ATHENS SCIENCE FESTIVAL
#asf

Τα ίχνη του DNA φωτίζουν το παρελθόν

Δρ. Χρήστος Γιαπιτζάκης,DMD,BS,MS,PhD

Επίκουρος Καθηγητής Βιολογίας-Νευρογενετικής
Α΄ Παιδιατρική Κλινική, Ιατρική Σχολή
Εθνικό Καποδιστριακό Πανεπιστήμιο Αθηνών
Νοσοκομείο Παίδων “Αγία Σοφία”, Αθήνα

Διευθυντής
Κέντρο “Κεφαλογενετική”, Αθήνα

Τα ίχνη του DNA φωτίζουν το παρελθόν

- Ποια είναι η θέση του ανθρώπου στην Ιστορία του Σύμπαντος;
- Ποια ήταν τα σημαντικότερα βήματα της ανθρωπότητας προς την κατεύθυνση της κατανόησης της φύσης της;
- Τι ιδιαίτερες ιδιότητες έχει το “μόριο της ζωής” DNA;
- Τι είναι οι γενετικοί δείκτες του DNA;
- Ποια είναι η σχέση του σύγχρονου ανθρώπου με άλλα συγγενικά είδη (πχ με τους Νεάντερταλ);
- Πώς οι μετακινήσεις των ανθρώπων επηρέασαν την γενετική των πληθυσμών;
- Πώς μελετούνται οι αρχαίες επιδημίες;
- Ποιοι μύθοι καταρρίπτονται από την μελέτη του DNA;

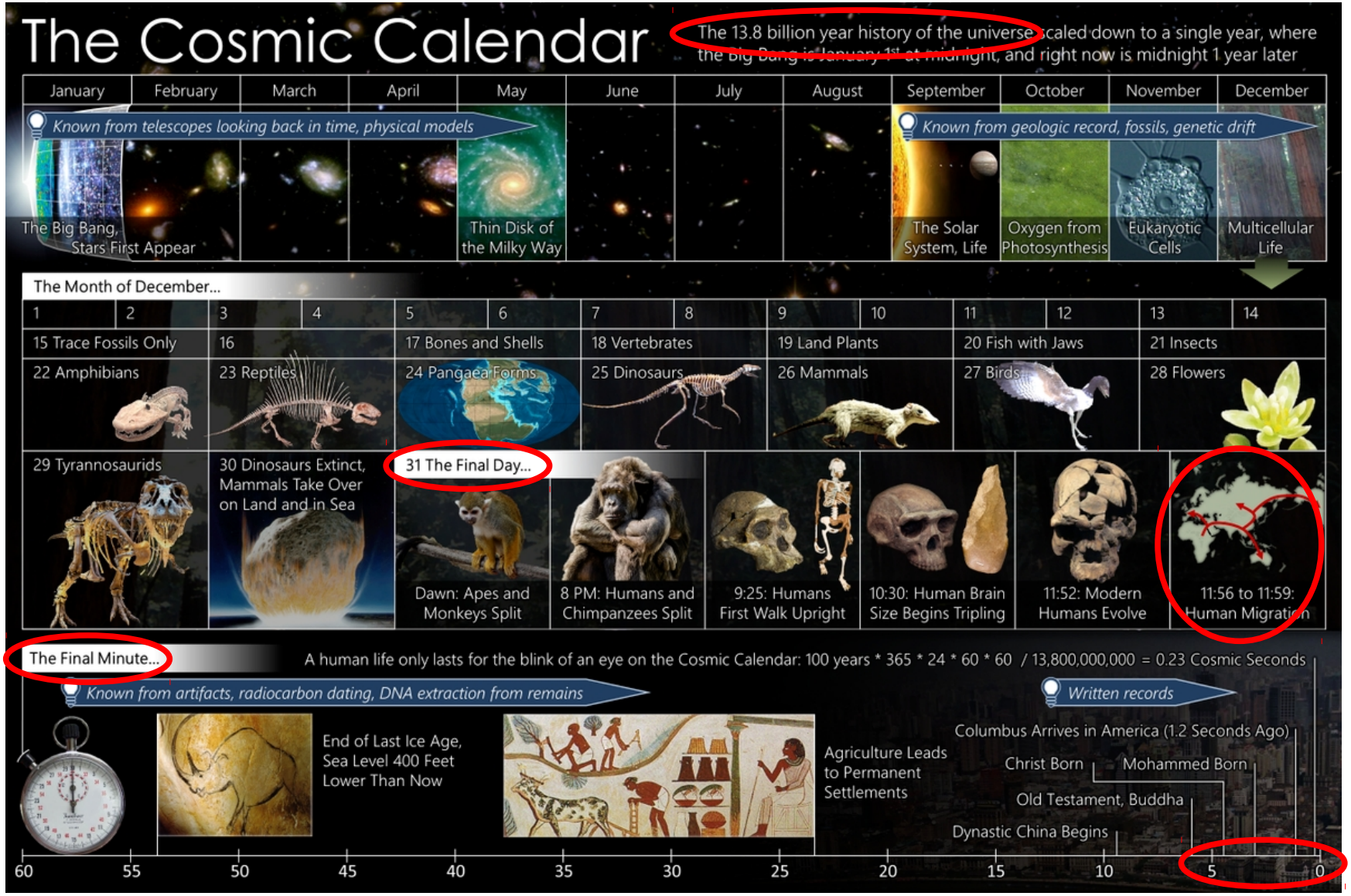
Η Ιστορία ως τώρα

Τηλεοπτική σειρά “Cosmos” (ΗΠΑ)
(13.8 δισ. Έτη/1Έτος)

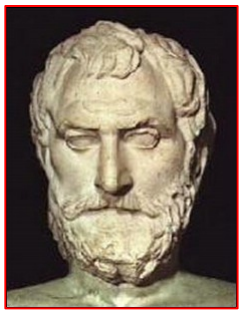
Carl Sagan

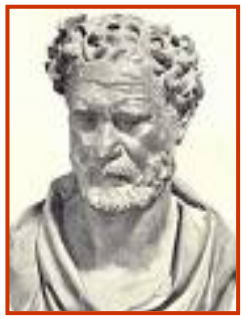
Neil deGrasse Tyson

Η Ιστορία ως τώρα

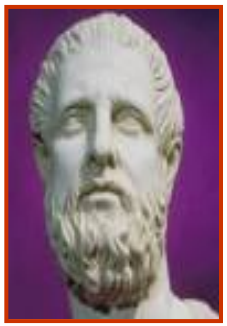


Ιστορικά Βήματα Κατανόησης της Φύσης



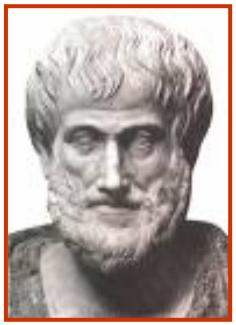


Θαλής (624-546 πΧ)
• Φιλοσοφία

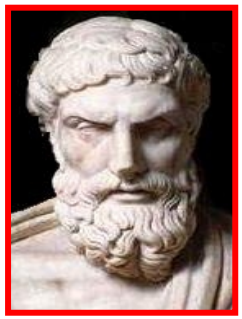


Ιπποκράτης (460-377 πΧ)
• Ιατρική

Δημόκριτος (π460-π370 πΧ)
• Ατομική Φυσική



Αριστοτέλης (384-322 πΧ)
• Ζωολογία, Βιολογική Ηθική



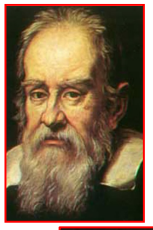
Επίκουρος (341-270 πΧ)
• Χημεία, Γενετική, Εξέλιξη

Ασκληπιάδης ο Βιθυνός (124-40 πΧ)
• Μοριακή Ιατρική

Yapijakis C. **Hippocrates the father of clinical medicine, Asclepiades the father of molecular medicine**. *In Vivo* 23: 507-514, 2009.

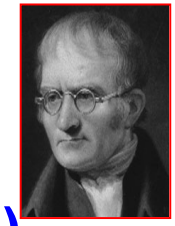
Yapijakis C. **Ancestral Concepts of Human Genetics and Molecular Medicine in Epicurean Philosophy**. In: *History of Human Genetics,* Petermann, Harper (Eds), Springer 2017

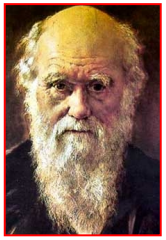
Ιστορικά Βήματα Κατανόησης της Φύσης







Αναγέννηση (1600-1700)
- Γαλιλαίος, Γκασσαντί, Λοκ, Νεύτων

Διαφωτισμός (1700-1800)
- ΛαΜετρί, Ντιντερό, Λαβουαζιέ

Αρχές Επιστήμης (1800-1900)
- Ντάλτον, Παστέρ, Μέντελ, Δαρβίνος

Ενηλικίωση Επιστήμης (1900-2000)
- Κβαντική Φυσική, Δομή DNA (Γουάτσον-Κρικ)
- Γενετική Ανθρώπου, Μοριακή Ιατρική
- Πρόγραμμα Ανθρώπινου Γονιδιώματος (“γνώθι σαυτόν”)

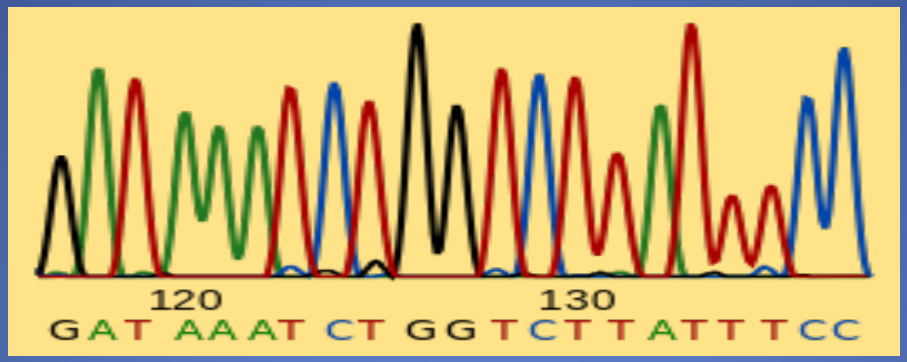
Σινσάιμερ, Πρύτανης University of California Santa Cruz (1985)

Sinsheimer R. **The Santa Cruz Workshop, May 1985**. *Genomics.* 5:954–956, 1989.
Harper PS. **A Short History of Medical Genetics**. Oxford University Press, 2008.

