

Variabilità genetica e migrazioni umane

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Archeogenetica e migrazioni umane

Alessandro Achilli, PhD

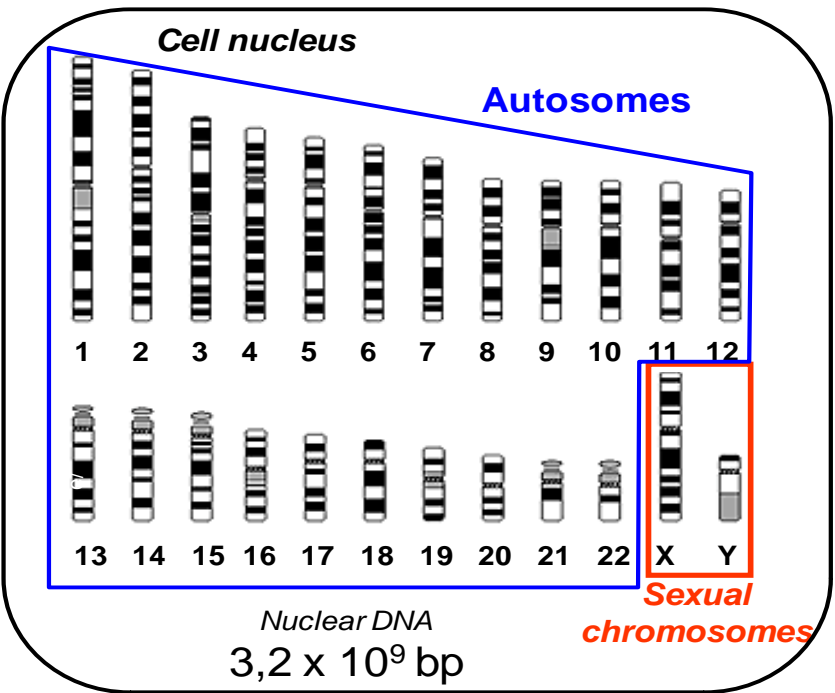
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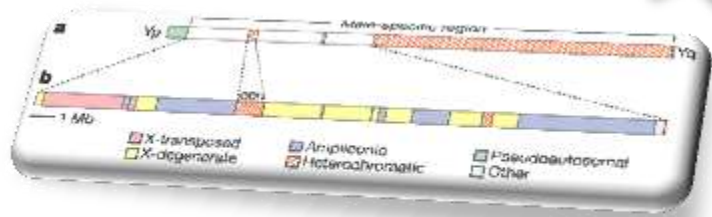
- **Archeogenetica (Renfrew 2010)**
 - Applicazione delle tecniche molecolari e filogenetiche per lo studio dell'origine dell'Uomo e dei processi genetici e demografici che hanno portato alle popolazioni moderne
- **Strumenti d'indagine**
 - Marcatori uniparentali: **DNA mitocondriale** e cromosoma Y
- **Approccio Filogeografico**
 1. Costruzione albero filogenetico
 2. Distribuzione geografiche delle linee (rami dell'albero)
 3. Stima temporale dell'età di ciascuna linea

The human genome

23 chromosome pairs + mtDNA

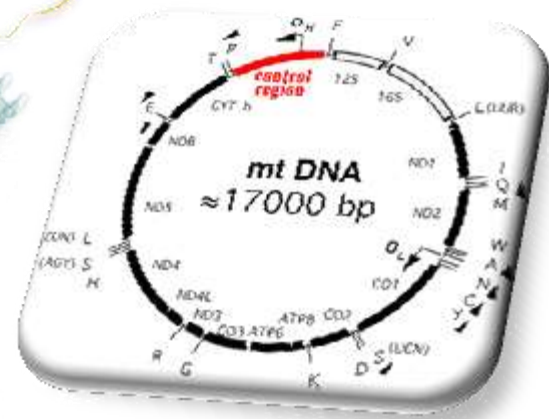
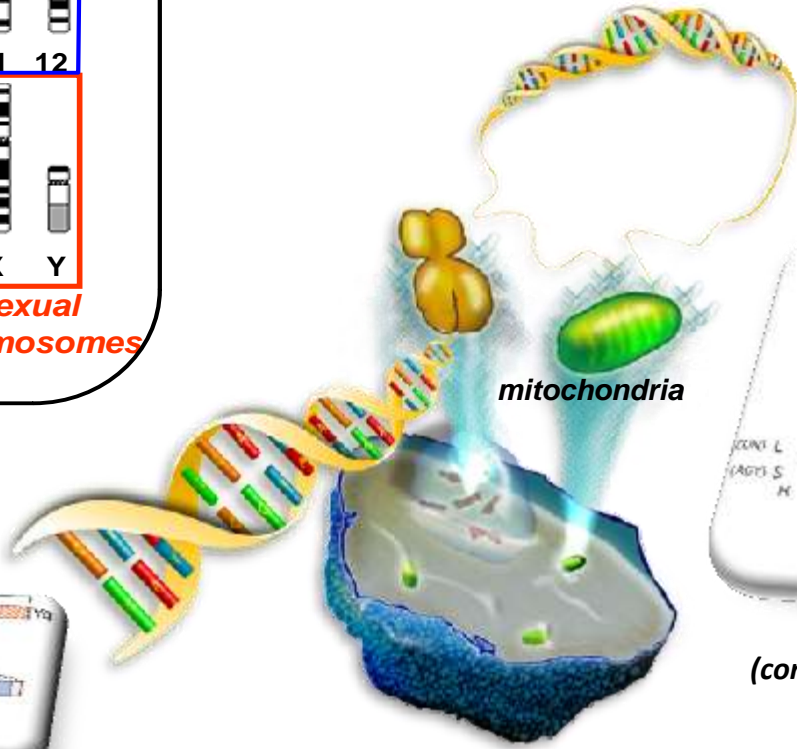


("completely" sequenced in 2001)



Y-Chromosome
(54 Mb in humans)

**Uniparental genetic systems
in mammals**

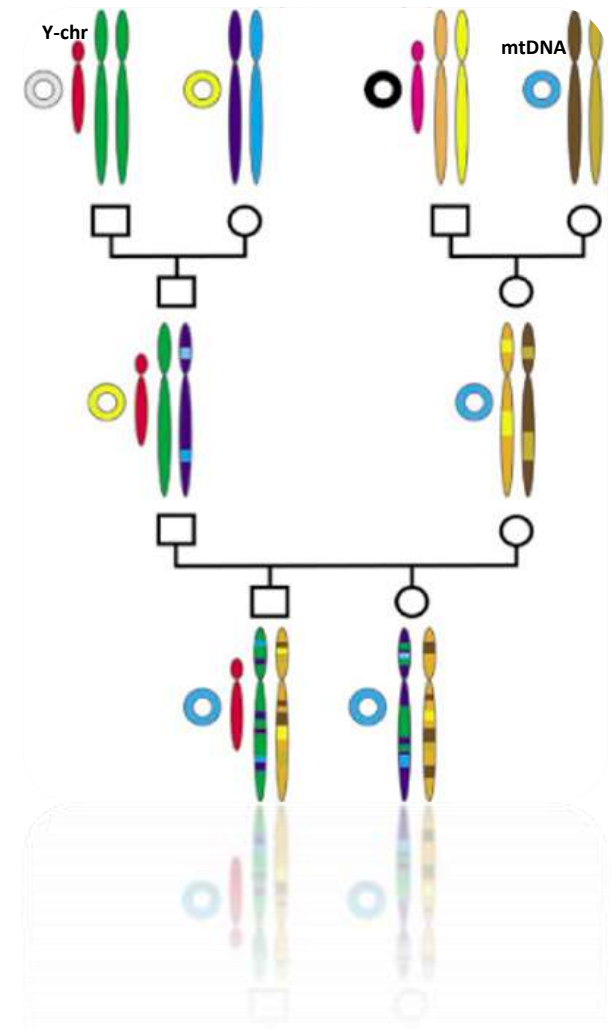


(completely sequenced in 1981)

MtDNA
(16.6 Kb in humans)

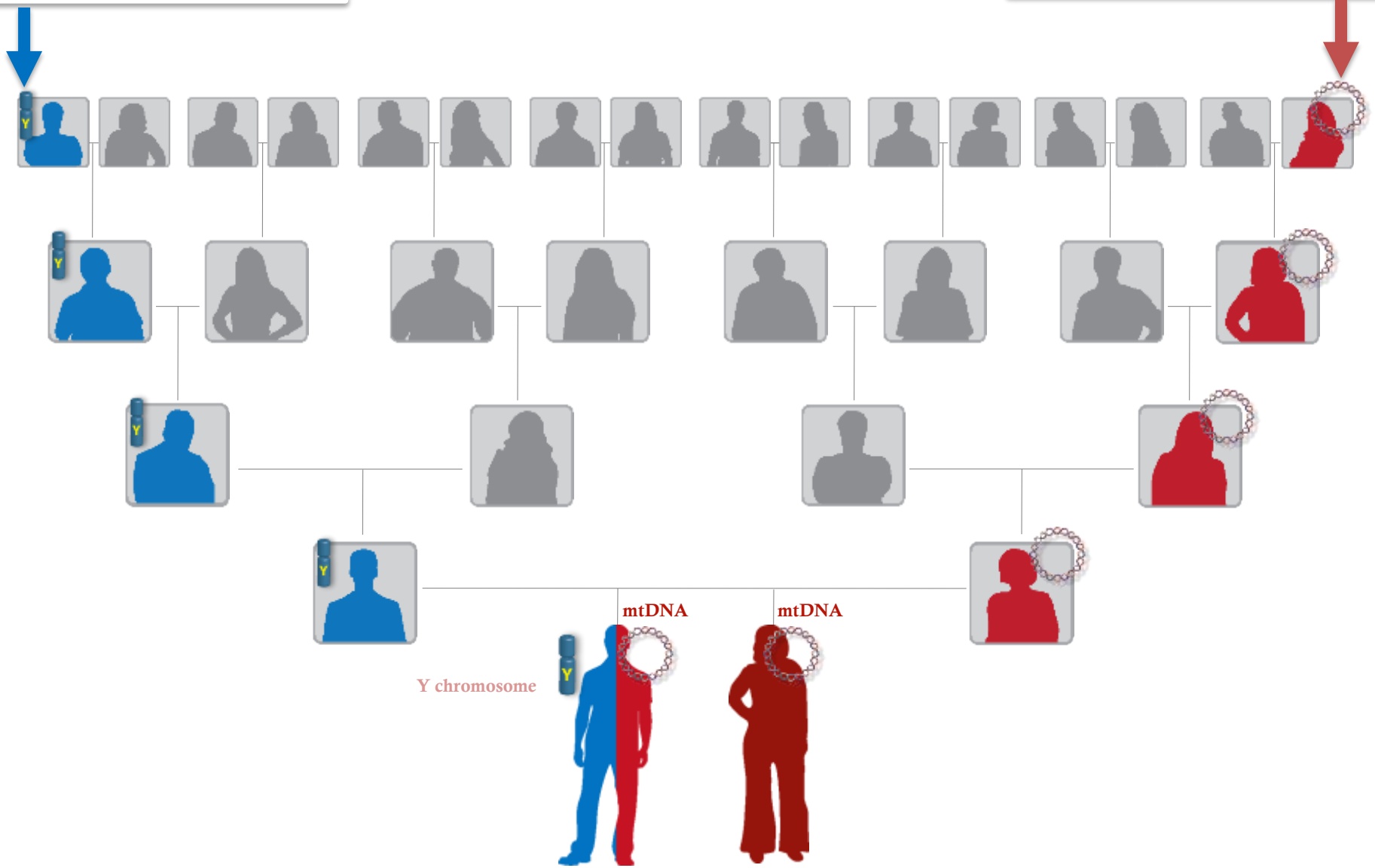
Why are uniparental markers employed?

- Uniparental transmission
- Not reshuffled by meiotic recombination



Ancestral Y-Chr

Ancestral mtDNA



Why are uniparental markers employed?

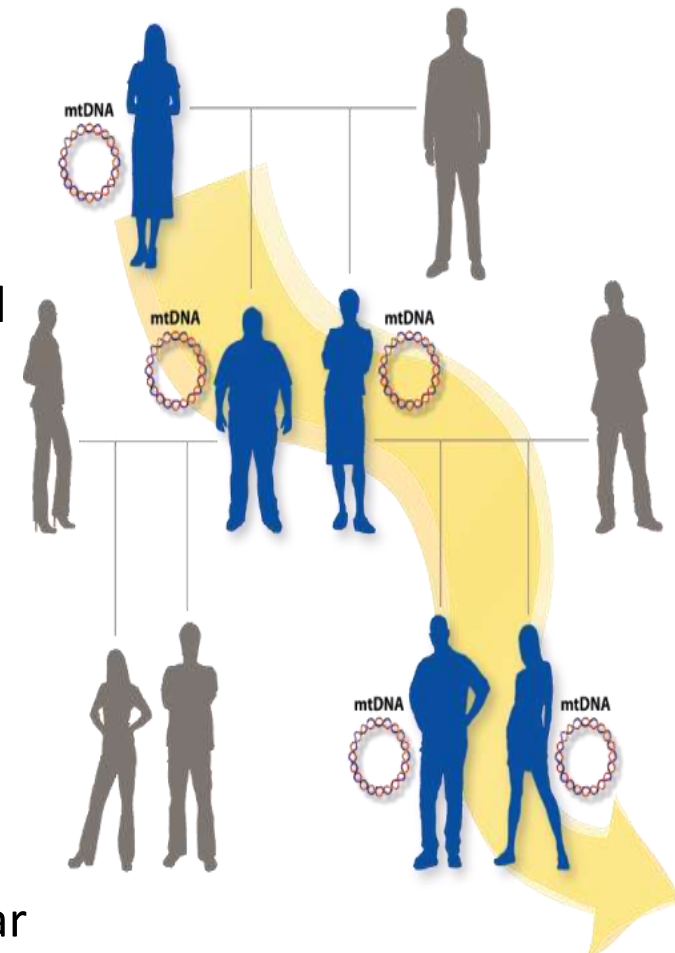
- Uniparental transmission
- Not reshuffled by meiotic recombination



- Their molecular differentiation has been generated only by the sequential accumulation of new mutations along strict maternal and paternal lines of descent, while populations spread through regions and continents



- Over the course of time, this process of molecular divergence has given rise to monophyletic units (***haplogroups***) that tend to be restricted to particular geographic locations and population groups



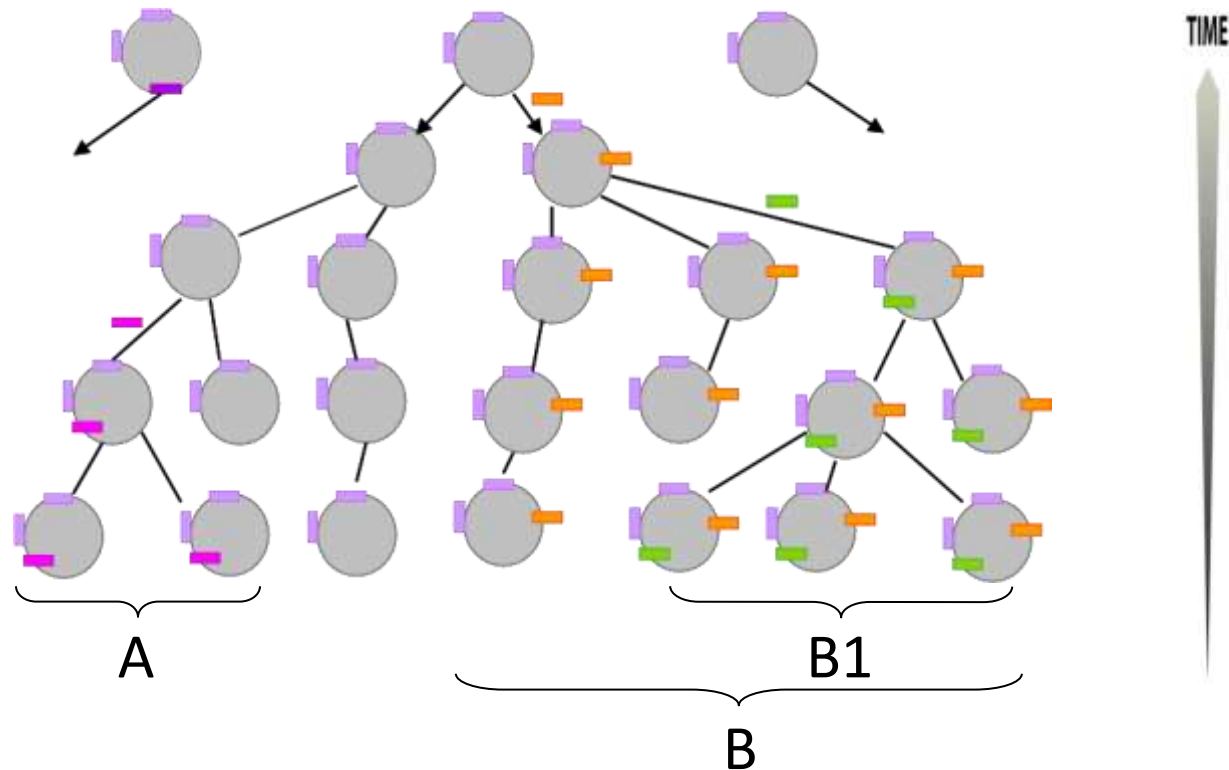
What is a (mtDNA) haplogroup?

