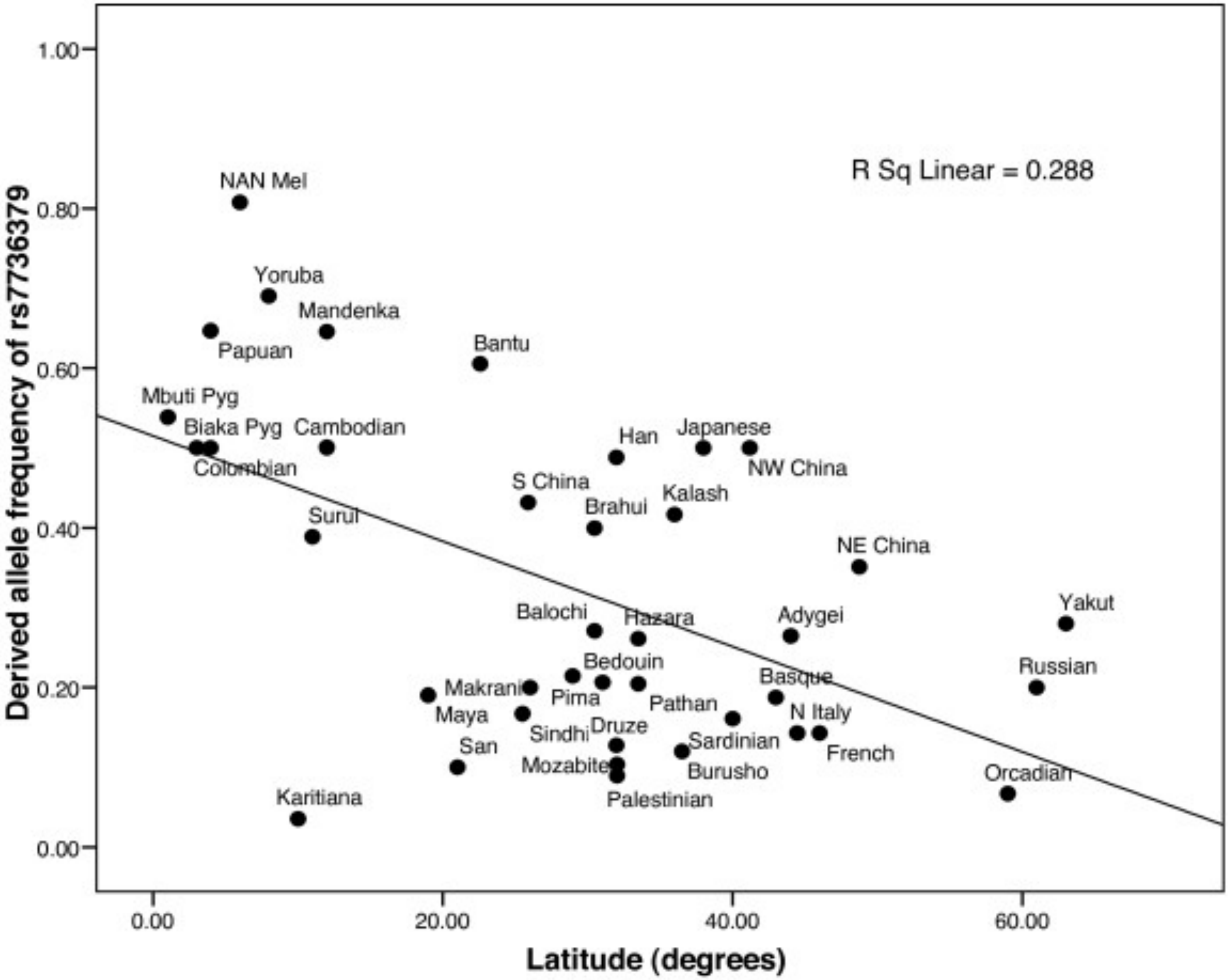
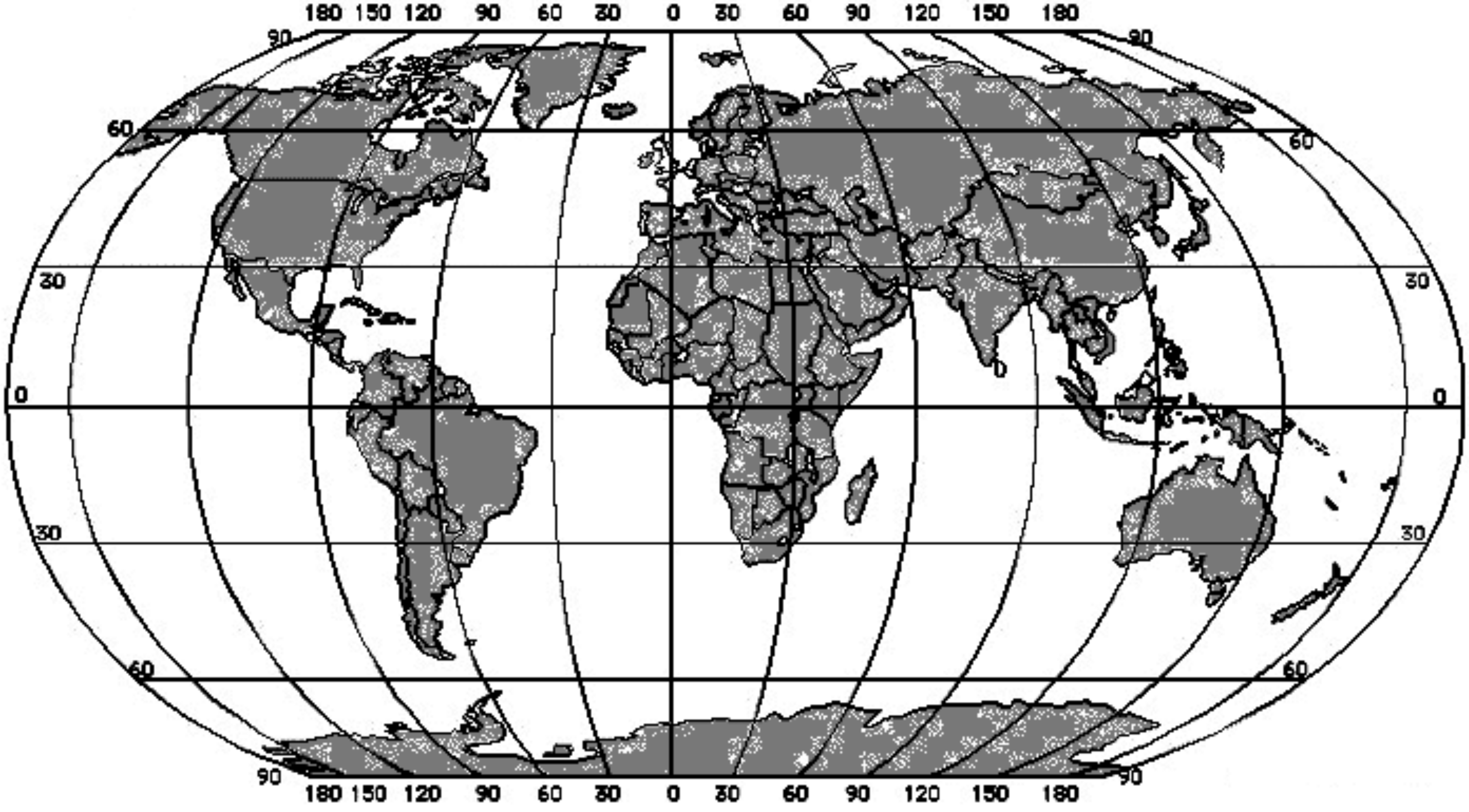