Μοριακή Βιολογία - Γενετική

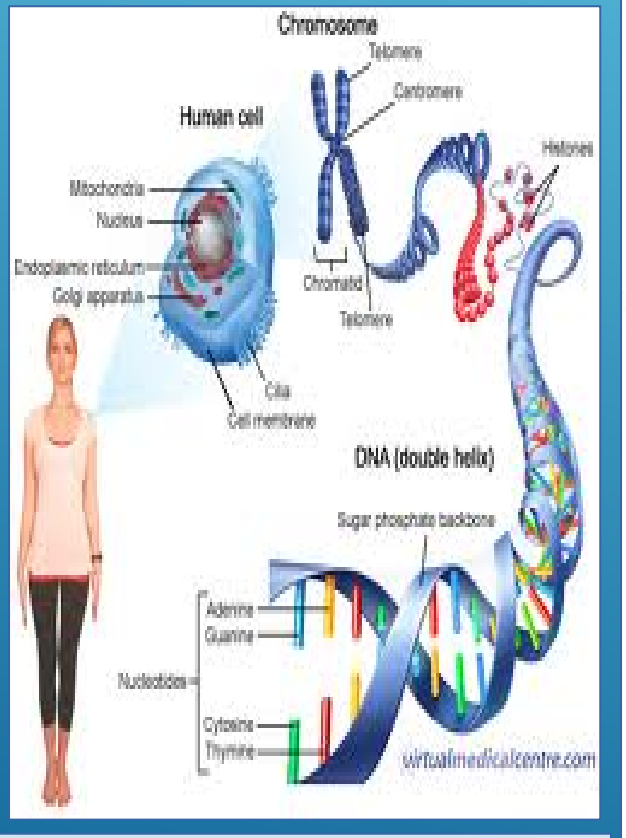
DNA - Το μόριο της ζωής

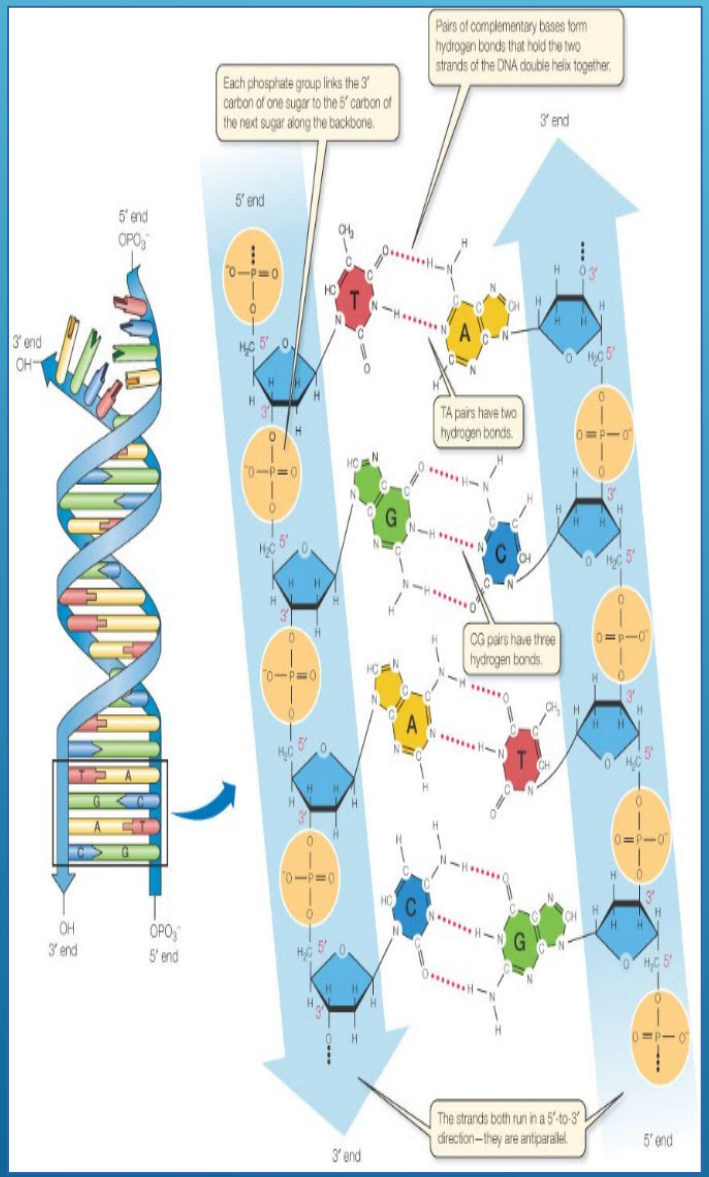
1. Μεταφέρει πληροφορίες

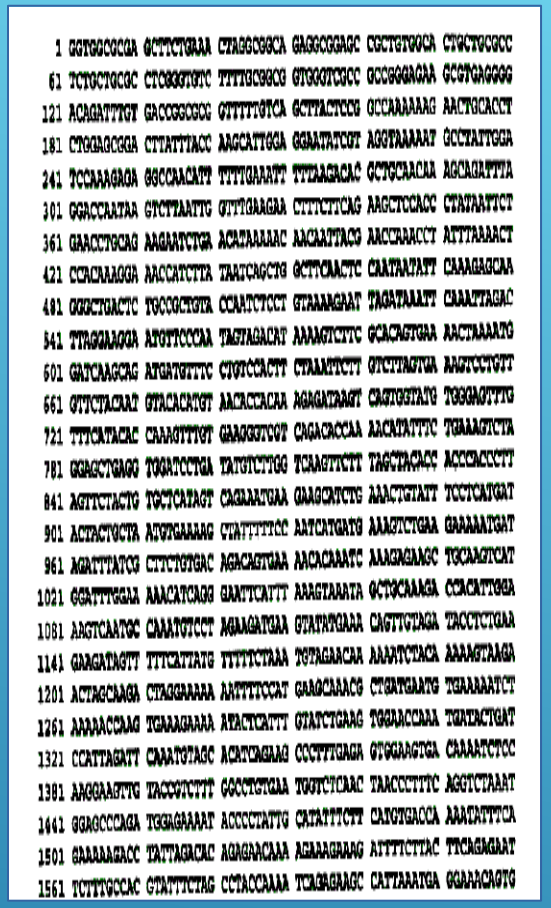


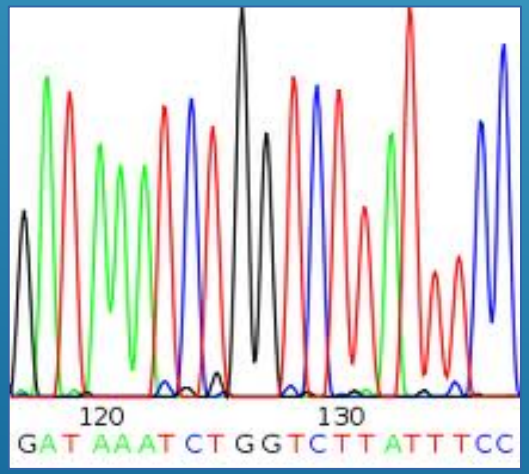
2. Αποκτά πανομοιότυπους απογόνους

Μοριακή Βιολογία



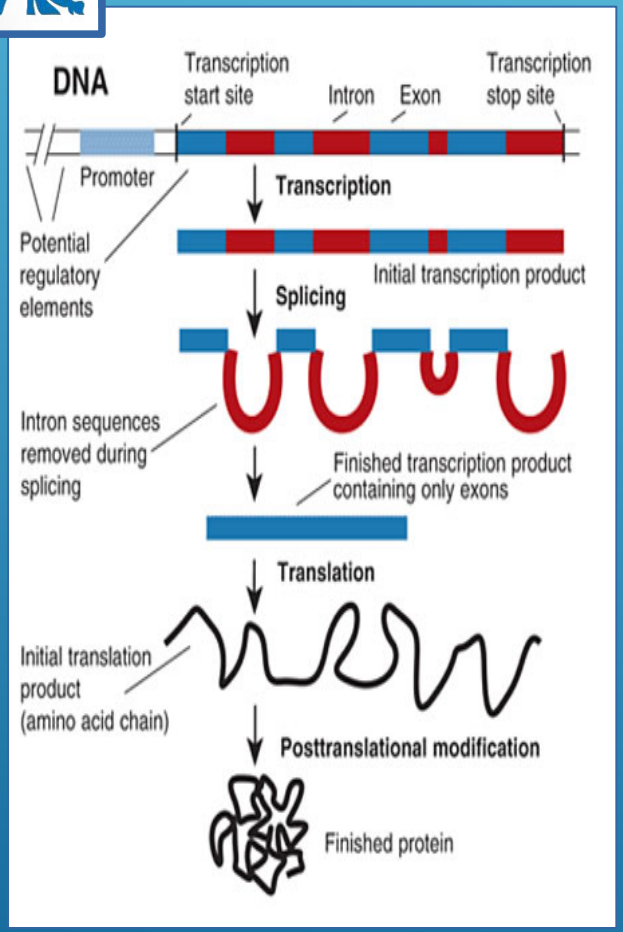


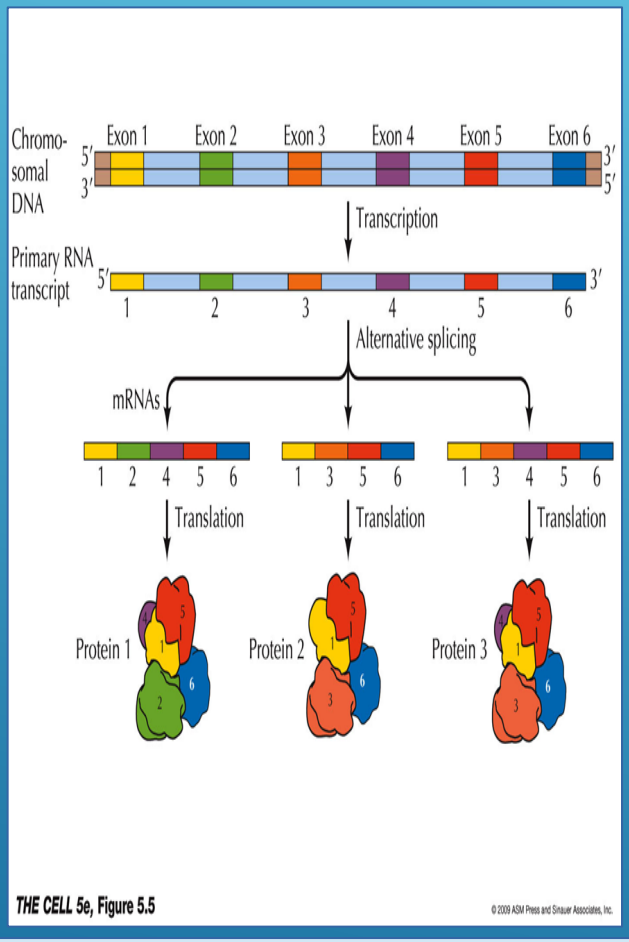