Haplogroup = Haplotype Group

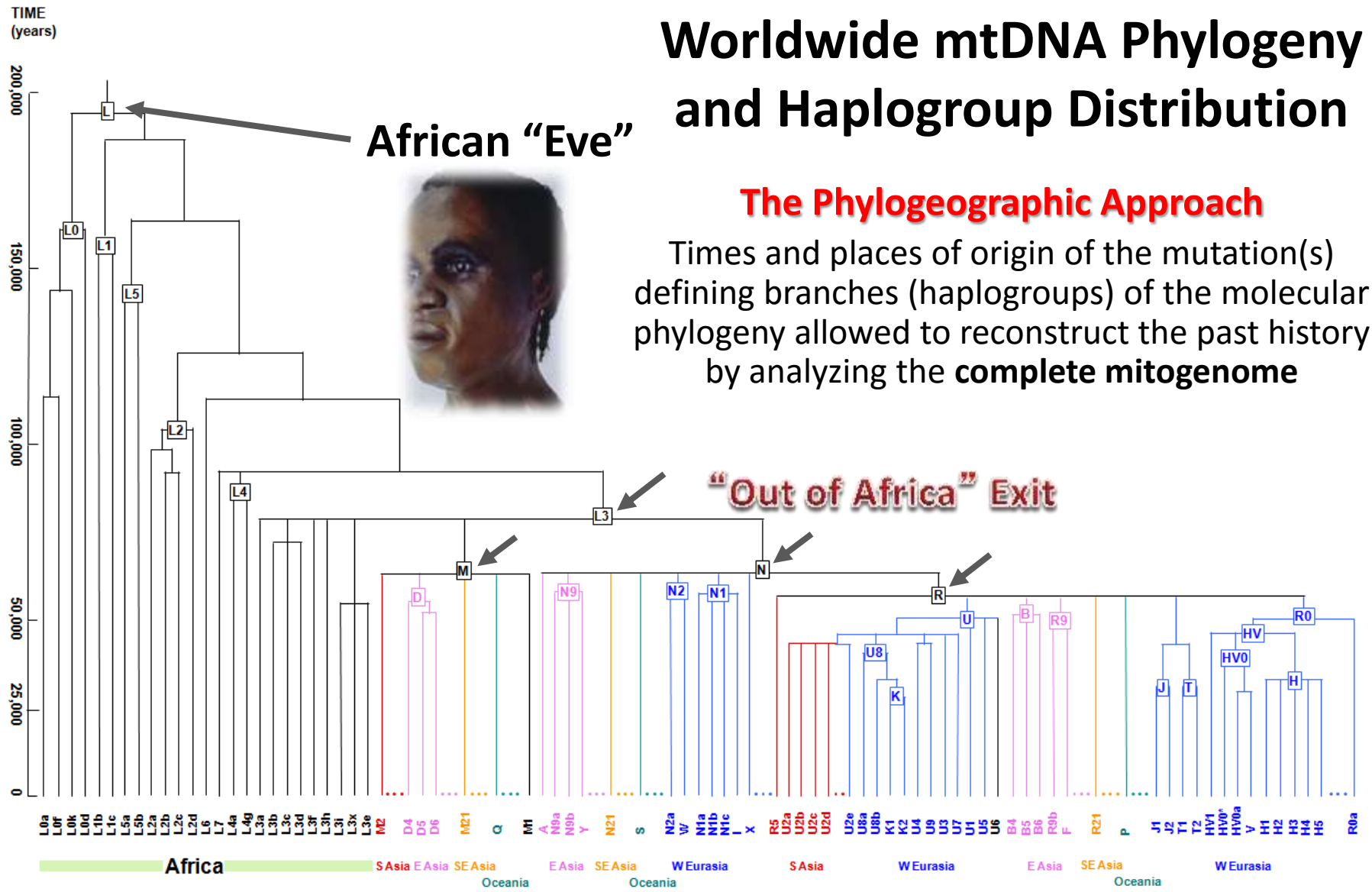
Asian Affinities and Continental Radiation of the Four Founding Native American mtDNAs

Torroni et al. Am J Hum Genet 53: 563-590 (1993)

A group of mtDNAs which are defined by a unique set of variants acquired from the same common ancient (female) ancestor



Worldwide mtDNA Phylogeny and Haplogroup Distribution



(modified from Olivieri, Achilli et al. 2006, Science)



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Tema strategico di Ateneo
Verso una governance del fenomeno migratorio



YOU CAME



FROM HERE!



**“Out of Africa” Exit:
Which Way?**

60-70 Kya

N,R (~45.000 ya)

...and BACK AGAIN

The mtDNA Legacy of the Levantine Early Upper Palaeolithic in Africa

Anna Olivieri,¹ Alessandro Achilli,¹ Maria Pala,¹ Vincenza Battaglia,¹ Simona Fornarino,¹ Nadia Al-Zahery,^{1,2} Rosaria Scozzari,³ Fulvio Cruciani,³ Doron M. Behar,⁴ Jean-Michel Dugoujon,⁵ Clotilde Coudray,⁵ A. Silvana Santachiara-Benerecetti,¹ Ornella Semino,¹ Hans-Jürgen Bandelt,⁶ Antonio Torroni^{1*}

www.sciencemag.org SCIENCE VOL 314 15 DECEMBER 2006

M,N,R (~60.000 ya)

Out of Africa

Southern route

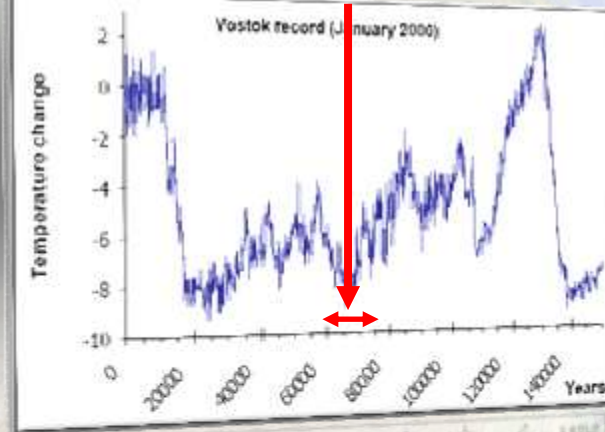
L3 → M,N → R (~70.000 ya)

ONE local source population

L3 (~83.000 ya)

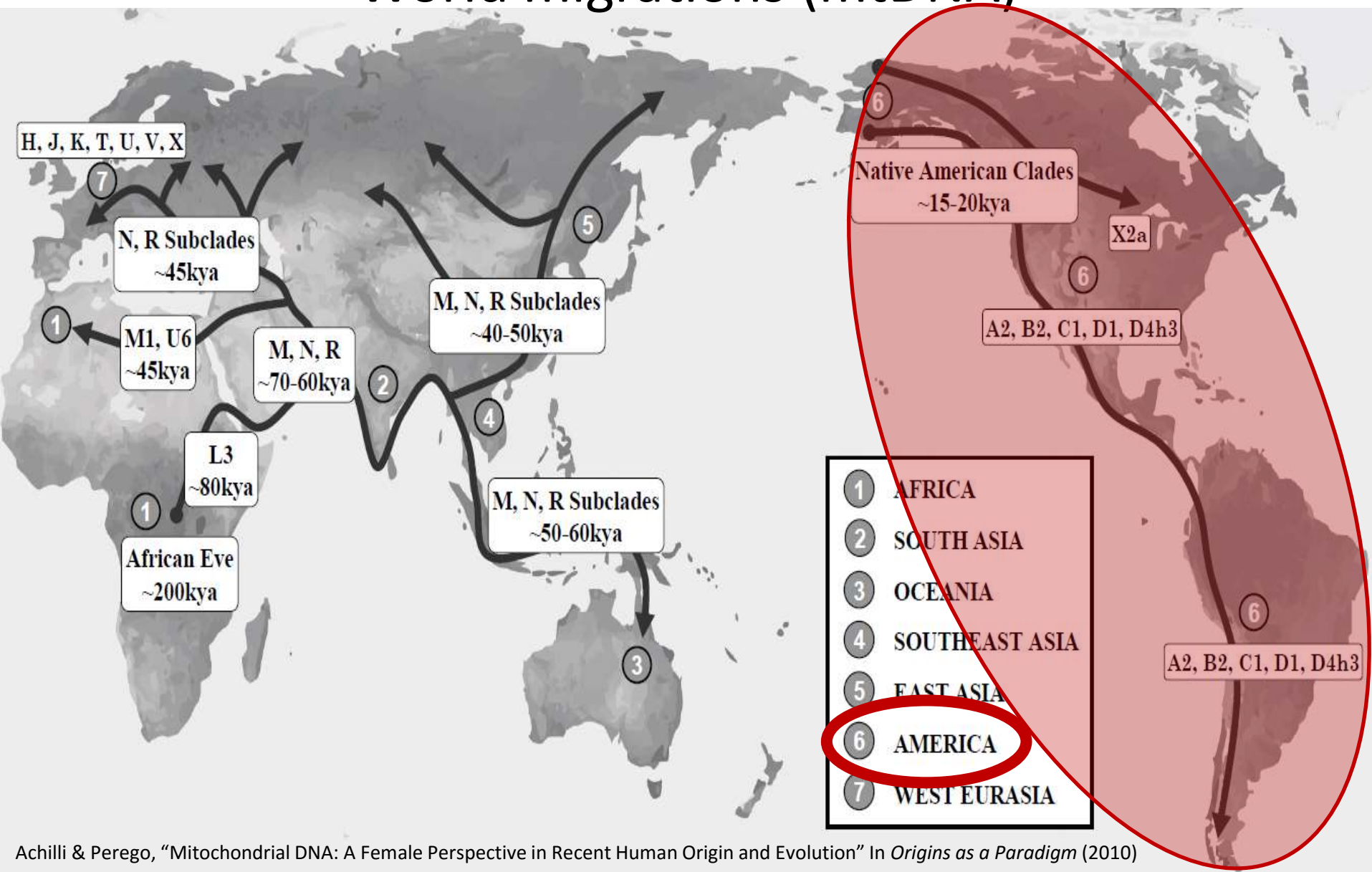
Single, Rapid Coastal Settlement of Asia Revealed by Analysis of Complete Mitochondrial Genomes

Vincent Macaulay,^{1*} Catherine Hill,² Alessandro Achilli,³ Chiara Rengo,³ Douglas Clarke,² William Meehan,² James Blackburn,² Ornella Semino,³ Rosaria Scozzari,⁴ Fulvio Cruciani,⁴ Adi Taha,⁵ Norazila Kassim Shaari,⁶ Joseph Maripa Raja,⁶ Patimah Ismail,⁶ Zafarina Zainuddin,⁷ William Goodwin,⁸ David Bulbeck,⁹ Hans-Jürgen Bandelt,¹⁰ Stephen Oppenheimer,¹¹ Antonio Torroni,³ Martin Richards^{12*}





World migrations (mtDNA)





into The Americas...

Genetics

Linguistics

Archaeology

From where did they arrive?

Who were Native Americans?

When?

What migratory routes did they follow?

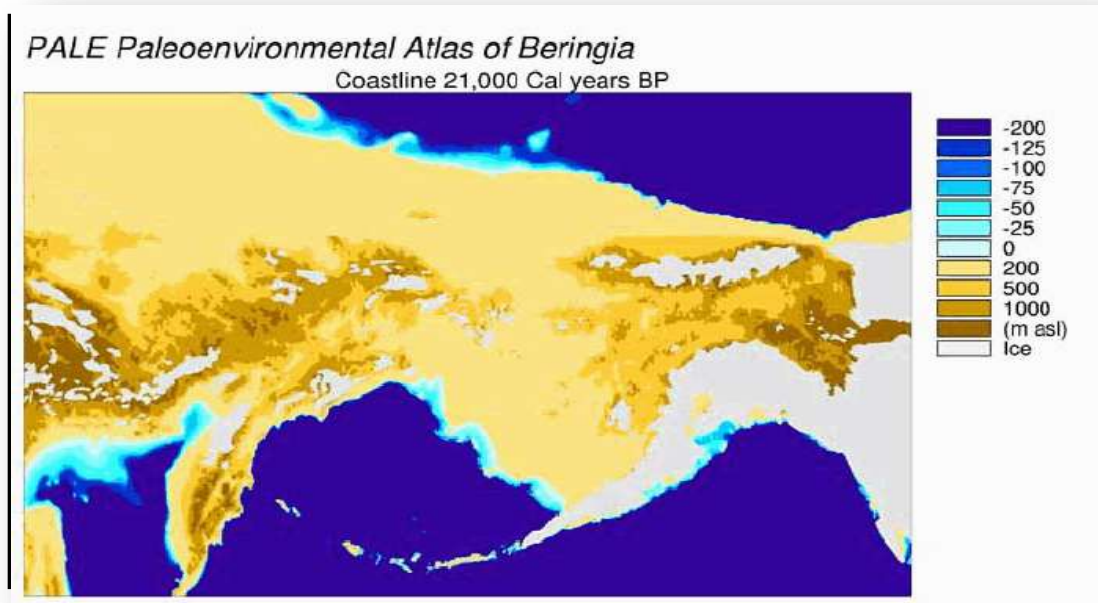
Anthropology

Climatology

The Americas: the continent most recently colonized by humans

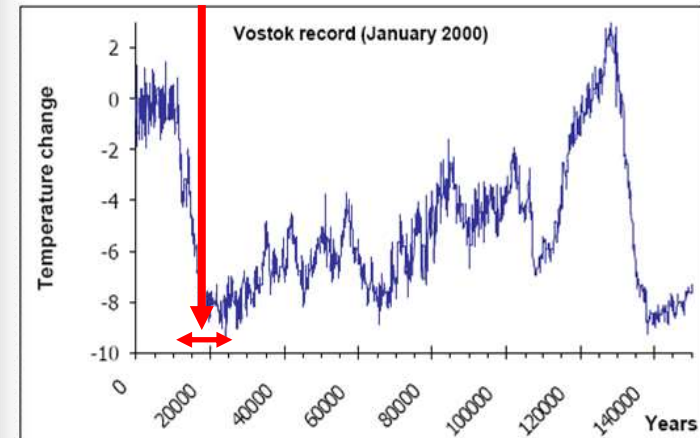
From where did they arrive?

Climatology



Bridging the gap!!!

Temperature Changes

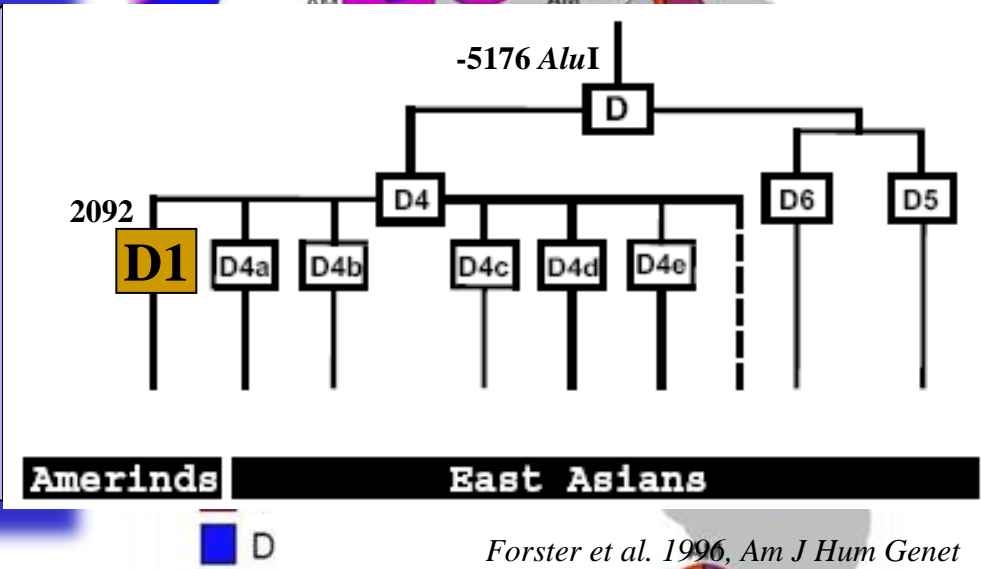
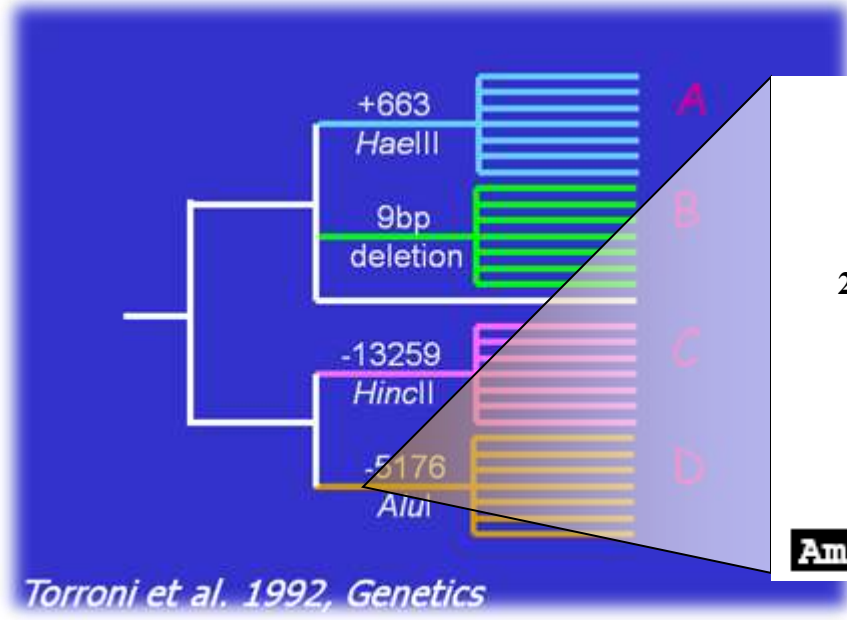
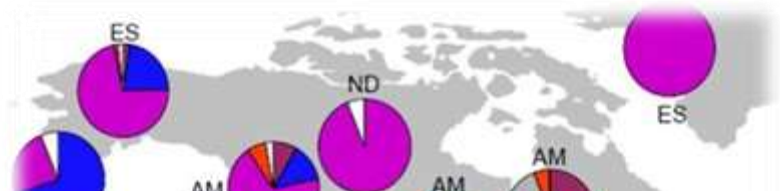


Last Glacial Maximum (~20kya)

Starting from ~35,000 ya the whole Siberian subcontinent was vastly enlarged in the northeast due to lower levels of the Bering and Chukchi Sea, creating the Beringian subcontinent in the ice-free part connecting Siberia and Alaska, permitting human migrations into the New World.