|iHS|
0
1
2
3
4
5
168.5
169.0
169.5
170.0
170.5
SLIT3
CCDC99
LCP2
RANBP17
DOCK2
KCNIP1
FOXI1
GABRP
-log10 CLR p-value
0.0
0.5
1.0
1.5
2.0
2.5
Position [Mb]

Figure 4



R Sq Linear = 0.288
Derived allele frequency of rs7736379
Latitude (degrees)
0.00
0.20
0.40
0.60
0.80
1.00
0.00
20.00
40.00
60.00
NAN Mel
Yoruba
Mandenka
Papuan
Bantu
Mbuti Pyg
Biaka Pyg
Cambodian
Colombian
Surui
Han
Japanese
NW China
S China
Kalash
Brahui
NE China
Yakut
Balochi
Hazara
Adygei
Bedouin
Russian
Basque
Makrani
Pima
Pathan
N Italy
Maya
Sindhi
Druze
Sardinian
French
San
Mozabite
Burusho
Orcadian
Karitiana
Palestinian


180
150
120
90
60
30
0
30
60
90
120
150
180
90
60
30
0
30
60
90

Conclusions

- Linkage Disequilibrium in African Populations
  - Recent Selection
- Correlation between Lattitude and frequency of rs7736379
  - Very Recent Selection?

References

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- Moreno-Estrada, Andrés, et al. "African signatures of recent positive selection in human FOXI1." BMC evolutionary biology 10.1 (2010): 267.

Discussion

- Are the conclusions justified?
- Will studies of more SNPs show non-neutral variation?
- Climate change and economics