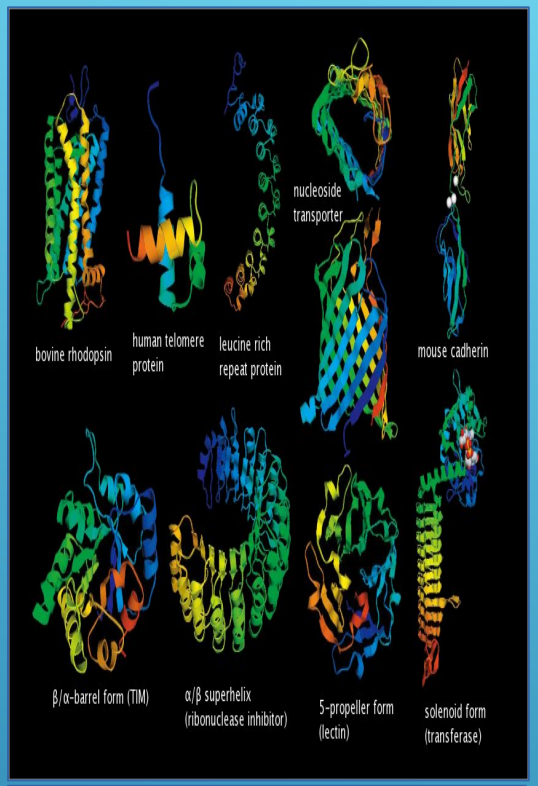


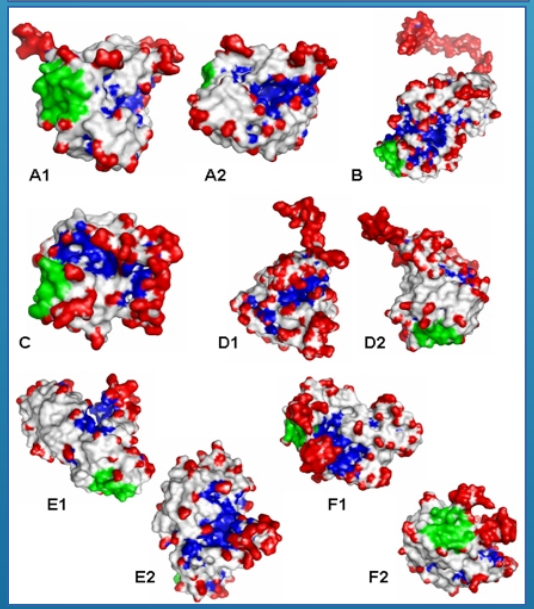
- 1 μόριο DNA περιελιγμένο σε 1 χρωμόσωμα
- Γενετικός Κώδικας (G,A,T,C)
- Ανάλυση αλληλουχίας DNA

Μοριακή Βιολογία



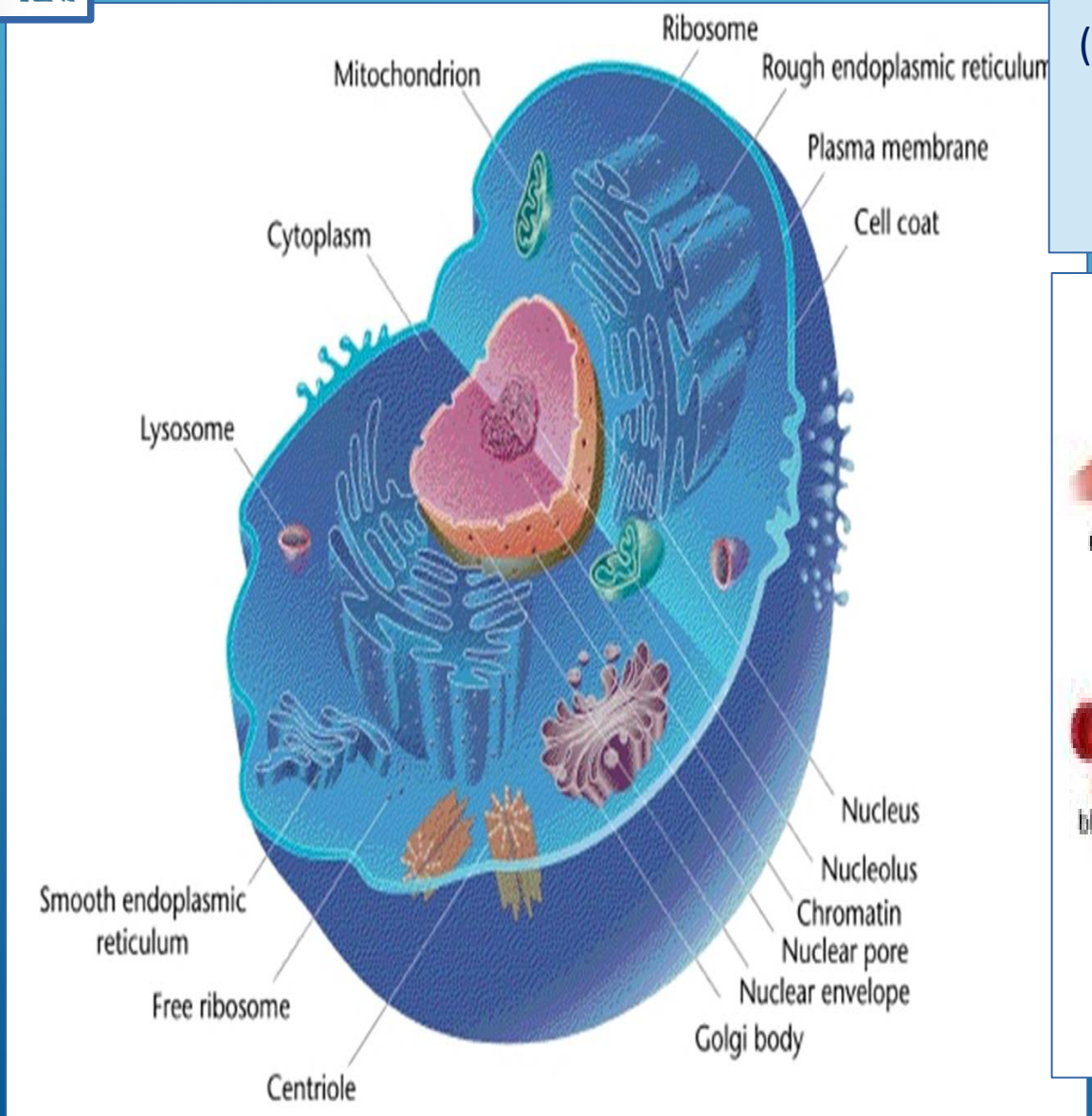




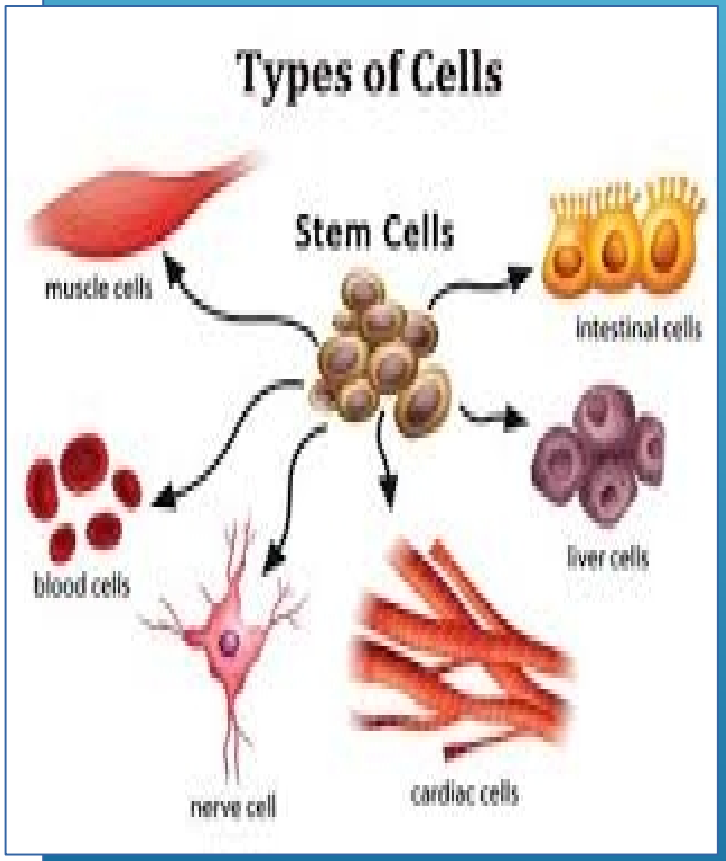


- Γονίδιο με κωδικοποιούσες περιοχές (εξόνια)
- Μεταγραφή mRNA - Αποκοπή ιντρονίων
- Μετάφραση σε Πρωτεΐνη **(ΔΟΜΗ=ΛΕΙΤΟΥΡΓΙΑ)**