Who were Native Americans?

The Asian connection



More than 95% of living Native Americans belong to four clades, which can be considered "pan-American"
 (A,B,C,D then renamed A2, B2, C1,D1)

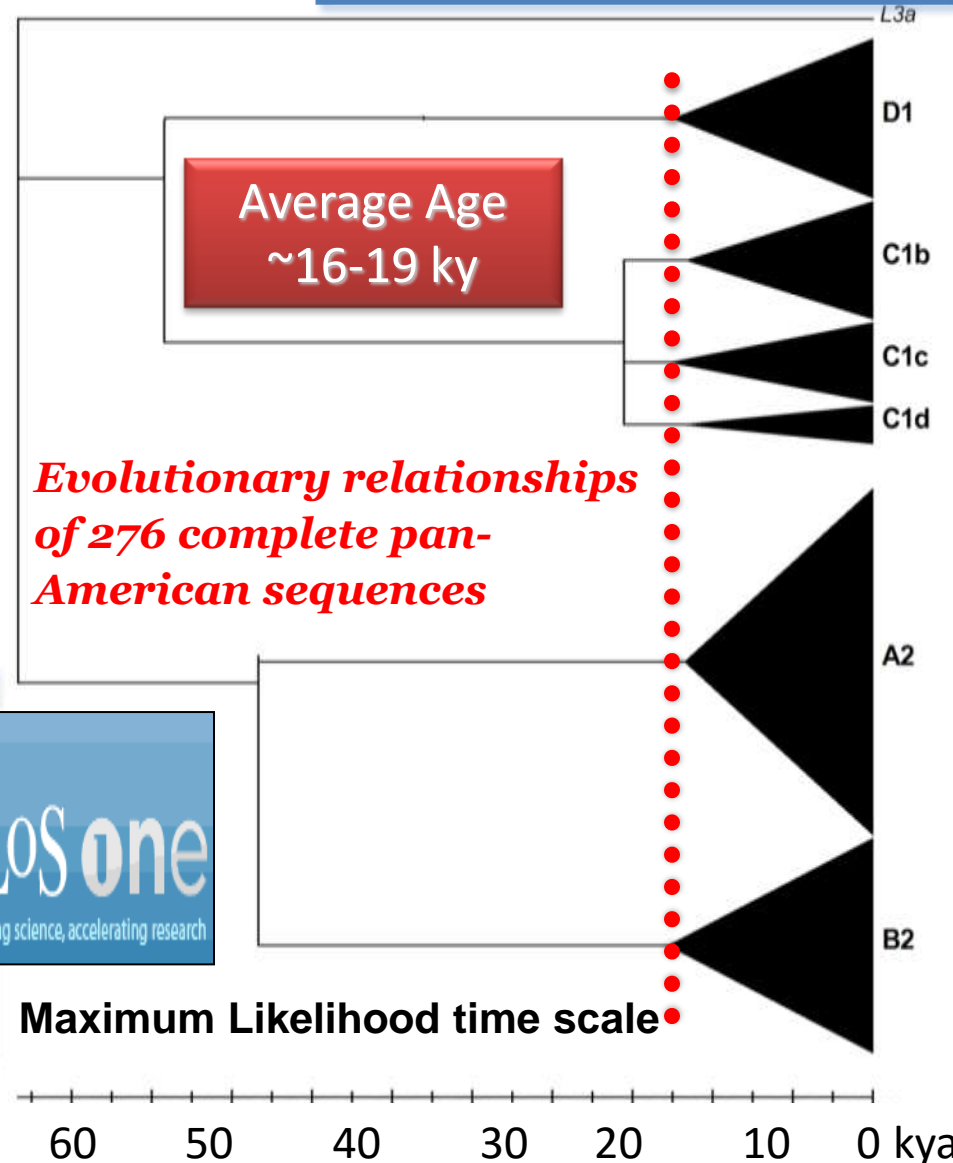
The "Native American" haplogroups are nested within a tree of East Asian mtDNA haplogroups



When did they arrive?

Conclusion (?)

- The estimated age divergence of the pan-American clades are quite similar (~16-19 ky)
- They entered together into the Americas, possibly right after the peak of the LGM



RESEARCH ARTICLE

The Phylogeny of the Four Pan-American MtDNA Haplogroups: Implications for Evolutionary and Disease Studies

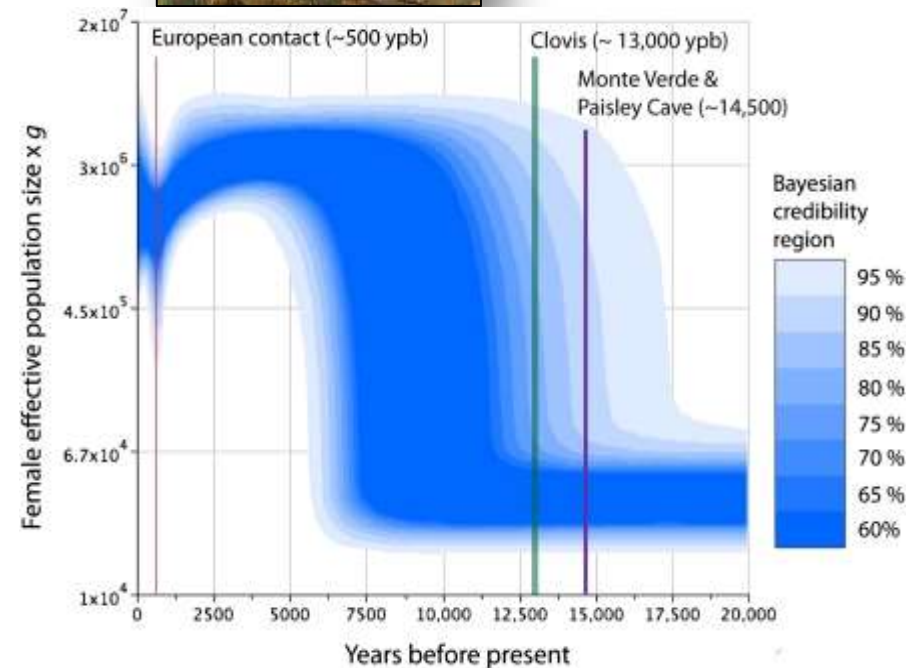
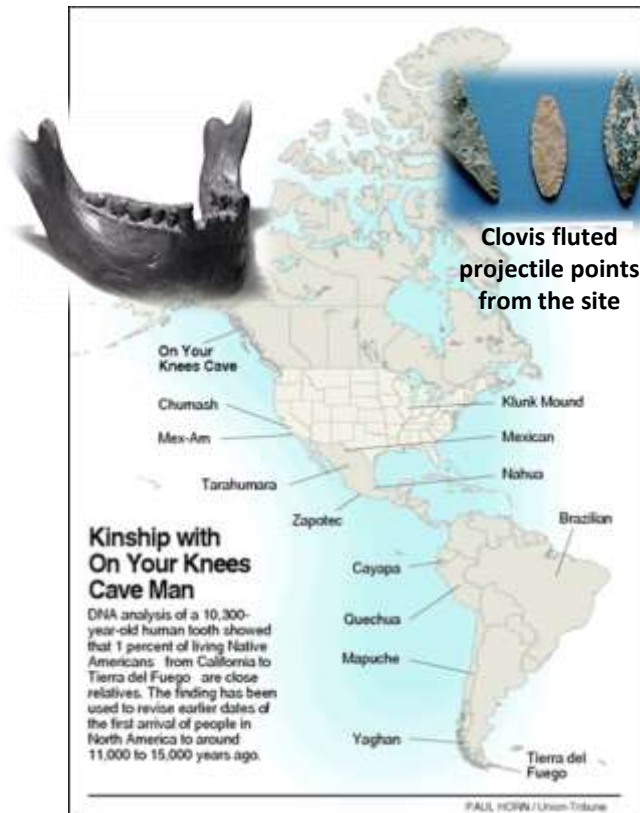
2008



Alessandro Achilli^{1,2}, Ugo A. Perego^{1,3}, Claudio M. Bravi⁴, Michael D. Coble⁵, Qing-Peng Kong^{6,7}, Scott R. Woodward³, Antonio Salas⁸, Antonio Torroni^{1*}, Hans-Jürgen Bandelt²

The importance of being rare!!!

- Later, additional rare haplogroups were discovered, which are restricted only to some Native American populations or geographic areas, e.g. **X2a and D4h3**



Bayesian skyline plot of female effective population size was reduced by ~50%.



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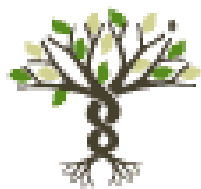
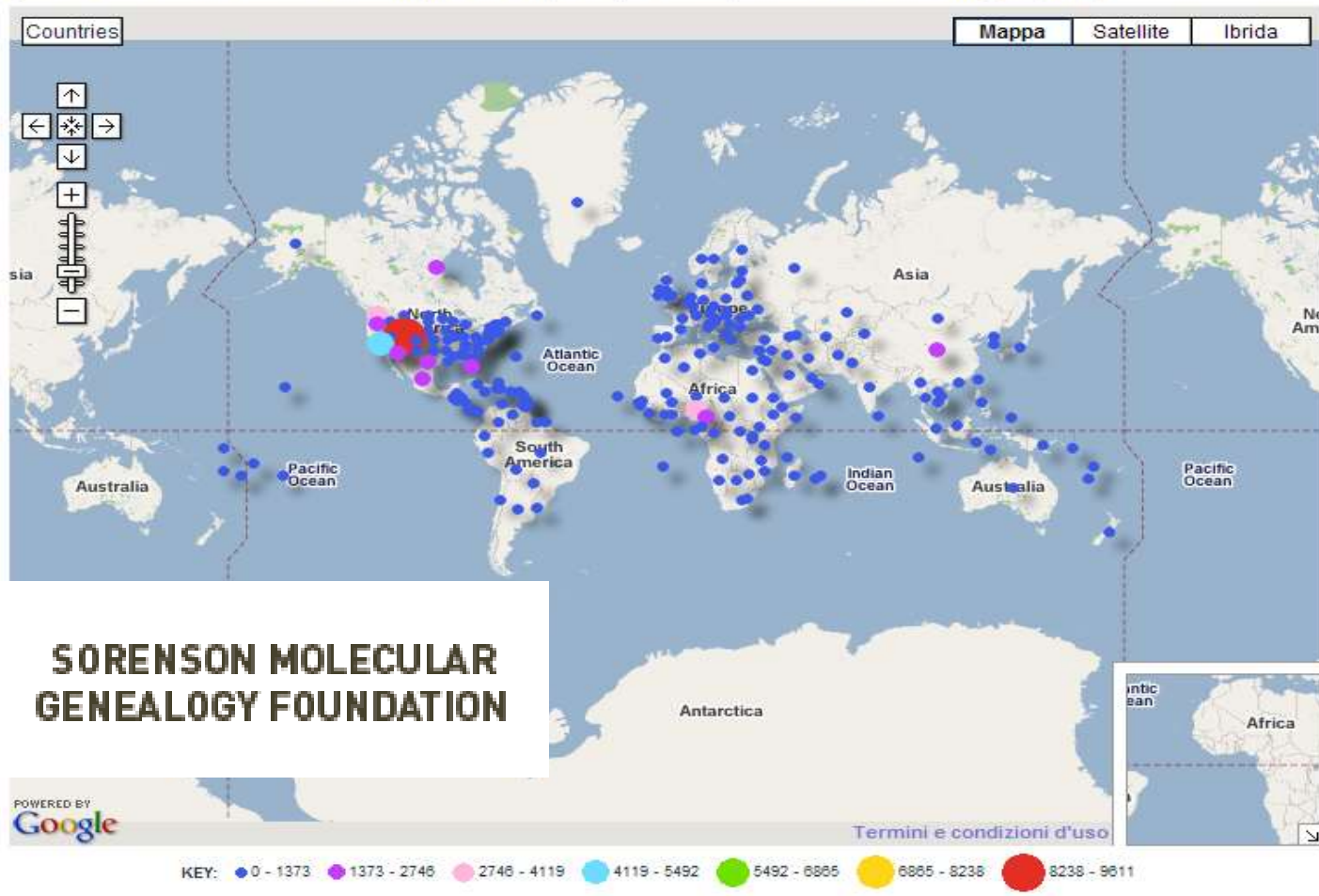
Tema strategico di Ateneo
Verso una governance del fenomeno migratorio



Sample Collection Map

www.SMGF.org

SMGF is committed to building a database that is truly global. Click on the dots below to view the number of samples collected in particular locations. To assist in collecting more samples in your area, please contact us at info@smgf.org.



SORENSEN MOLECULAR
GENEALOGY FOUNDATION

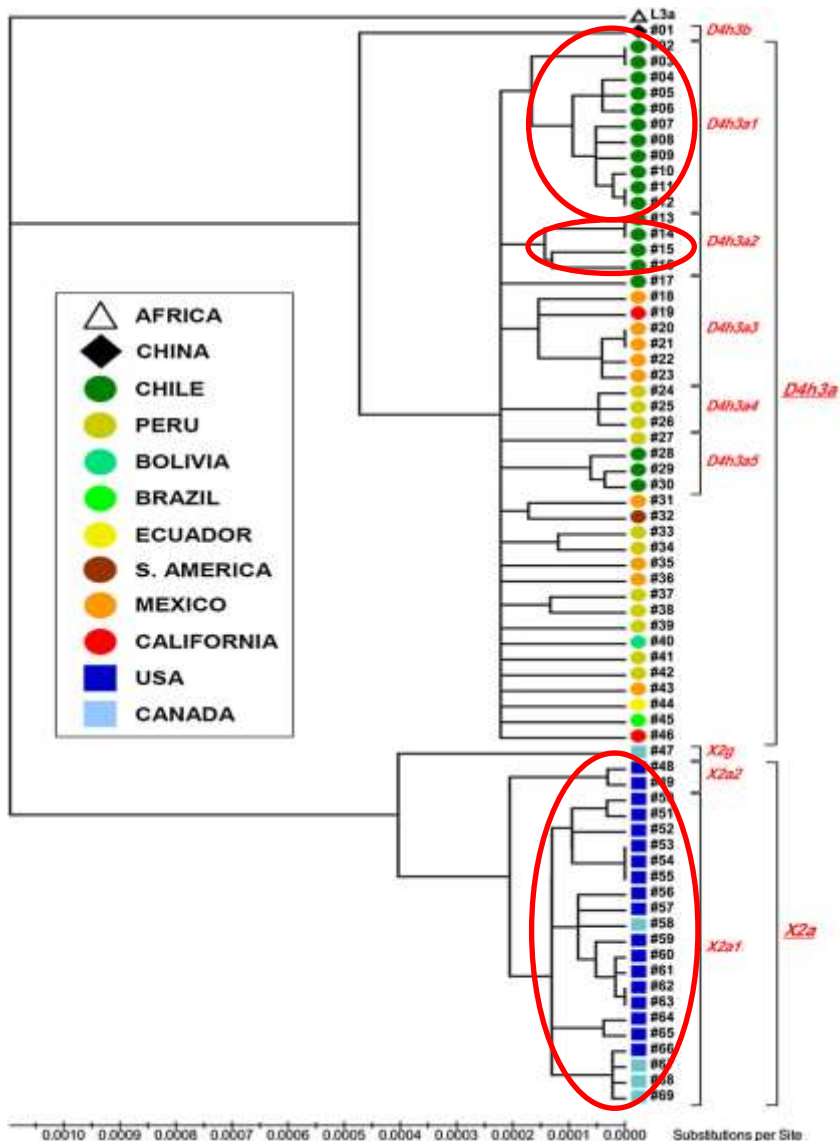
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[Termini e condizioni d'uso](#)

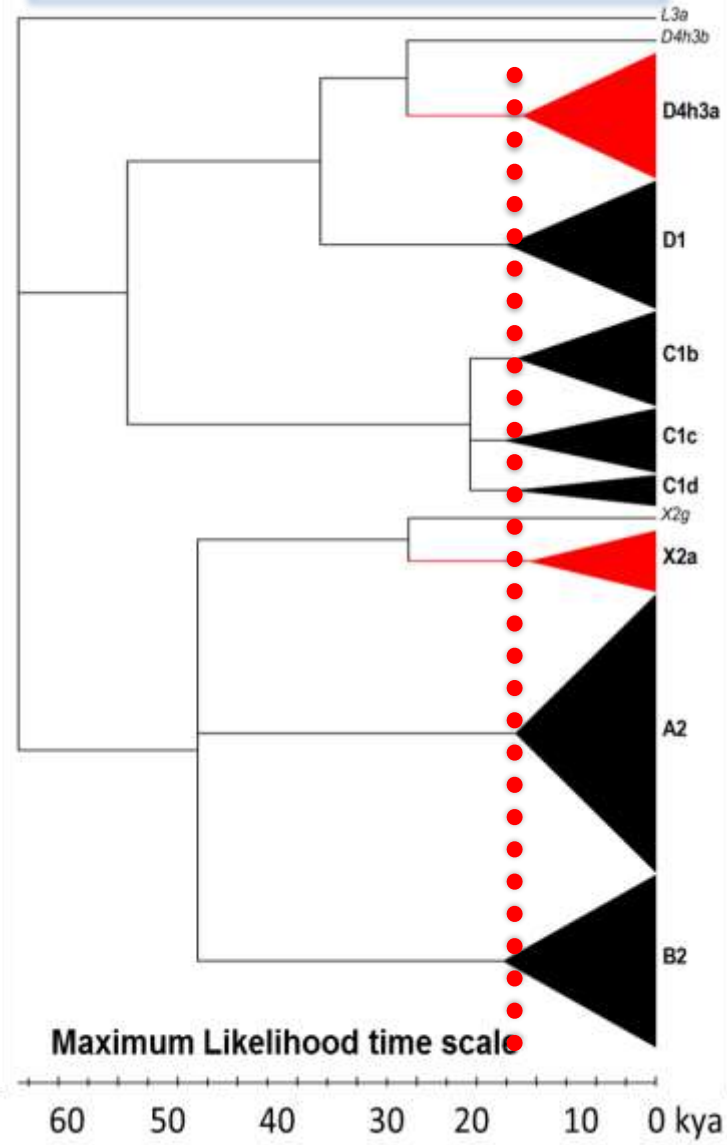
~110,000 DNA samples representing 117 countries



46 D4h3 & 23 X2a mtDNAs



When did they arrive?