Κυτταρική Βιολογία



- **37 τρισεκατομμύρια κύτταρα στο ανθρώπινο σώμα** (Bianconi et al. *Ann Hum Biol* 2013)
- **>200 τύποι κυττάρων** (McCarthy , Enquist *Evol Ecol Res* 2005)

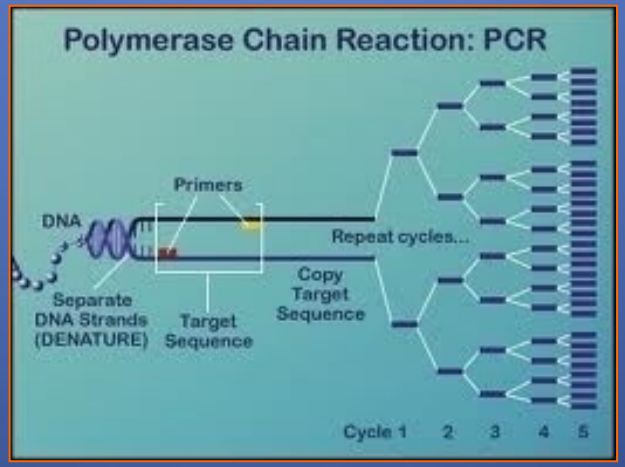


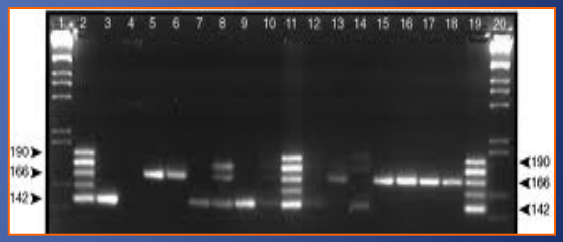
Γενετική
Ανάλυση DNA

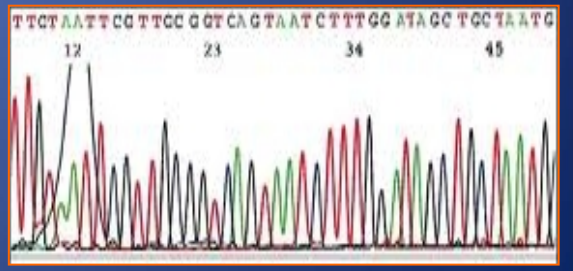
αίμα

σάλιο

βιοψία







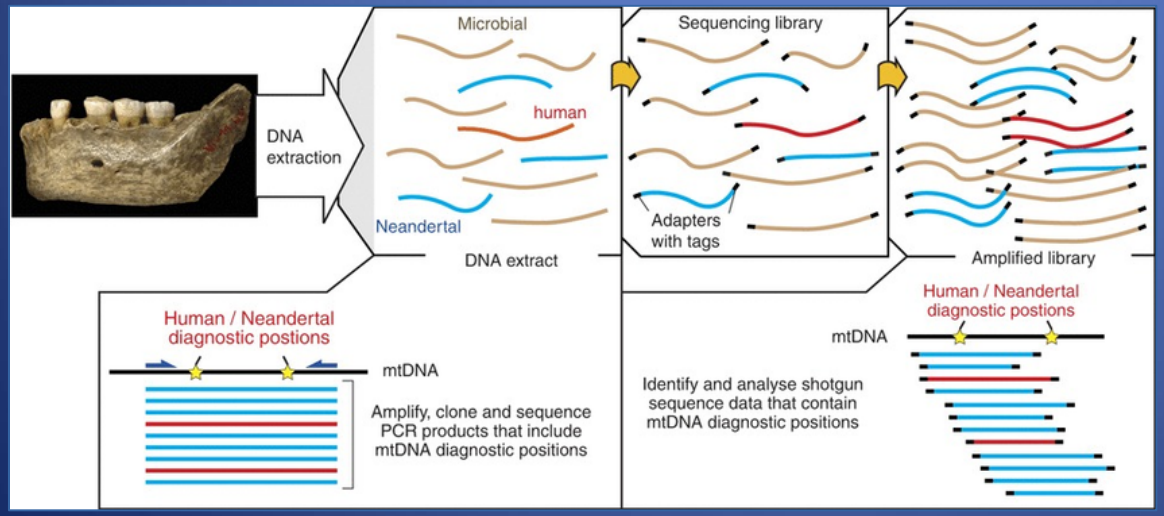
Γενετική
Ανάλυση Αρχαίου DNA

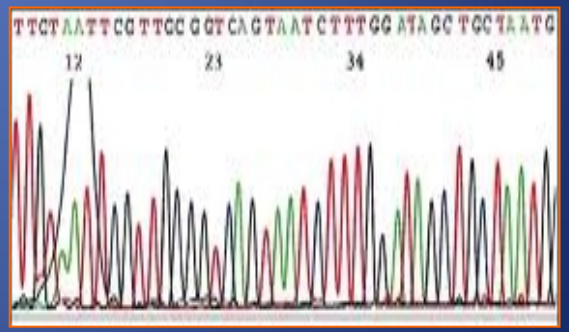
δείγμα μούμιας

οστούν

δόντι

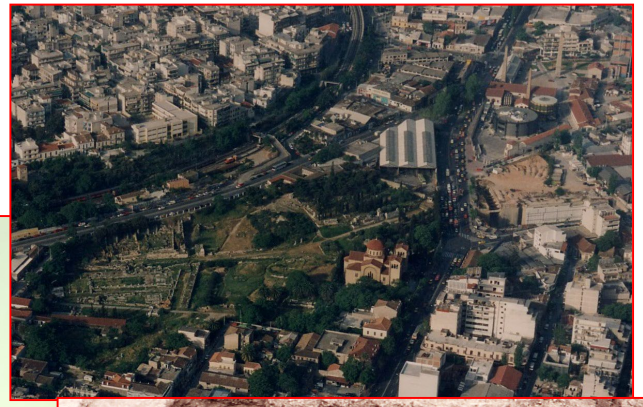
κεχριμπάρι

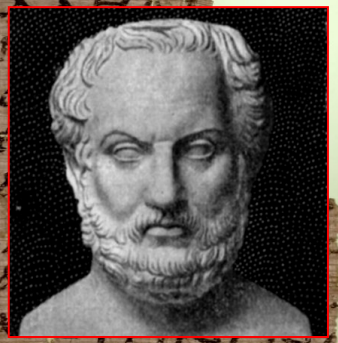


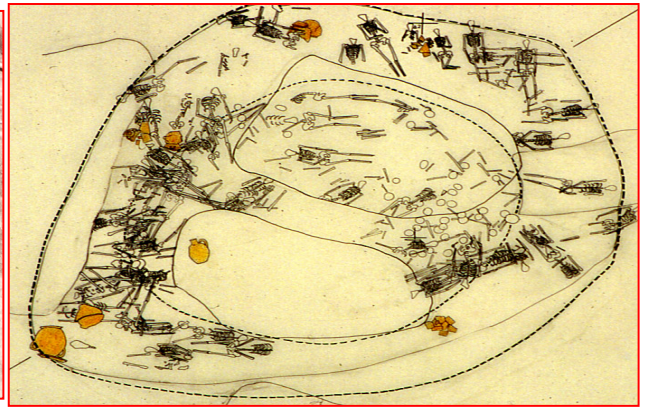


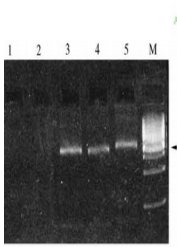
Αρχαίο DNA – Λοιμός των Αθηνών

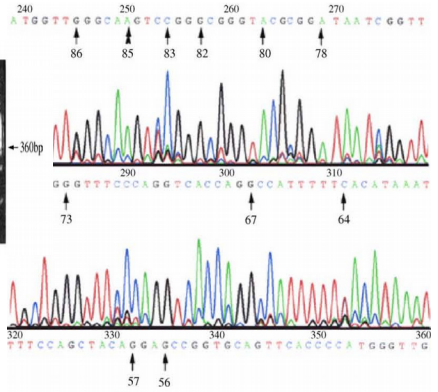
Papagrigorakis, Yapijakis, Synodinos, Baziotopoulou *Int J Infect Dis* 2006



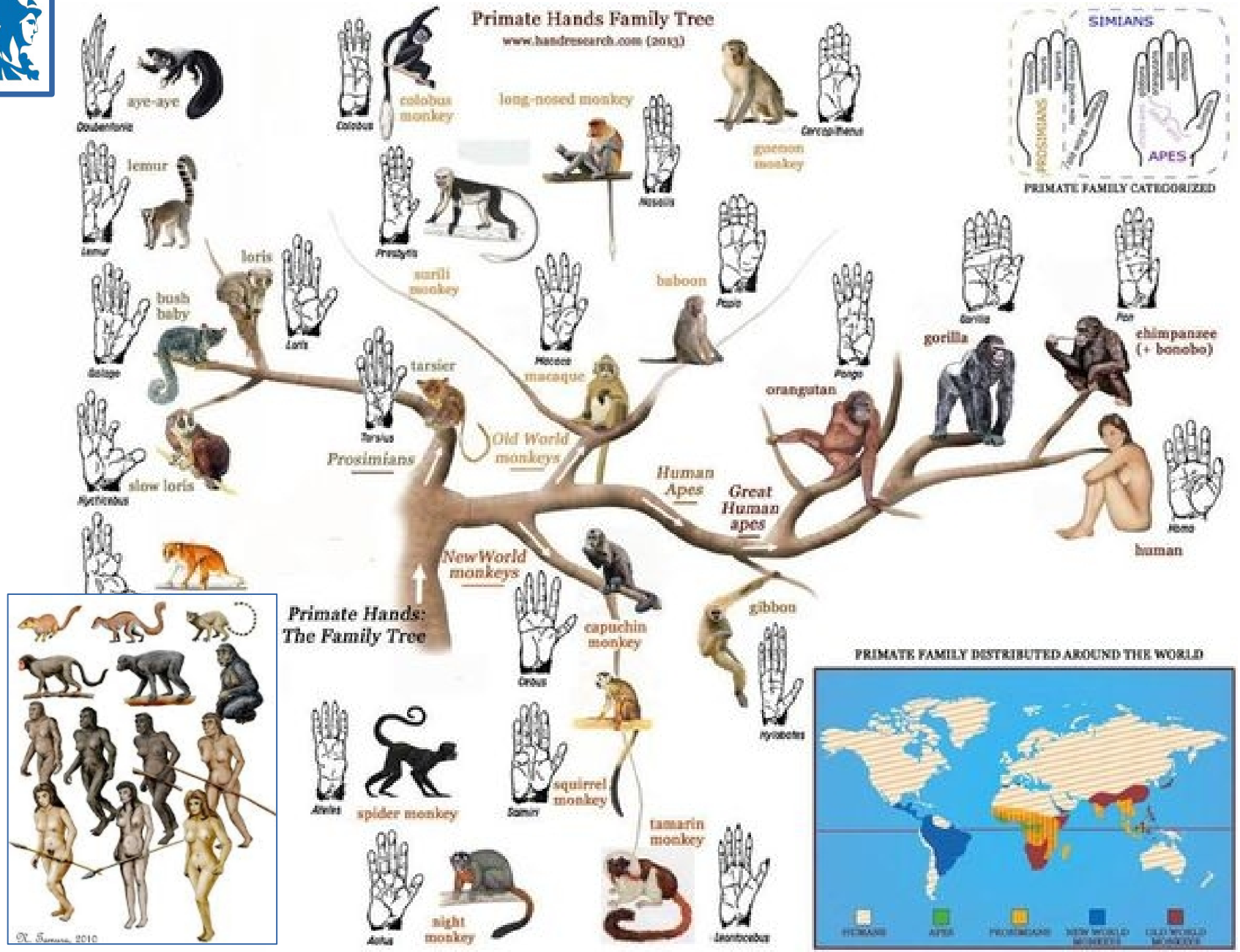




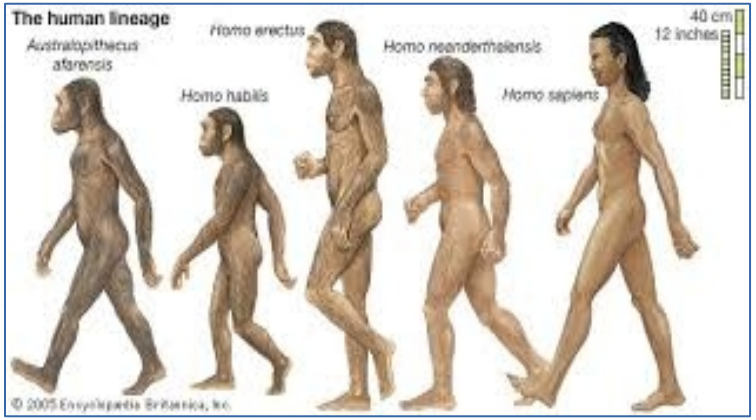


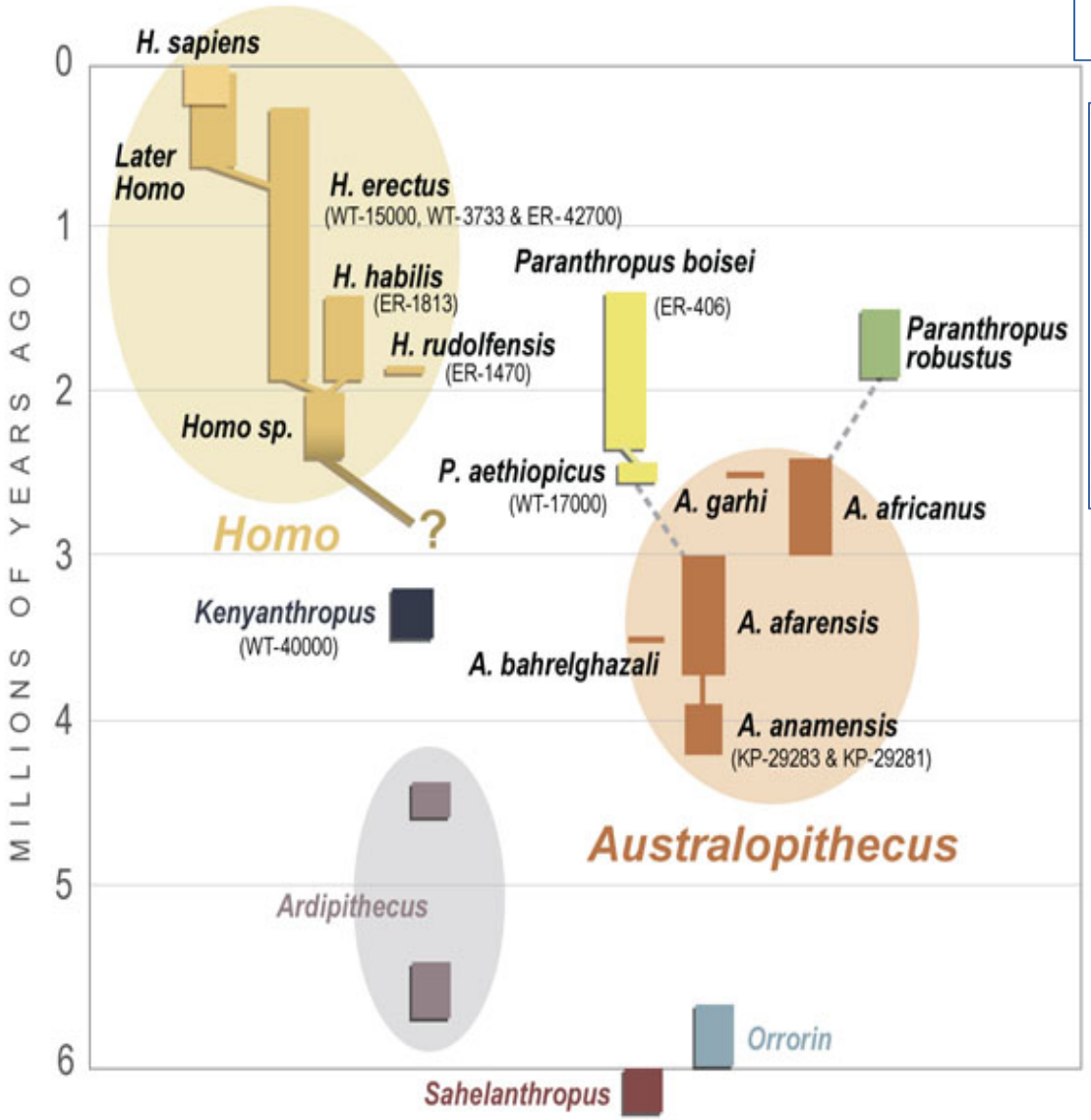


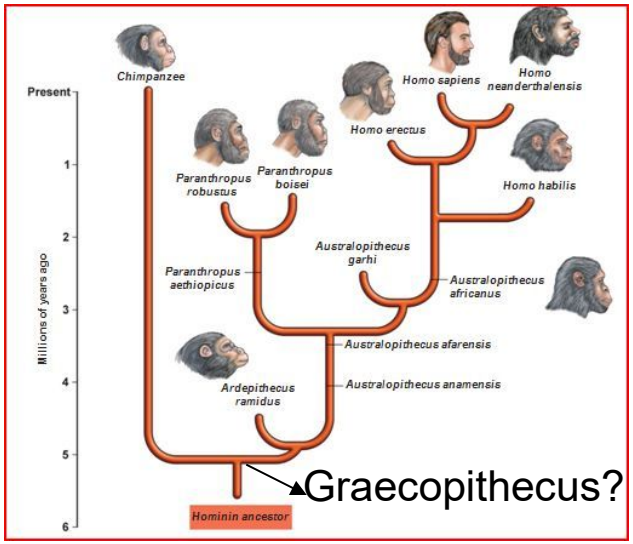
Πρωτεύοντα – Φυλογενετικό Δένδρο



Hominin Phylogeny
A Perspective View

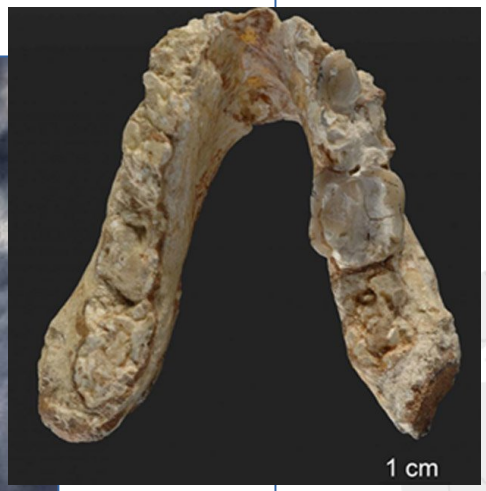