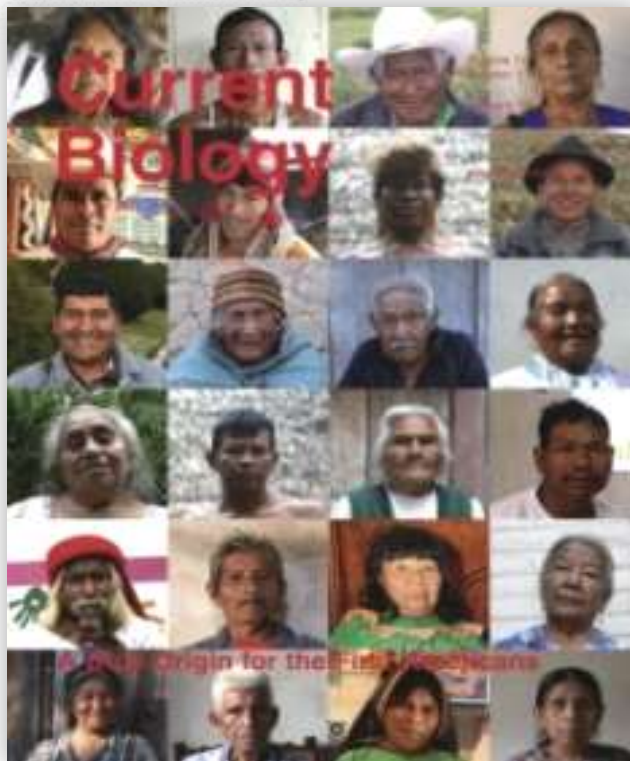




Distinctive Paleo-Indian Migration Routes from Beringia Marked by Two Rare mtDNA Haplogroups

What migratory routes did they follow?

Ugo A. Perego,^{1,2,9} Alessandro Achilli,^{1,3,9}
Norman Angerhofer,² Matteo Accetturo,¹ Maria Pala,¹
Anna Olivieri,¹ Baharak Hooshiar Kashani,¹
Kathleen H. Ritchie,² Rosaria Scozzari,⁴ Qing-Peng Kong,^{5,6}
Natalie M. Myres,² Antonio Salas,⁷ Ornella Semino,¹
Hans-Jürgen Bandelt,⁸ Scott R. Woodward,²
and Antonio Torroni^{1,*}



LETTER

doi:10.1038/nature13025

The genome of a Late Pleistocene human from a Clovis burial site in western Montana

Morten Rasmussen^{1*}, Sarah L. Anzick^{2,8}, Michael R. Waters³, Pontus Skoglund⁴, Michael DeGiorgio^{1,4}, Thomas W. Stafford Jr^{1,4}, Simon Rasmussen⁷, Ida Moltke^{6,9}, Anders Albrechtsen⁵, Shane M. Doyle¹⁰, G. David Poznik¹¹, Valborg Gudmundsdottir⁷, Rachita Yadav⁷, Anna-Sapfo Malaspinas¹, Samuel Stockton White V¹², Morten E. Allentoft¹, Omar E. Cornejo¹³, Kristina Tambets¹⁴, Anders Eriksson^{15,16}, Peter D. Heintzman¹⁷, Monika Karmin¹⁸, Thorfinn Sand Kornelussen¹, David J. Meltzer¹⁹, Tracey L. Pierre¹, Jesper Stenderup¹, Lauri Saag¹⁴, Vera M. Warmuth^{10,19}, Margarida C. Lopes¹⁹, Ripan S. Malhi²⁰, Soren Brunak², Thomas Sicheritz-Ponten¹, Ian Barnes^{17,1}, Matthew Collins²¹, Ludovic Orlando¹, Francois Balloux²², Andrea Manica¹⁵, Rammeek Gupta², Mait Metspalu²³, Carlos D. Bustamante^{21,24}, Mattias Jakobsson^{4,25}, Rasmus Nielsen⁵ & Eske Willerslev¹

13 FEBRUARY 2014 | VOL 506 | NATURE | 225

LETTER

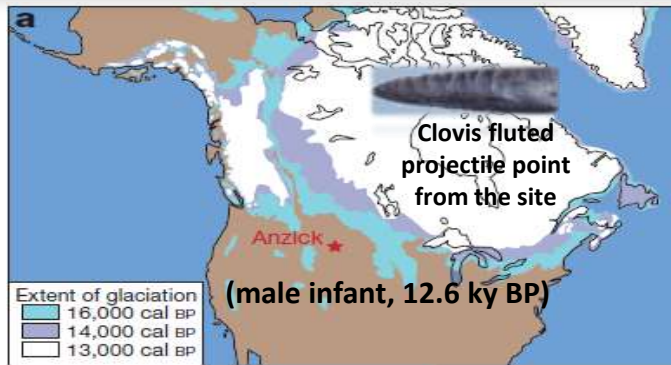
OPEN

doi:10.1038/nature14625

The ancestry and affiliations of Kennewick Man

Morten Rasmussen^{1,2}, Martin Sikora^{3*}, Anders Albrechtsen^{5*}, Thorfinn Sand Kornelussen^{1*}, J. Victor Moreno-Mayar^{6*}, G. David Poznik⁴, Christoph P. E. Zöllikofer⁷, Marcia S. Ponce de León⁸, Morten E. Allentoft¹, Ida Moltke⁹, Håkon Jónsson¹⁰, Cristina Valdiosera^{11*}, Ripan S. Malhi¹², Ludovic Orlando¹, Carlos D. Bustamante¹³, Thomas W. Stafford Jr¹⁴, David J. Meltzer¹⁵, Rasmus Nielsen^{1,11} & Eske Willerslev¹

23 JULY 2015 | VOL 523 | NATURE | 455



CONCLUSION: ...Our results are also **consistent with previous models derived from mtDNA**, which imply that Native American populations primarily derive from a single-source population, but that there was a secondary movement to northern North America.

NOTE: mtDNA haplogroup D4h3a.

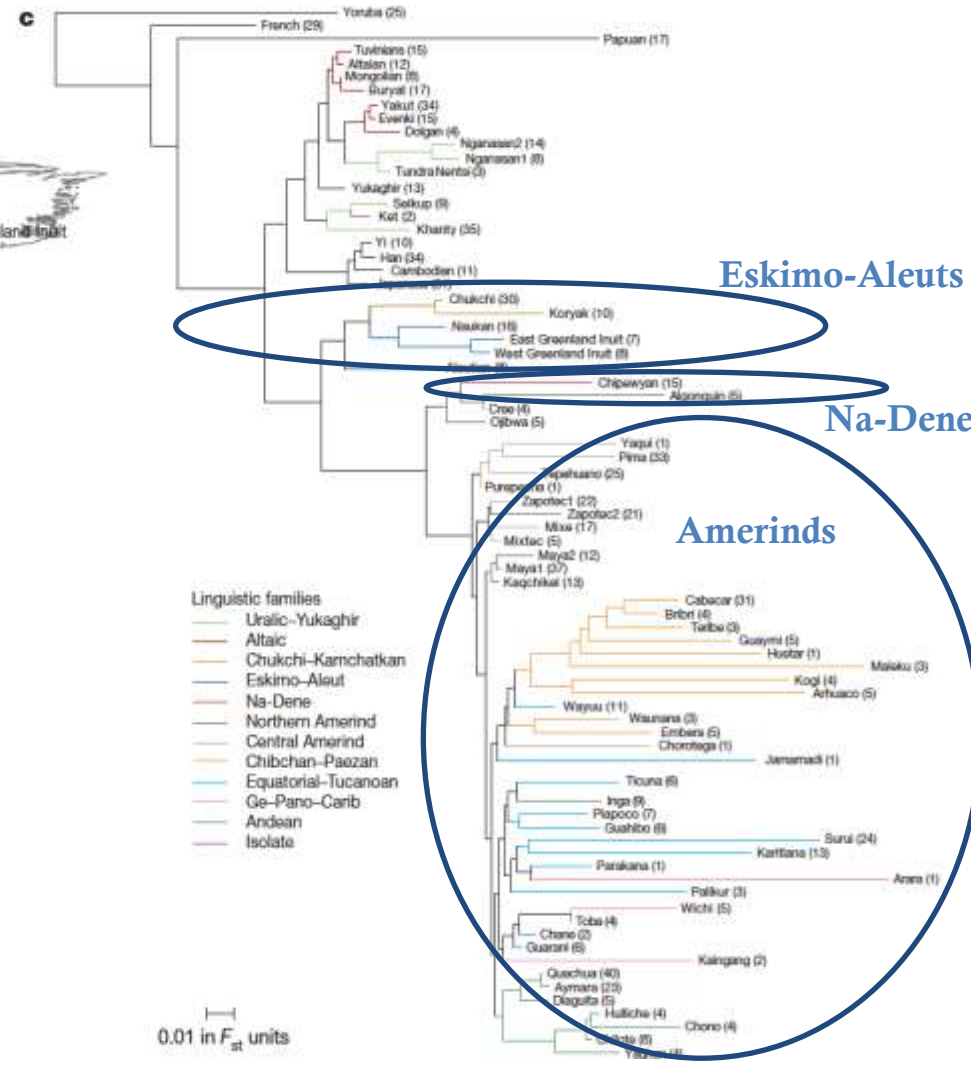
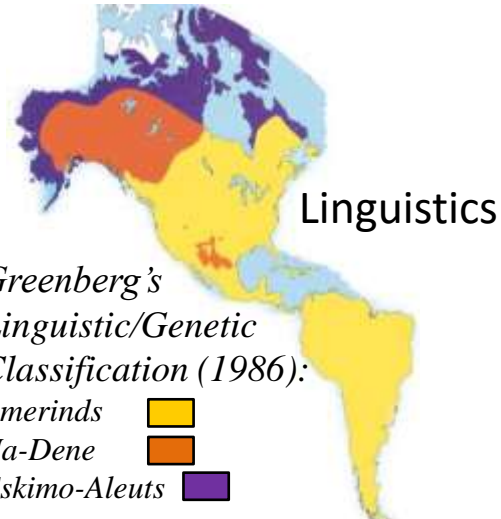
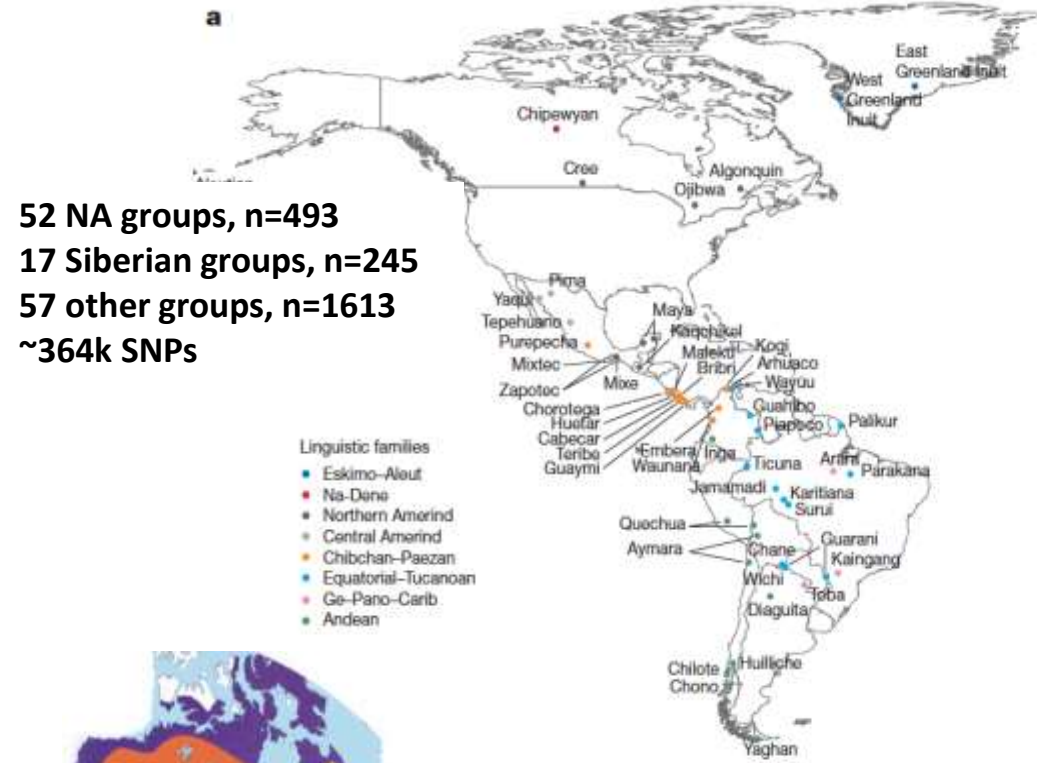


Kennewick Man, referred to as the “Ancient One” by Native Americans, is a male human skeleton discovered in Washington state (USA) in 1996 and initially radiocarbon-dated to 8,340–9,200 years BP.
NB: A very disputed case for repatriation under the Native American Graves Protection and Repatriation Act (NAGPRA)!!

NOTE: mtDNA haplogroup X2a.

Reconstructing Native American population history

David Reich, et al. *Nature* (2012)

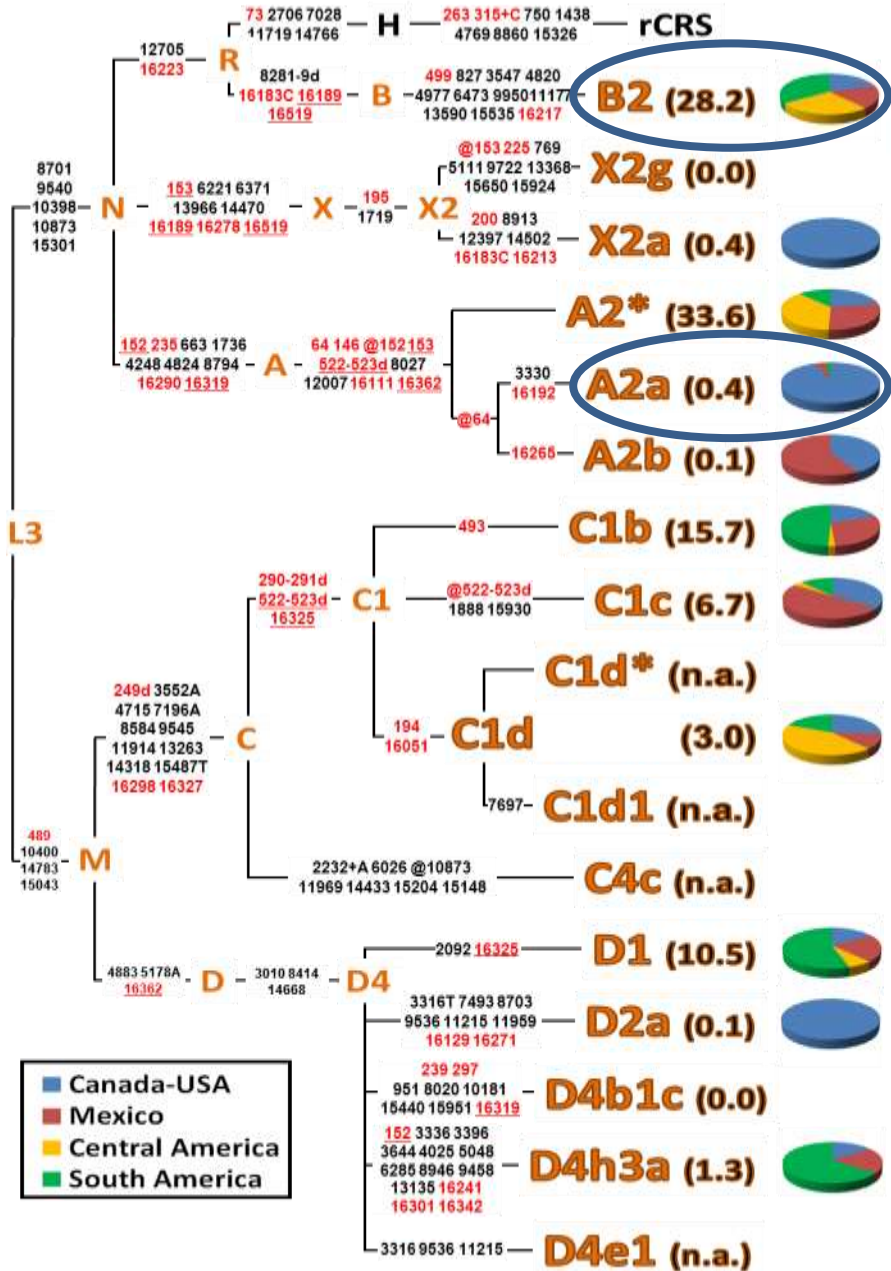


Three distinct lineages (of Asian origin): Eskimo-Aleuts, Na-Dene and Amerinds

...consistent with a three-wave model...