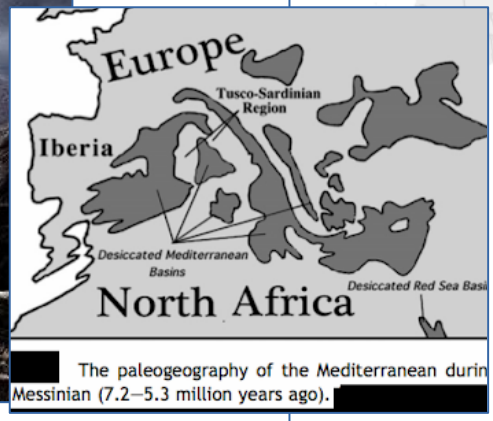




Graecopithecus

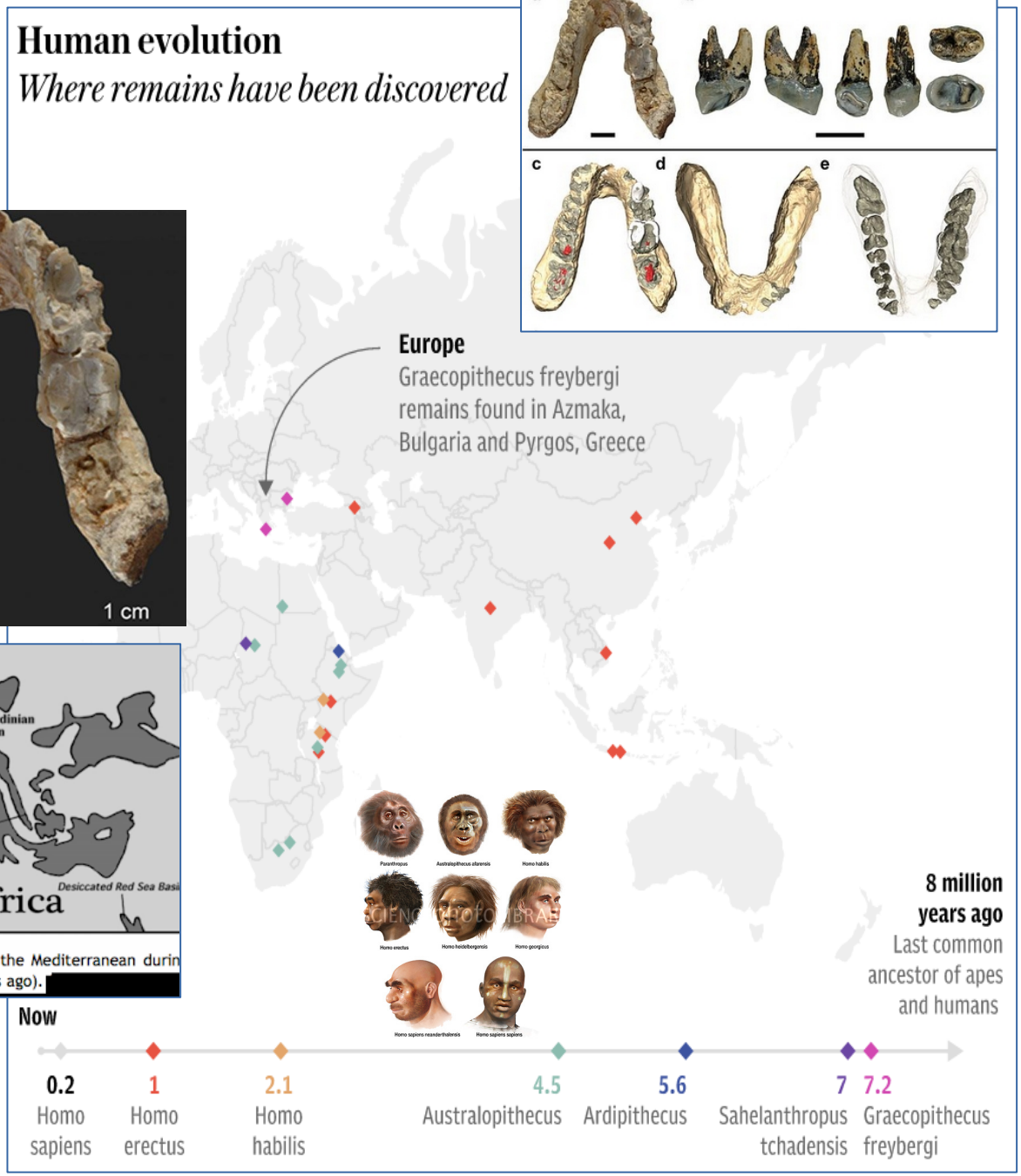
Πύργος Βασιλίσσης Ίλιον



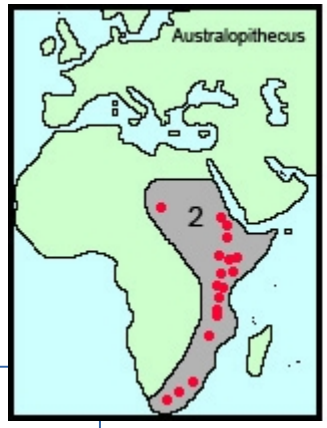


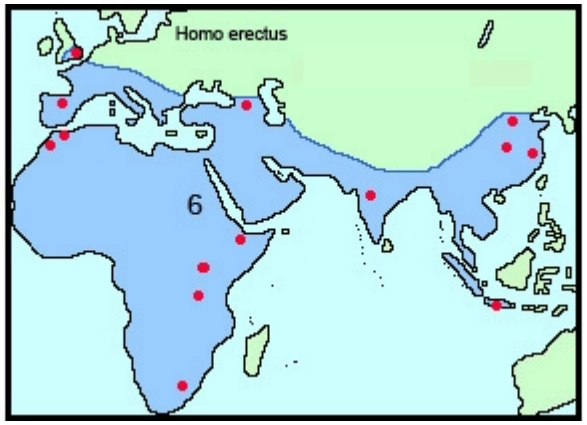
The paleogeography of the Mediterranean durin
Messinian (7.2–5.3 million years ago).

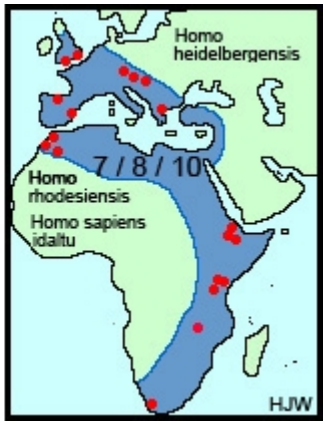
Fuss et al. *PLOS* 2017

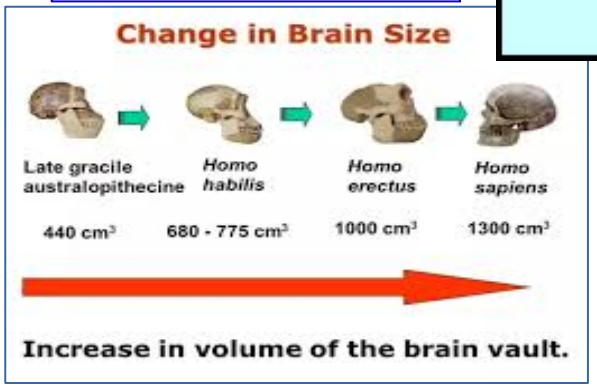


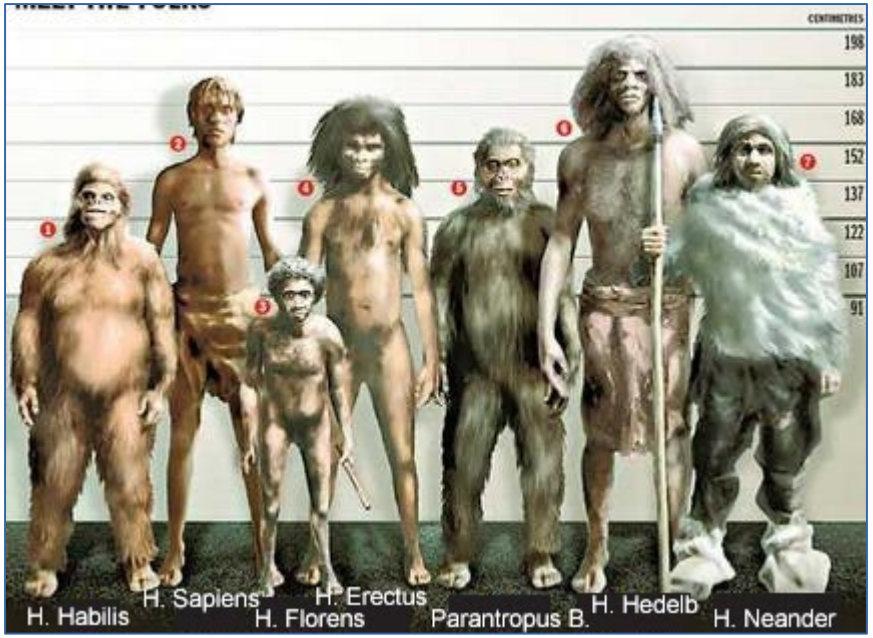
Slatkin, Racimo
PNAS 2016

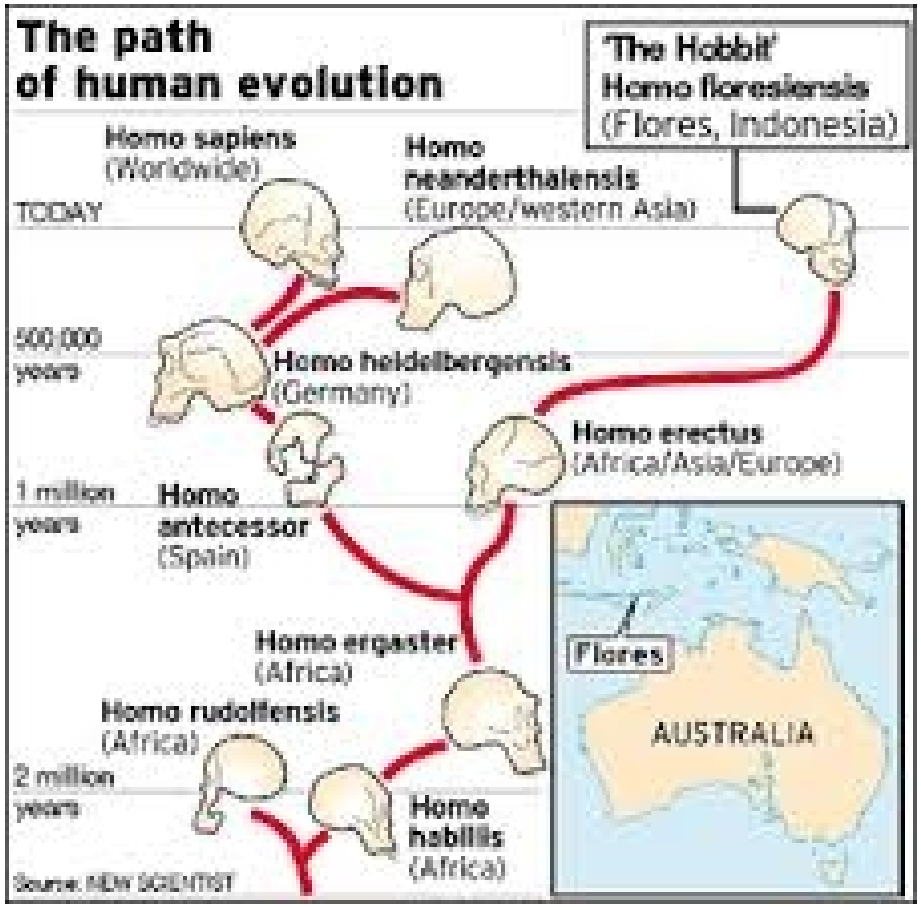












Homo sapiens

Slatkin, Racimo
PNAS 2016

THE MIGRATION OF ANATOMICALLY MODERN HUMANS

Evidence from fossils, ancient artefacts and genetic analyses combine to tell a compelling story

Oued Djebbana (Algeria) Shell beads >35k
Peştera cu Oase (Romania) ~40k
Skhul and Qafzeh (Israel) 120-90k Shell beads ~110k
ATLANTIC CROSSING
'Lagar Velho boy' (Portugal)
Taforalt (Morocco) Shell beads ~82k
Herto (Ethiopia) ~160k
Omo Kibish (Ethiopia) ~195k
Singa (Sudan) ~155k
Blombos Caves (South Africa) 75-65k 2 pieces of engraved ochre ~77k Shell beads ~75k
Fa Hien Cave and Batadomba Lena Cave (Sri Lanka) Bones and artifacts ~35k
Klasies River (South Africa) 90-65k Cultural artifacts ~70k
Lake Mungo (Australia) ~46k
Tianyuan (China) ~40k
Niah Caves (Sarawak) ~45k
BERINGA ROUTE
16k
PACIFIC COASTAL ROUTE
PACIFIC COASTAL ROUTE
Wally's Beach (US) Human occupation ~13k
ATLANTIC CROSSING
Arlington Springs (US) Leg bone ~13k
Cactus Hill (US) Small blades 20-17k
South-east of Puebla (Mexico) Ancient footprints ~38k (contested)
Quebrada Jaguay (Peru) Human settlement ~13k
15k
Monte Verde (Chile) Flake tools and stone points ~15k
PACIFIC CROSSING
40k
60k
50k
65k
NORTHERN ROUTE
SOUTHERN ROUTE
BAB EL-MANDEB STRAIT
Flow of genes around globe
Routes of migration
Alternative/contested routes
~13k Anatomically modern humans
10k 10,000 years ago

Homo altai (denisovan)

Homo neanderthalensis

Homo floresiensis

Two routes jump out as prime candidates for the human exodus out of Africa. A northern route would have taken our ancestors from their base in eastern sub-Saharan Africa across the Sahara desert, then through Sinai and into the Levant. An alternative southern route may have charted a path from Djibouti or Eritrea in the Horn of Africa across the Bab el-Mandeb strait and into Yemen and around the Arabian peninsula. The plausibility of these two routes as gateways out of Africa has been studied as part of the UK's Natural Environment Research Council's programme "Environmental Factors in the Chronology of Human Evolution & Dispersal" (EFCHED).

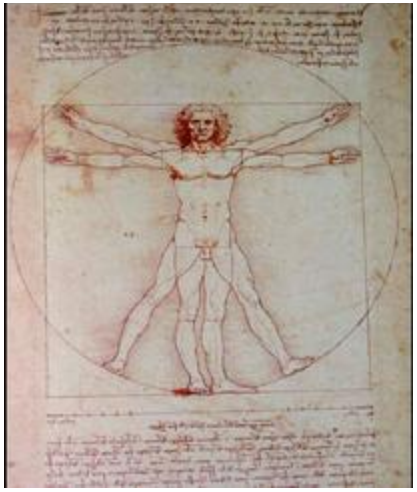
During the last ice age, from about 80,000 to 11,000 years ago, sea levels dropped as the ice sheets grew, exposing large swathes of land now submerged under water and connecting regions now separated by the sea. By reconstructing ancient shorelines, the EFCHED team found that the Bab el-Mandeb strait, now around 30 kilometres wide and one of the world's busiest shipping lanes, was then a narrow, shallow channel.

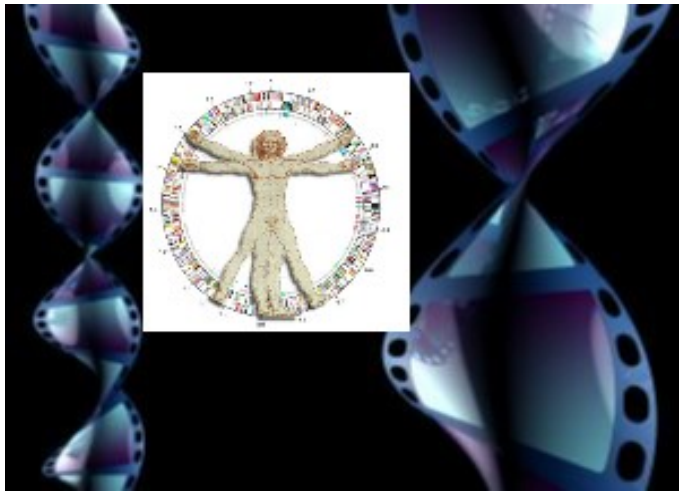
Early humans may have taken this southern route out of Africa. The northern route appears easier, especially given the team's finding that the Suez basin was dry during the last ice age. But crossing the Sahara desert is no small matter. EFCHED scientist Simon Armitage of the Royal Holloway University of London has found some clues as to how this might have been possible. During the past 150,000 years, North Africa has experienced abrupt switches between dry, arid conditions and a humid climate. During the longer wetter periods huge lakes existed in both Chad and Libya, which would have provided a "humid corridor" across the Sahara.

Armitage has discovered that these lakes were present around 10,000 years ago, when there is abundant evidence for human occupation of the Sahara, as well as around 115,000 years ago, when our ancestors first made forays into Israel. It is unknown whether another humid corridor appeared between about 65,000 and 50,000 years ago, the most likely time frame for the human exodus. Moreover, accumulating evidence is pointing to the southern route as the most likely jumping-off point.

Γενετική Ποικιλομορφία

- Φάσμα γονοτύπων
- Πλούσια κληρονομιά





DNA Ανθρώπου

GATTTAGATCGCGATAGAG

GATTTAGATCTCGATAGAG

99.9% ίδιο DNA
0.1% διαφορετικό

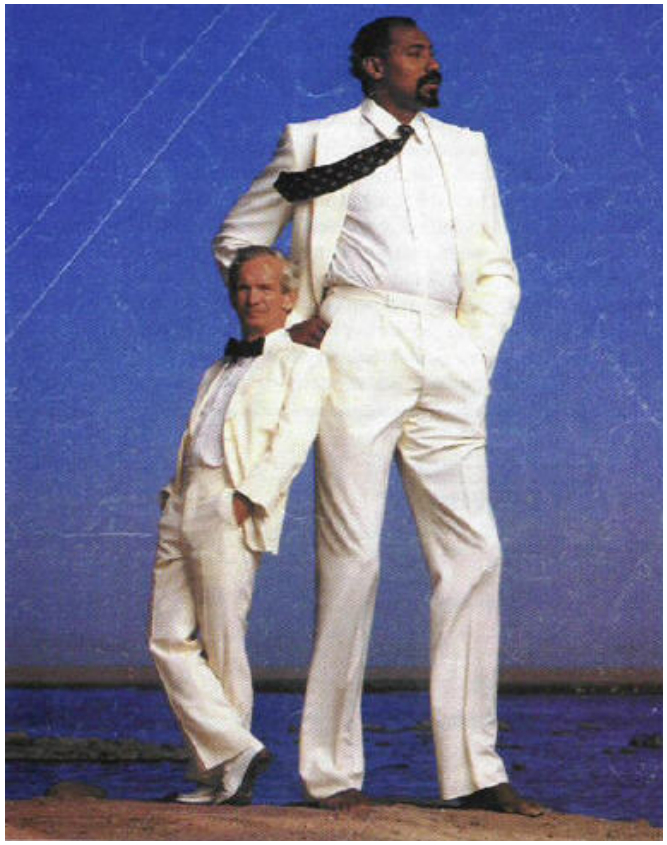
Μεταλλαγές

Πολυμορφισμοί DNA
(Μονοκλεοτιδιακοί SNPs
90% γενετικών παραλλαγών)