The initial peopling of the Americas: A growing number of founding mitochondrial genomes from Beringia

Ugo A. Perego,^{1,2} Norman Angerhofer,¹ Maria Pala,² Anna Olivieri,² Hovirag Lancioni,³ Baharak Hooshyar Kashani,² Valeria Carossa,² Jayne E. Ekins,¹ Alberto Gómez-Carballa,⁴ Gabriela Huber,⁵ Bettina Zimmermann,⁵ Daniel Corach,⁶ Nora Babudri,³ Fausto Panara,³ Natalie M. Myres,¹ Walther Parson,⁴ Ornella Semino,² Antonio Salas,⁵ Scott R. Woodward,¹ Alessandro Achilli,^{2,3,7,8} and Antonio Torroni^{2,7,8} 2010



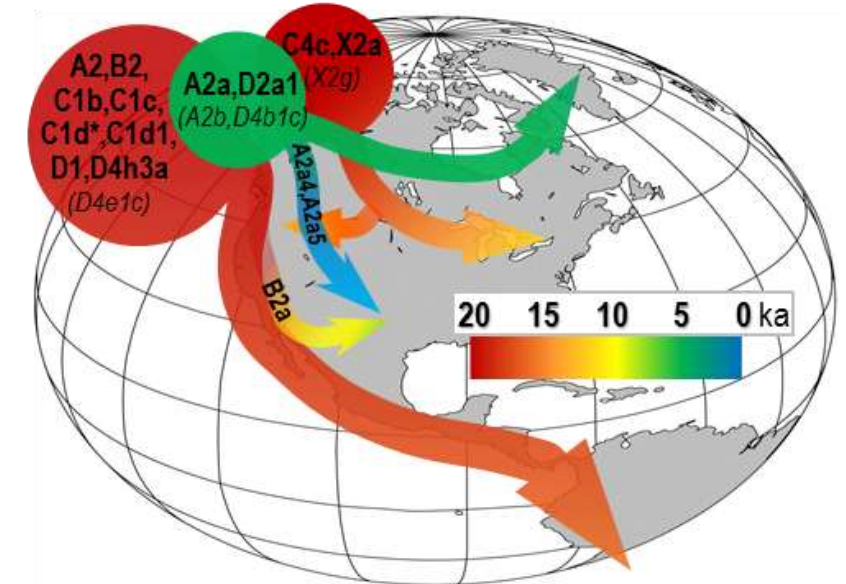
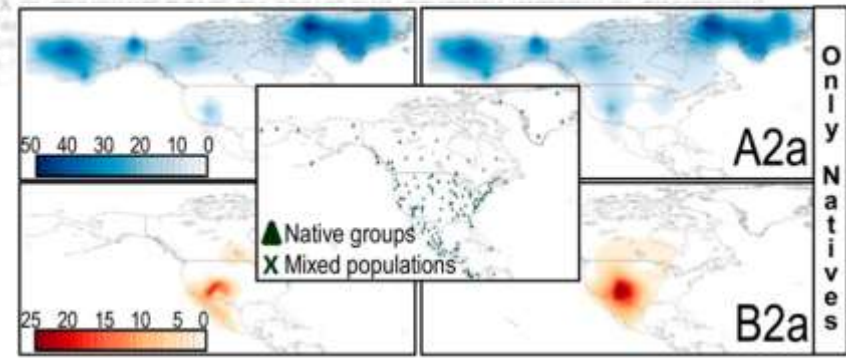
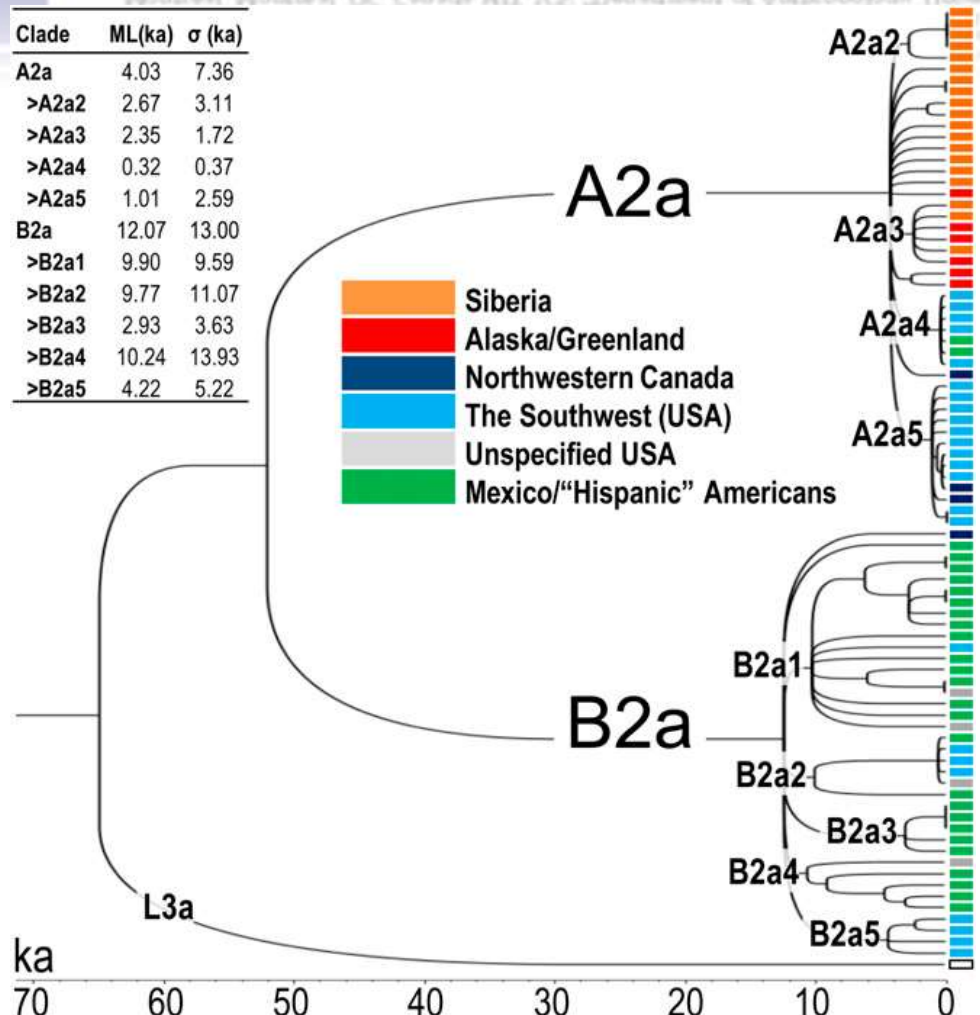
Reconciling migration models to the Americas with the variation of North American native mitogenomes

2013

Alessandro Achilli^{a,1}, Ugo A. Perego^{b,c}, Hovirag Lancioni^a, Anna Olivieri^b, Francesca Gandini^b, Baharak Hooshiar Kashani^b, Vincenza Battaglia^b, Viola Grugni^b, Norman Angerhofer^c, Mary P. Rogers^d, Rene J. Herrera^e, Scott R. Woodward^{c,f}, Damian Labuda^g, David Glenn Smith^h, Jerome S. Cybulskiⁱ, Ornella Semino^b, Ripan S. Malhi^{d,j}, and Antonio Torroni^{b,1}

^aDipartimento di Chimica, Biologia e Biotecnologie, Università di Perugia, 06123 Perugia, Italy; ^bDipartimento di Biologia e Biotecnologie "Lazzaro Spallanzani", Università di Pavia, 27100 Pavia, Italy; ^cSorenson Molecular Genealogy Foundation, Salt Lake City, UT 84115; ^dDepartment of Anthropology and Institute for Genomic Biology, University of Illinois, Champaign, IL 61801; ^eDepartment of Biological Sciences, Florida International University, Miami, FL 33199; ^fAncestryDNA, Provo, UT 84604; ^gDépartement de Pédiatrie, Centre de Recherche du Centre Hospitalier Universitaire Sainte-Justine, Université de Montréal, Montréal, QC, Canada H3T 1C5; ^hDepartment of Anthropology, University of California, Davis, CA 95616; and ⁱCanadian Museum of Civilization, Gatineau, QC, Canada K1A 0M8

Clade	ML(ka)	σ (ka)
A2a	4.03	7.36
>A2a2	2.67	3.11
>A2a3	2.35	1.72
>A2a4	0.32	0.37
>A2a5	1.01	2.59
B2a	12.07	13.00
>B2a1	9.90	9.59
>B2a2	9.77	11.07
>B2a3	2.93	3.63
>B2a4	10.24	13.93
>B2a5	4.22	5.22



The three-wave model is too restrictive!!!



Decrypting the Mitochondrial Gene Pool of Modern Panamanians

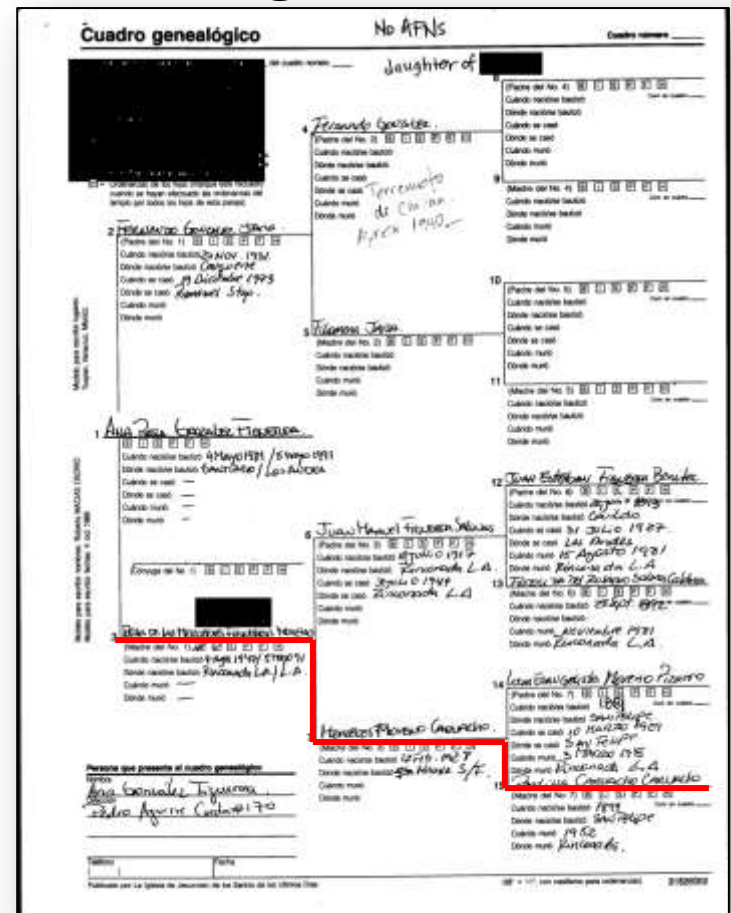
Ugo A. Perego^{1,3}, Hovirag Lancioni^{2,3}, Maribel Tribaldos^{3,7}, Norman Angerhofer^{1,4}, Jayne E. Ekins¹, Anna Olivieri⁵, Scott R. Woodward^{1,4}, Juan Miguel Pascale³, Richard Cooke⁶, Jorge Motta³, Alessandro Achilli^{2*}

Biological Specimen ~1500 samples

collected in collaboration with SMGF (Utah), The Smithsonian Institute and Instituto Conmemorativo Gorgas de Estudios de la Salud (Panama City)



Pedigree Chart



TMA = Terminal Maternal Ancestor

Emberà - Darien



Santa Fe - Darien



Puerto Armuelles - Chiriqui



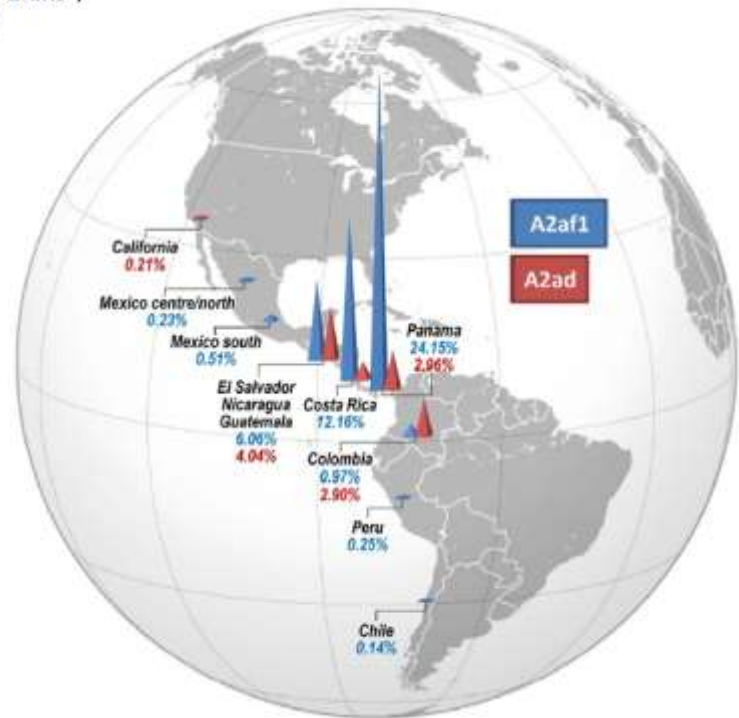
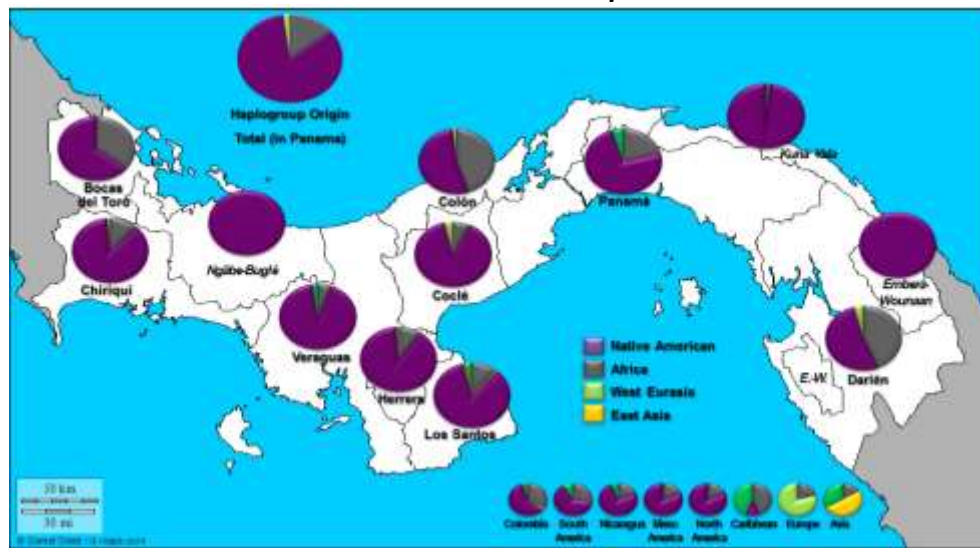
San Felix - Chiriqui



Decrypting the Mitochondrial Gene Pool of Modern Panamanians

Ugo A. Perego^{1,2}, Hovirag Lancioni^{2,3}, Maribel Tribaldos^{3,2}, Norman Angerhofer^{1,4}, Jayne E. Ekins¹, Anna Olivieri⁵, Scott R. Woodward^{1,4}, Juan Miguel Pascale³, Richard Cooke⁶, Jorge Motta³, Alessandro Achilli^{2*}

1565 Panamian samples



AN OVERWHELMING NATIVE AMERICAN LEGACY (84%)
 Last official census: 12.3% identified themselves as Natives
 EXTREMELY LOW EUROPEAN CONTRIBUTION (2%)
 Post-Columbian colonization was mostly male-mediated

Two A2 subclades (A2af1 & A2ad) CONFIRM
 THE MAJOR ROLE OF THE PACIFIC COASTAL PATH
 and testify the antiquity of native mtDNAs in Panama



RESEARCH ARTICLE

Exploring the Y Chromosomal Ancestry of Modern Panamanians

Viola Grugni¹, Vincenza Battaglia¹, Ugo Alessandro Perego^{2,3}, Alessandro Raveane¹, Hovirag Lancioni³, Anna Olivieri¹, Luca Ferretti¹, Scott R. Woodward², Juan Miguel Pascale⁴, Richard Cooke⁵, Natalie Myres^{2,6}, Jorge Motta⁴, Antonio Torroni¹, Alessandro Achilli^{1,2}, Ornella Semino^{1*}

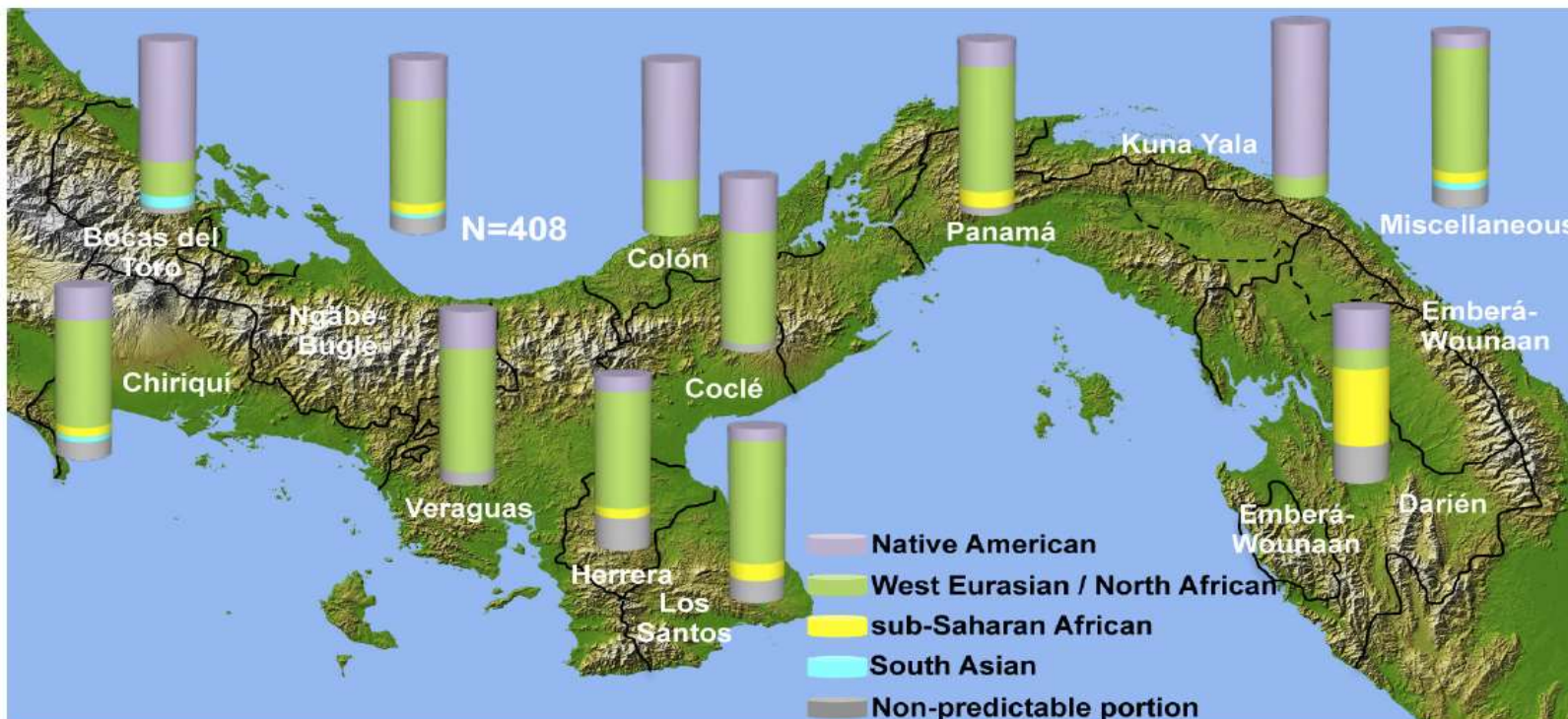
Received: March 31, 2015

Accepted: November 16, 2015

Published: December 4, 2015

Table 3. Y-chromosome components (%) in the Panamanian samples with PGF in Panama.

Province/ Comarca (n. of subjects)	Native American ^a	West Eurasian and North African ^b	sub-Saharan African ^c	South Asian ^d	Non-predictable portion ^e
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Tema strategico di Ateneo
Verso una governance del fenomeno migratorio

ARAM

ArtEmpire

ERC CoG 2014, N. 648535



This interdisciplinary project applies historical, archaeological and genetic methodologies to **evidence of encounters between peoples and goods from Europe, America, Africa and Asia that took place on the Isthmus of Panama during the sixteenth and seventeenth centuries.**

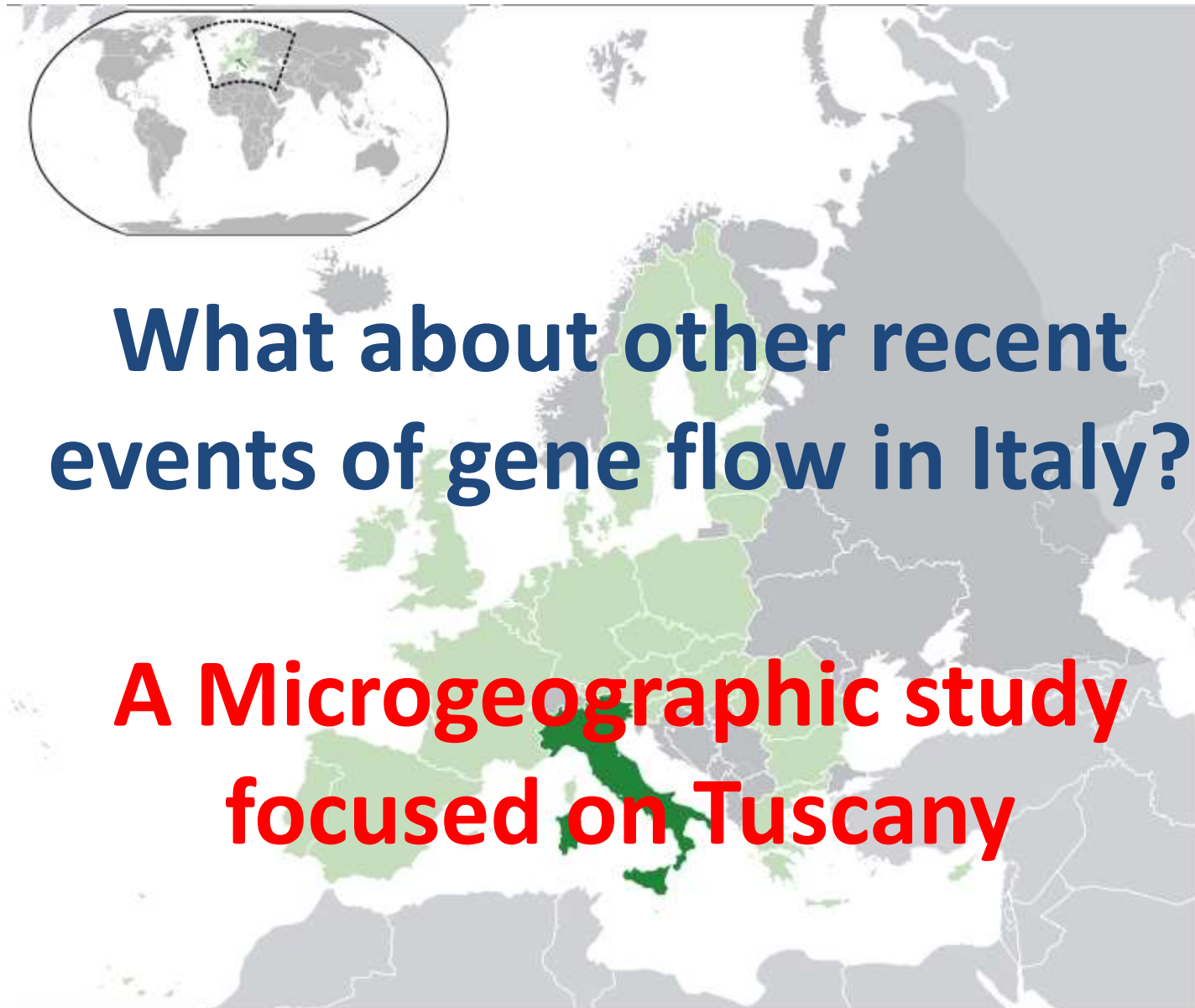
Project Acronym: ArtEmpire
Project Number: 648535
Project Title: "An ARTery of EMPIRE. Conquest, Commerce, Crisis, Culture and the Panamanian Junction (1513-1671)"
Principal Investigator: Bethany ARAM
Host Institution: Universidad Pablo de Olavide (Seville)
Additional Beneficiaries (if applicable): Curt-Engelhorn-Zentrum Archäometrie (Mannheim, Germany); Universidad del Norte (Barranquilla, Colombia)

... Any analysis of DNA must draw upon Dr. Achilli's expertise as one of the few scientists who have studied the genetic mutations in this geographical area....



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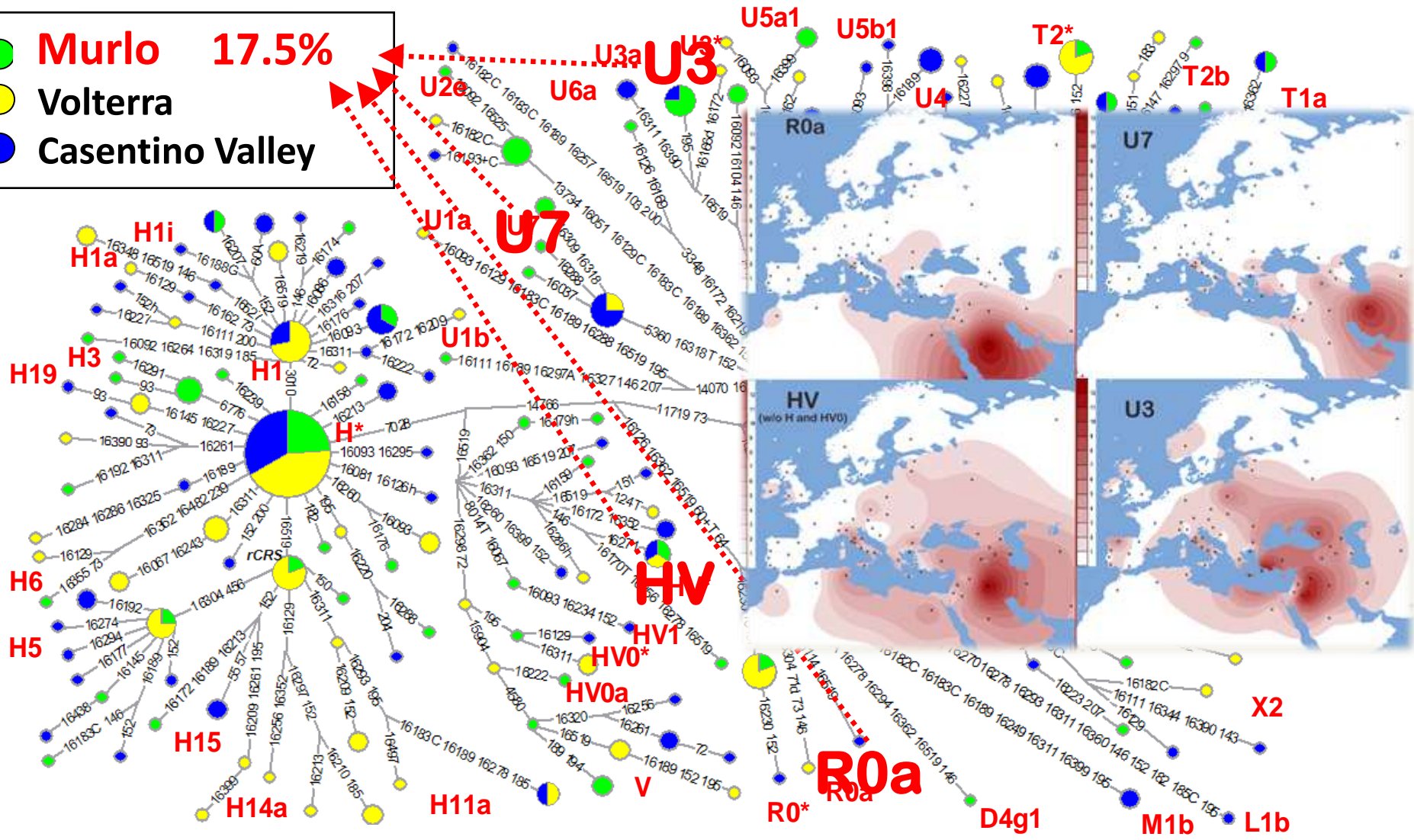
What about other recent events of gene flow in Italy?

A Microgeographic study focused on Tuscany

MtDNA tree of modern Tuscans

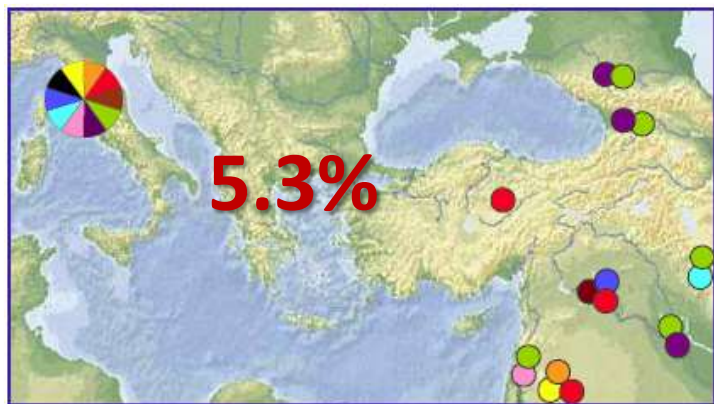
322 campioni → 39 haplogroups

● **Murlo 17.5%**
● **Volterra**
● **Casentino Valley**



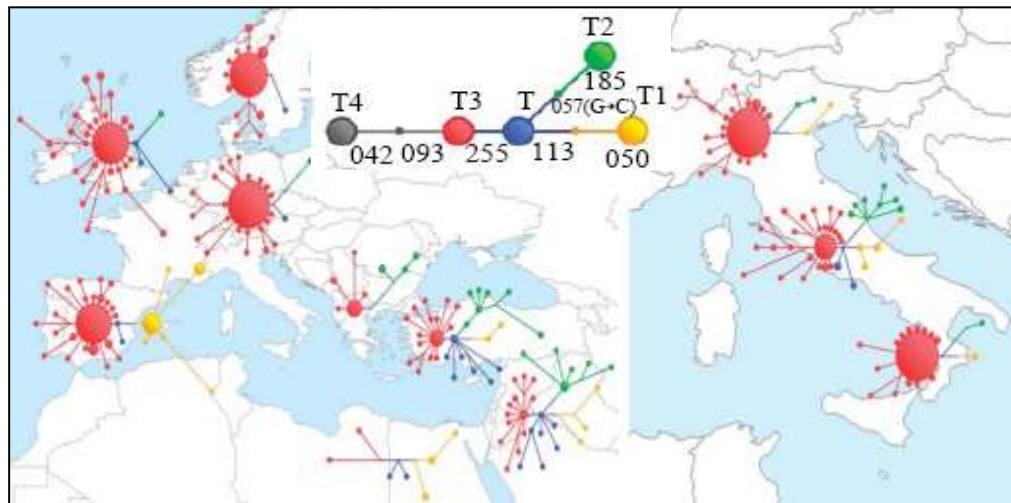


The origin of Etruscans: a parallel genetic history



(Achilli et al. 2007, Am J Hum Genet)

Data on modern Tuscans



(Pellecchia et al. 2007, Proc Biol Sci)

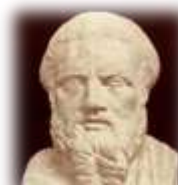
Data on cattle (Maremma and Chianina)

- A direct genetic input from the Near East to the present-day population of Tuscany
- A common past migration: **both humans and cattle** reached Etruria from the Eastern Mediterranean area by sea



A recent genetic link between Tuscany and the Near East

A scenario that is compatible with a Near Eastern origin of Etruscans as suggested by Herodotus (The Histories, c. 430 BCE, I.94)



Human Populations Genetics needs further inputs.....

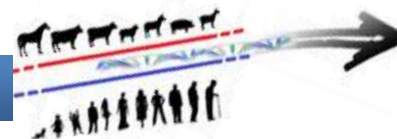


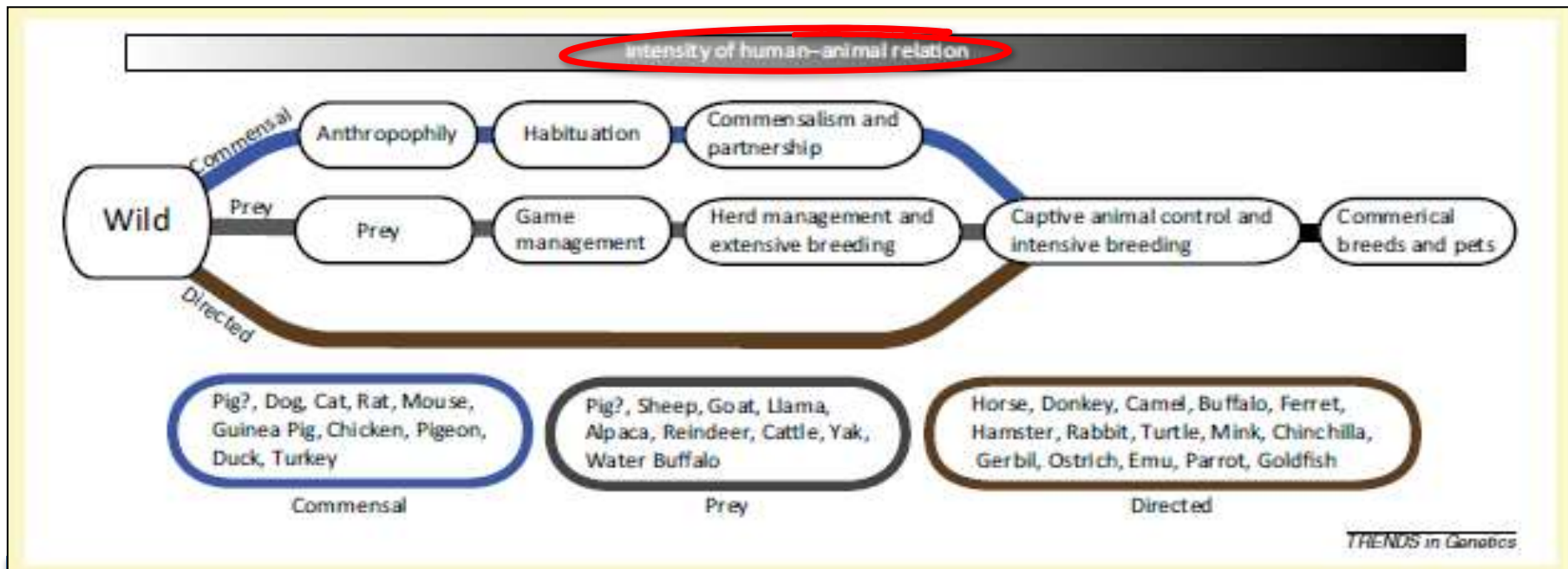
What about trying to reconstruct ...

“The parallel genetic history of humans and domesticated animals”???

Perhaps, the molecular and phylogenetic survey of complete mitogenomes could be also applied to study some livestock species...

FIRB2008: FUTURO IN RICERCA





WHEN?

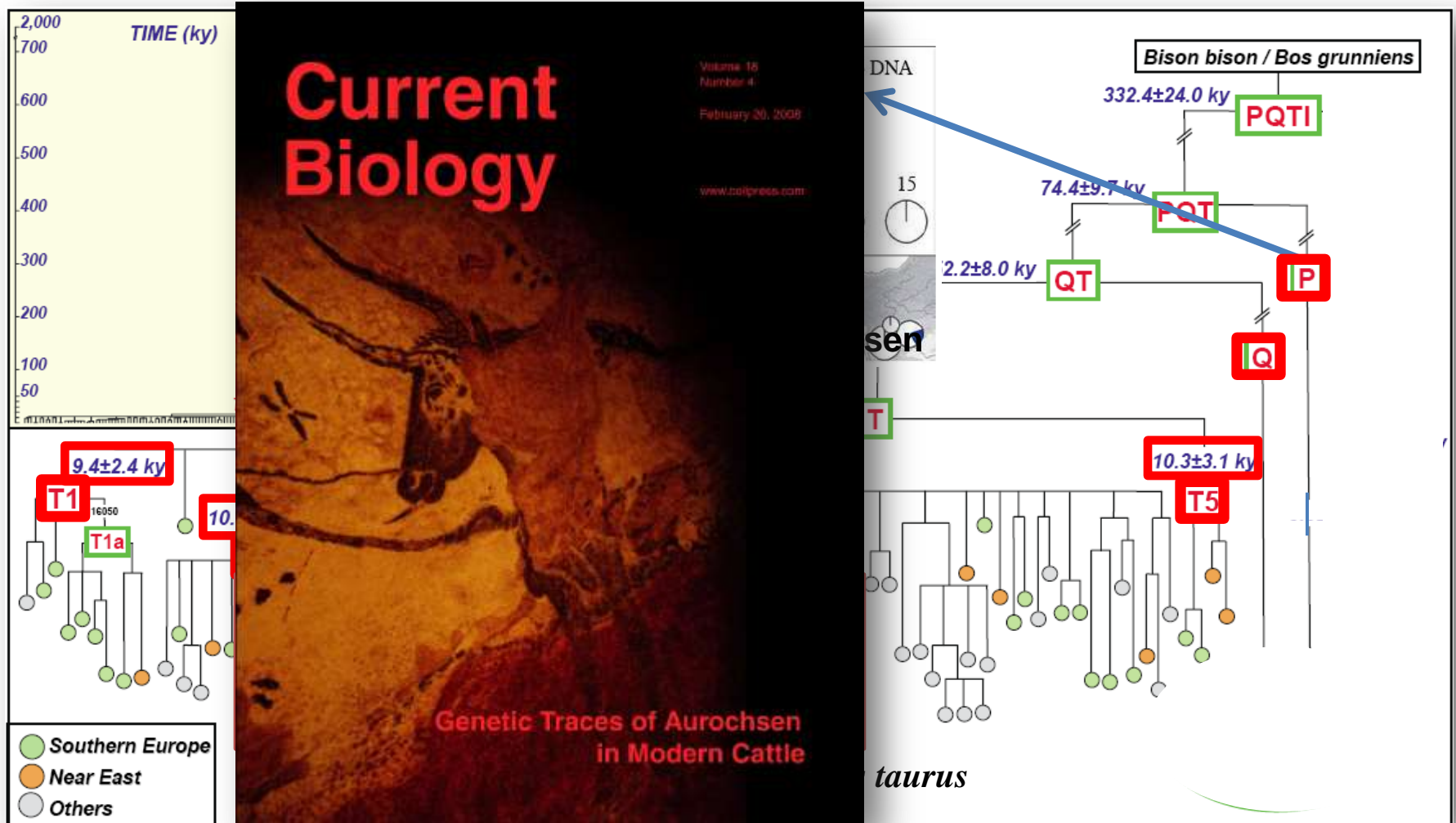
Where?



Which Lineages?

DOMESTICATION

Cattle mtDNA phylogeny (106 complete mtDNA sequences)



...the last recorded aurochs died in Poland in 1627

Achilli, Olivieri et al. 2008, *Curr Biol*

Mitochondrial genomes from modern horses reveal the major haplogroups that underwent domestication

Alessandro Achilli^{a,1}, Anna Olivieri^b, Pedro Soares^c, Hovirag Lancioni^a, Baharak Hooshiar Kashani^b, Ugo A. Perego^{b,d}, Solomon G. Nergadze^b, Valeria Carossa^b, Marco Santagostino^b, Stefano Capomaccio^e, Michela Felicetti^e, Walid Al-Achkar^f, M. Cecilia T. Penedo^g, Andrea Verini-Supplizi^e, Massoud Houshmand^h, Scott R. Woodward^d, Ornella Semino^b, Maurizio Silvestrelli^e, Elena Giulotto^b, Luísa Pereira^{c,i}, Hans-Jürgen Bandelt^j, and Antonio Torroni^{b,1}

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Who are the ancestors of modern horses?

Pictures of wild horses (Equus ferus) hunted for food



- Chauvet Cave
- Lascaux Cave
- ~30 Kya
- ~16 Kya

Domestication Event(s): where and when?



Archeological evidence of domestication comes from the **Botai culture**, found in north Kazakhstan, **~5500 ya**



Horse mtDNA Phylogeny 83 complete sequences

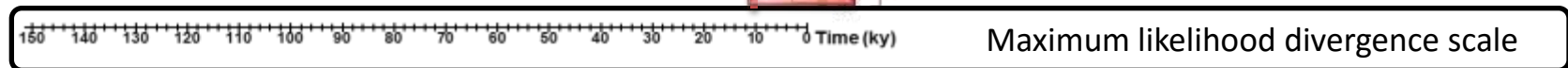
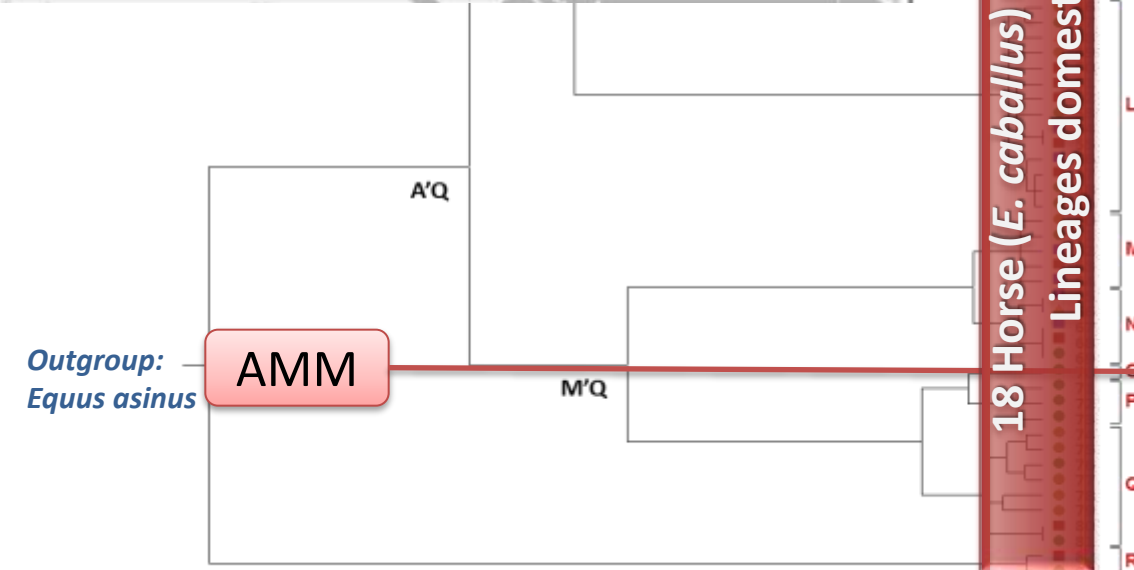
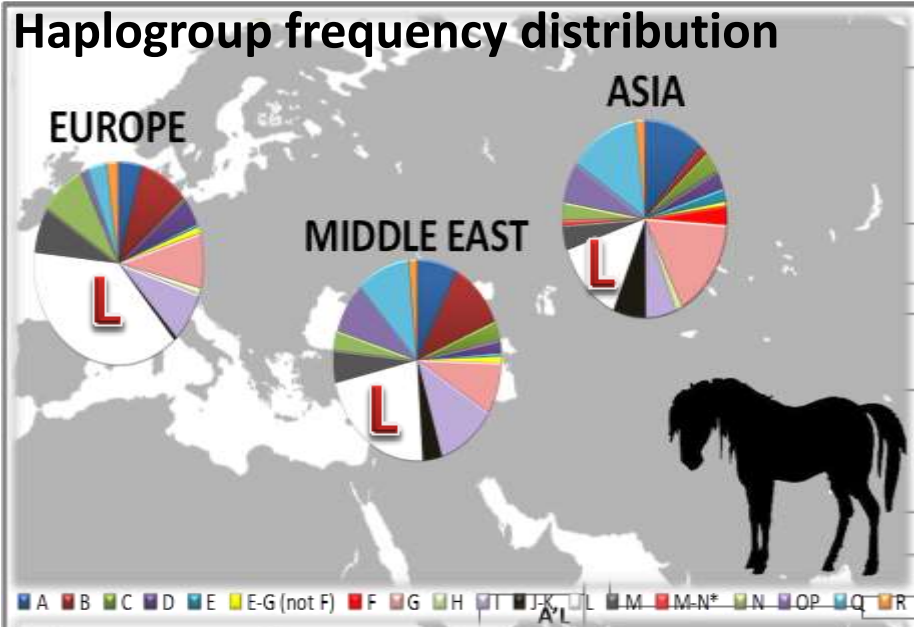
18 Horse MtDNA
Haplogroups «A-R»

Many different matrilineal lineages
underwent domestication,
throughout the Neolithic period

In multiple locations of Eurasia,
including West Europe (Iberia)

AMM
Ancestral Mare
Mitogenome
~160-130 kya

Neolithic timeline
18 Horse (*E. caballus*) mitochondrial haplogroups:
Lineages domesticated in the Neolithic

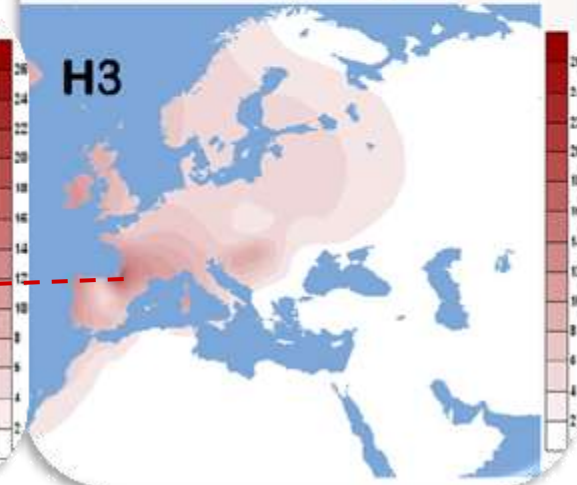
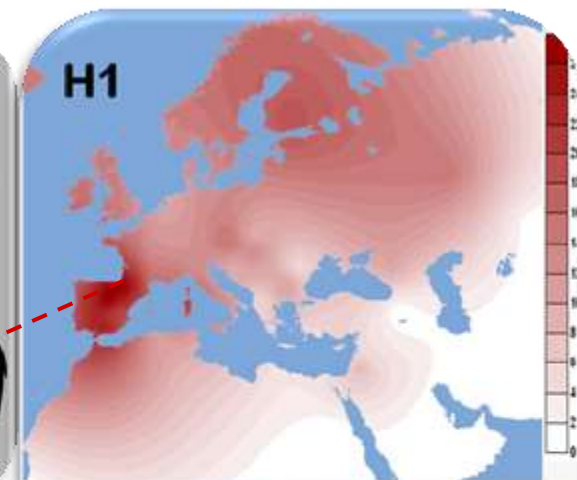
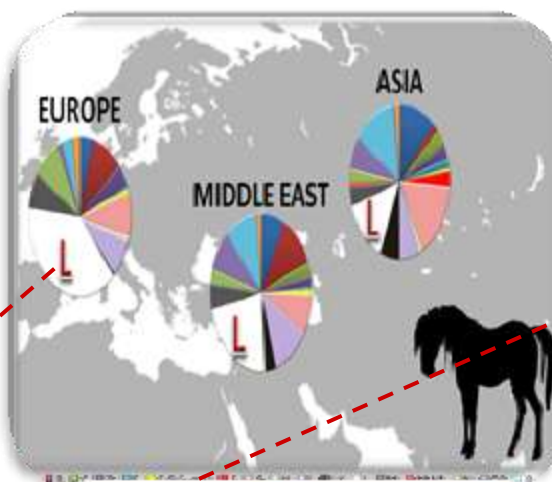


Maximum likelihood divergence scale



(Achilli et al. 2012, PNAS)

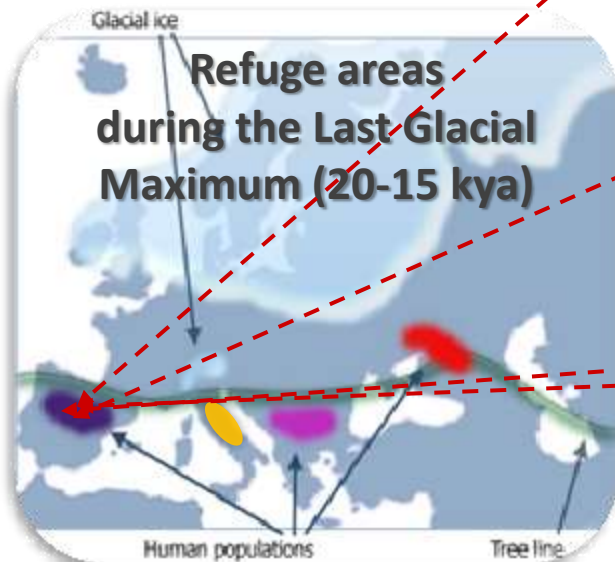
A Parallel Genetic History!!!



(Achilli et al. 2004, Am J Hum Genet)

(Achilli et al. 2005, Am J Hum Genet)

The role of the Franco-Cantabrian Refuge as a source for the Paleolithic hunter-gatherer populations that gradually repopulated central and northern Europe after the LGM





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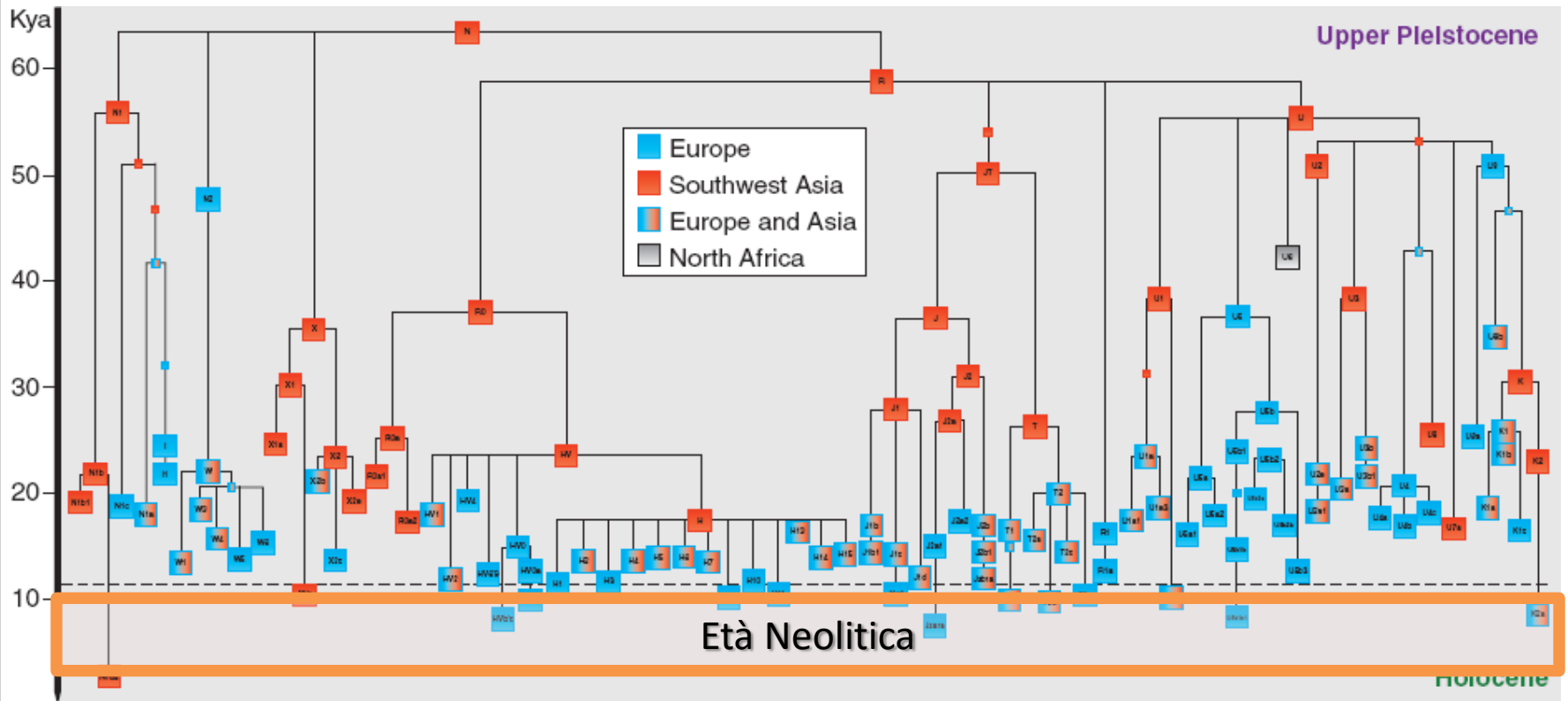
Tema strategico di Ateneo
Verso una governance del fenomeno migratorio



Cosa possiamo dire riguardo eventi migratori recenti/attuali???

Purtroppo ancora poco....

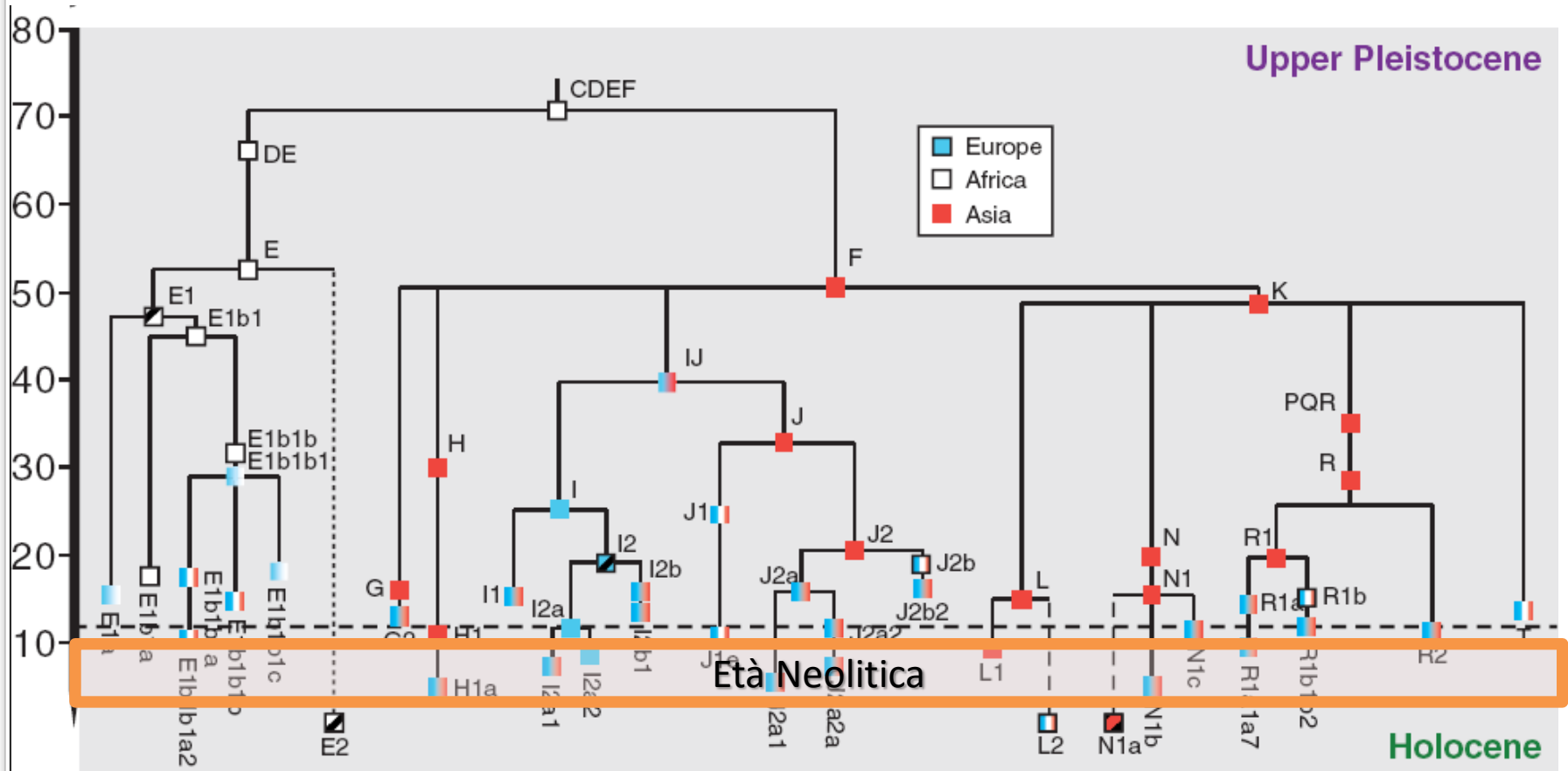
Filogenesi ed età dei principali aplogruppi mitocondriali osservati in Eurasia occidentale e Nord Africa



(Soares, Achilli et al. 2010, *Curr Biol* 70: R174-R183)

Linee Neolitiche dell' mtDNA? ... poche

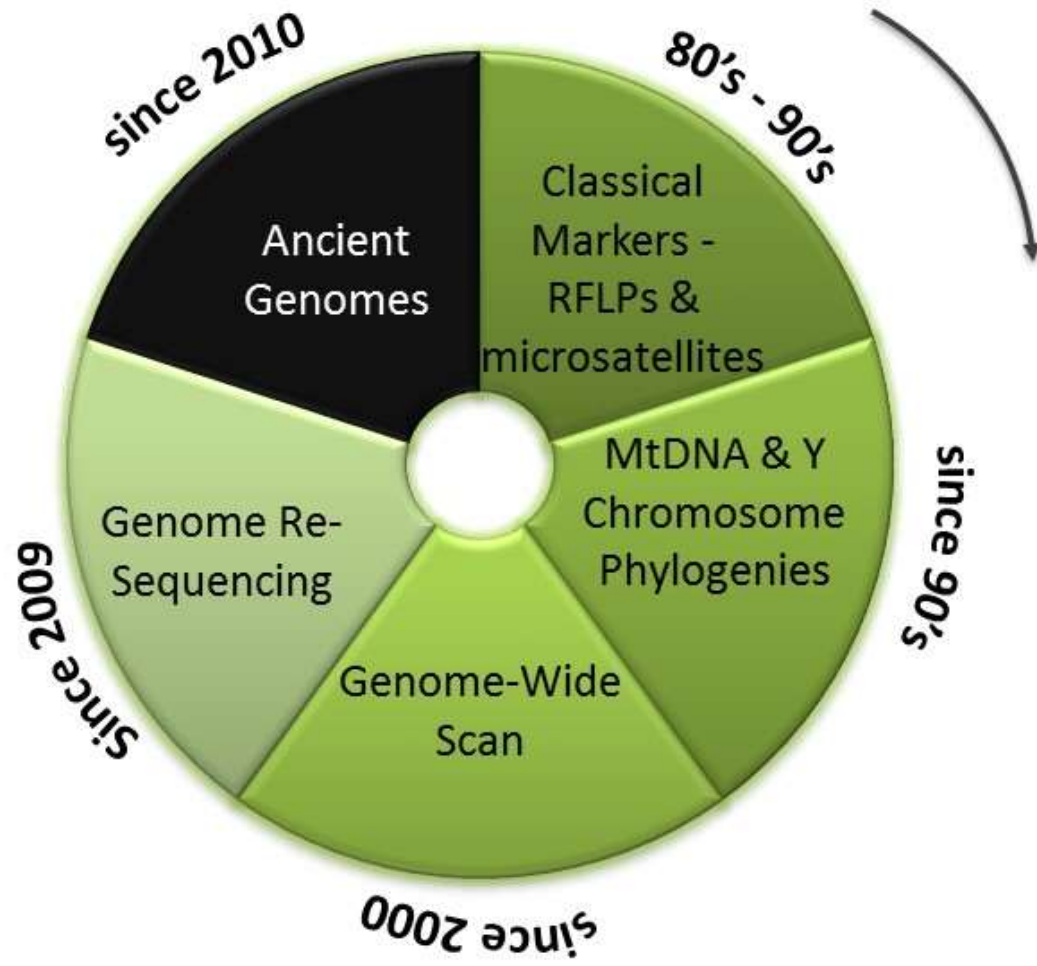
Filogenesi ed età dei principali aplogruppi del cromosoma Y osservati in Eurasia occidentale e Nord Africa



(Soares, Achilli et al. 2010, *Curr Biol* 70: R174-R183)

Linee Neolitiche del cromosoma Y? ... ancora meno

«Evoluzione» degli approcci genetici utilizzati per gli studi sulle popolazioni umane

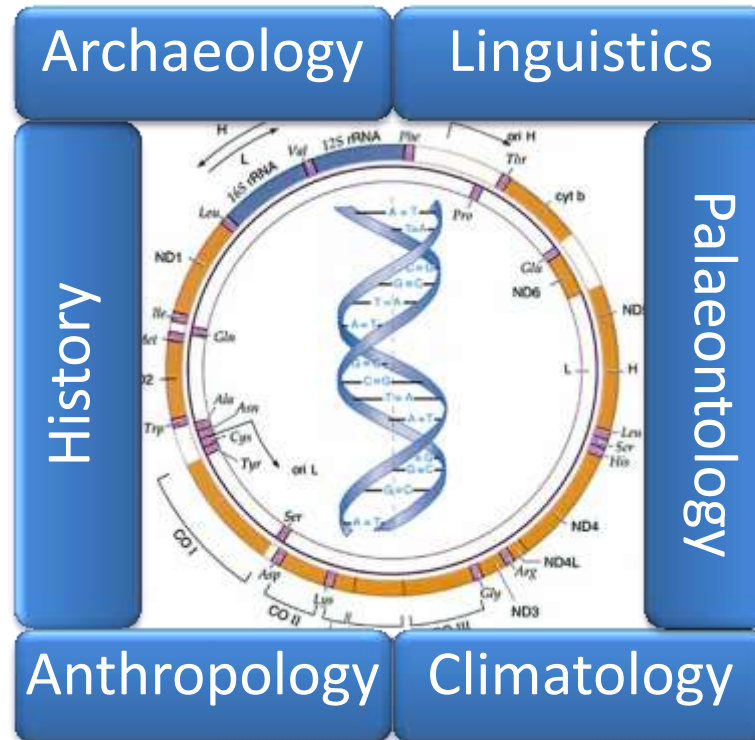


Conclusione

Gli studi molecolari e filogeografici sul DNA mitocondriale (sul cromosoma Y e sugli altri marcatori nucleari) possono fornire dati importanti sui principali eventi (di *longue durée*) che hanno caratterizzato la preistoria e la protostoria delle popolazioni umane, mentre per eventi recenti bisognerà incrementare il livello di risoluzione filogenetico e..

i nuovi dati acquisteranno valore solo se

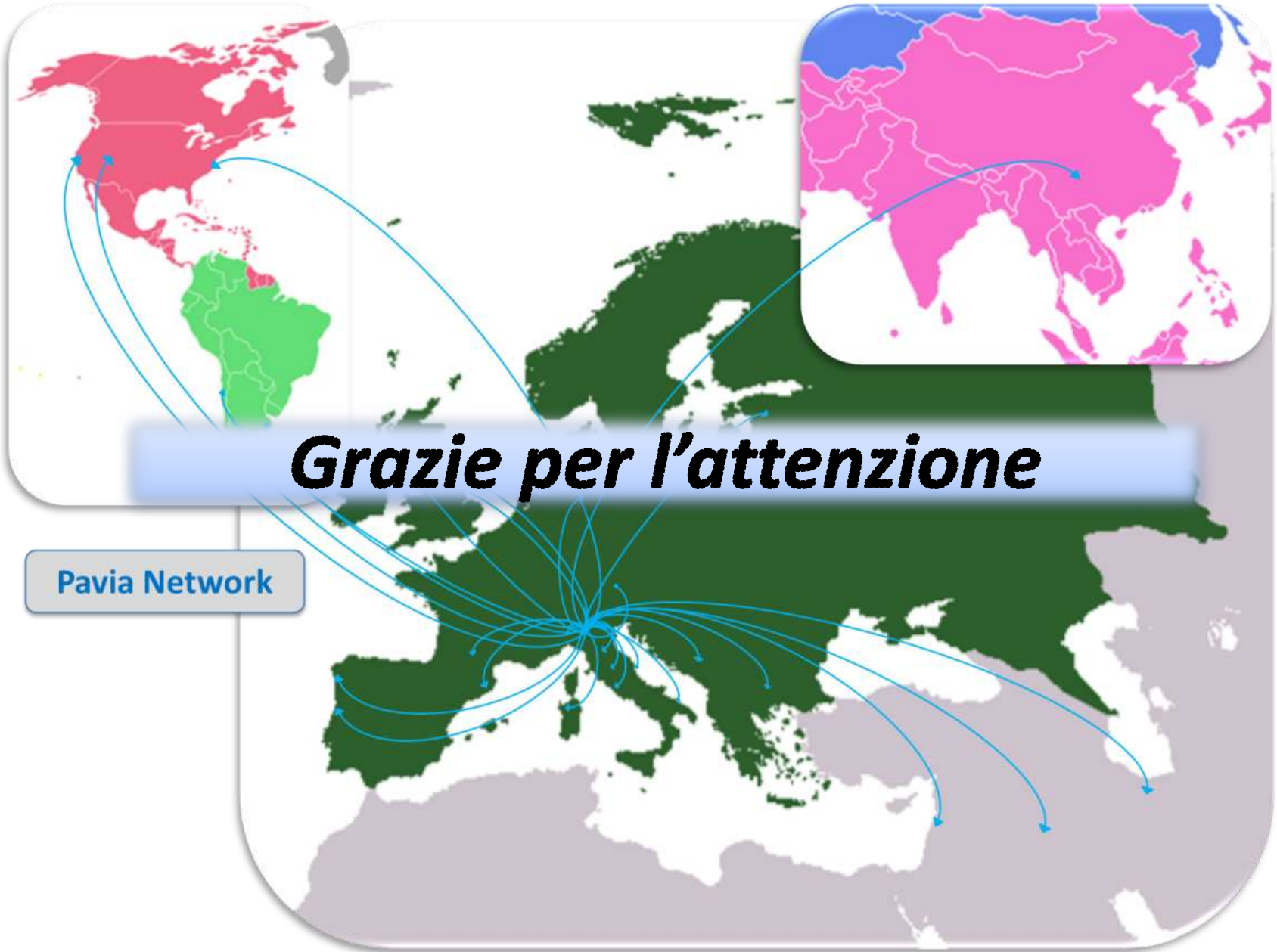
inquadri nell'ambito delle ipotesi fornite dalla storia, archeologia, antropologia, paleoclimatologia, etc. ossia in un contesto **multidisciplinare**.





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Tema strategico di Ateneo
Verso una governance del fenomeno migratorio



Grazie per l'attenzione

Pavia Network