Διαφορές με Νεάντερταλ
- 99.5% ίδιο DNA
- 0.8-1.6% γονίδια στους *H.s.*

Διαφορές με χιμπατζή
- 99% ίδιο DNA
- 200 γονίδια (ΚΝΣ)

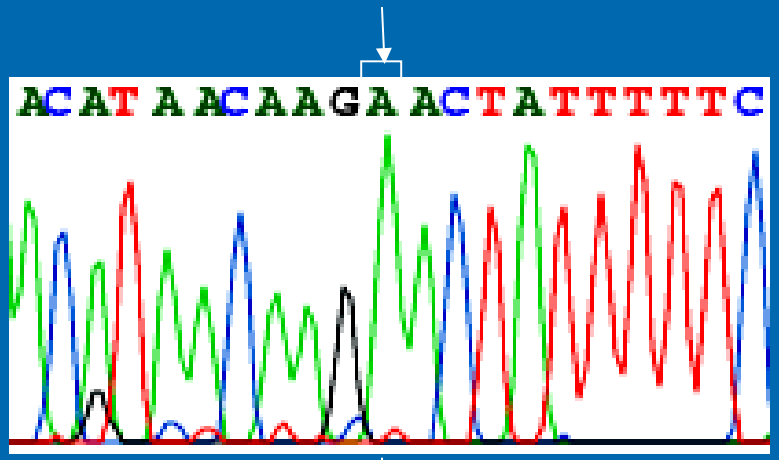
Ιστορία



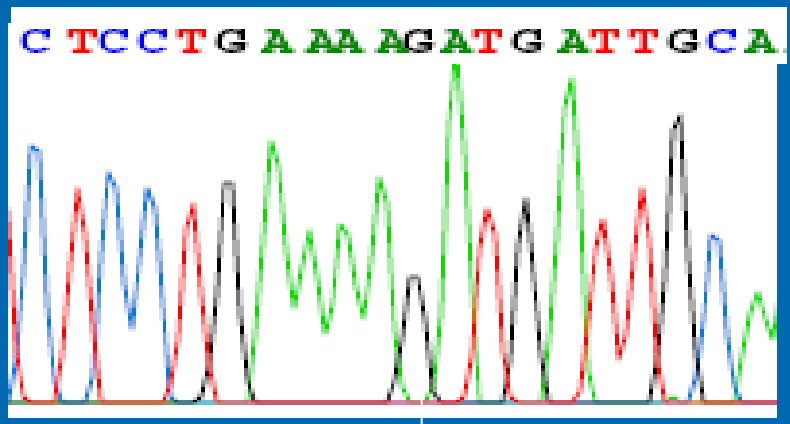
Wilt Chamberlain,
διάσημος
μπασκετμπολίστας
(216 cm; 125 κιλά)

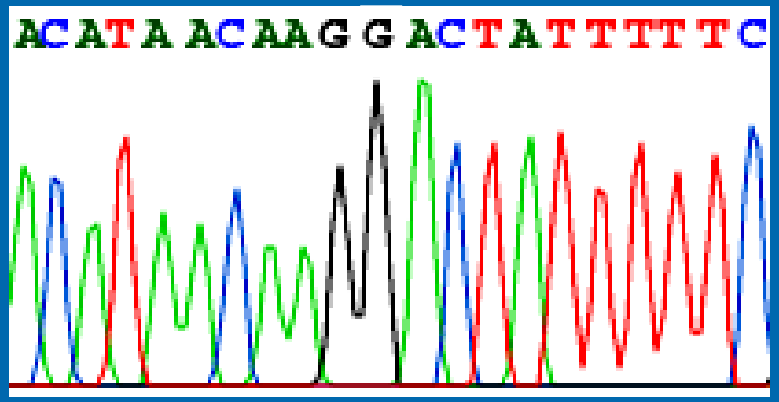
Willie Shoemaker,
διάσημος
τζόκεϋ ιπποδρομιών
(149 cm; 45 κιλά)

Απλότυποι A-G **ALPHA**
G-T **BETA**

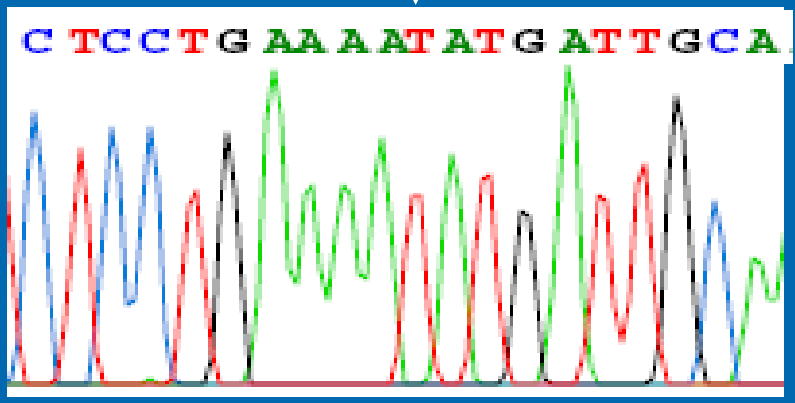


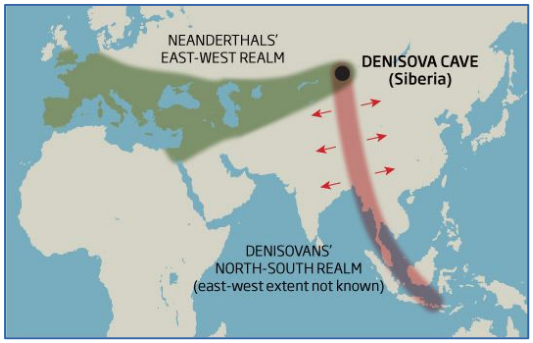
ALPHA





BETA

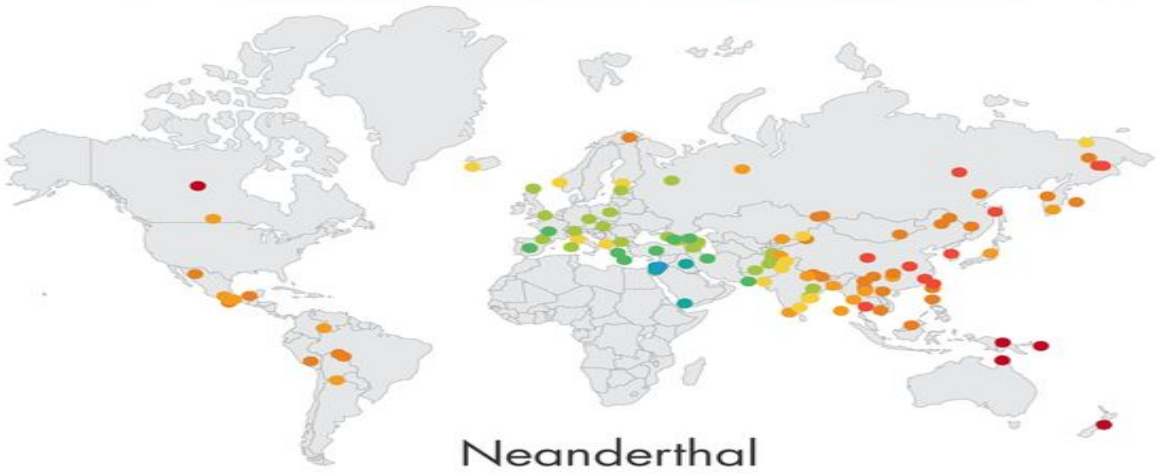


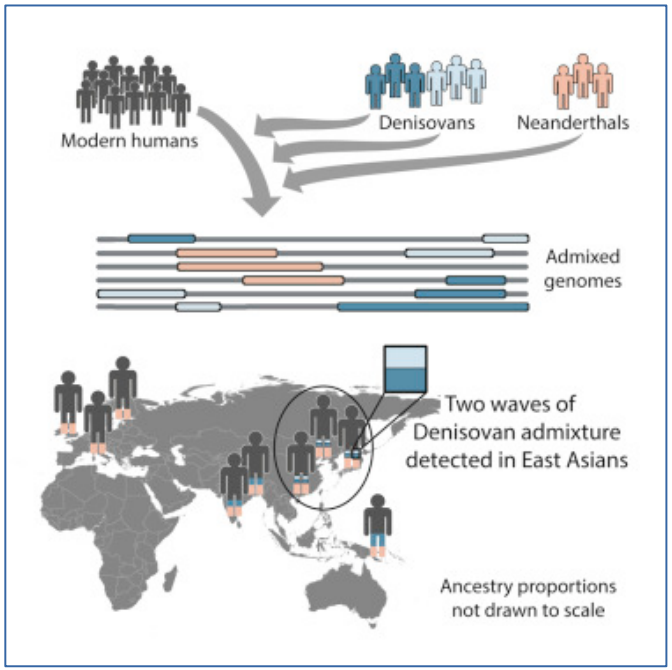


WHERE THE HOMININS ROAMED

As modern humans spread out of Africa, they interbred with Neanderthals and Denisovans. Traces of DNA from those archaic humans remains in our genomes, though some populations tend to have higher concentrations of our extinct ancestors' DNA than others.

Percentage of archaic DNA





Slatkin, Racimo
PNAS 2016

Homo sapiens

Cheddar man
Somerset,
SW England

8,000 y

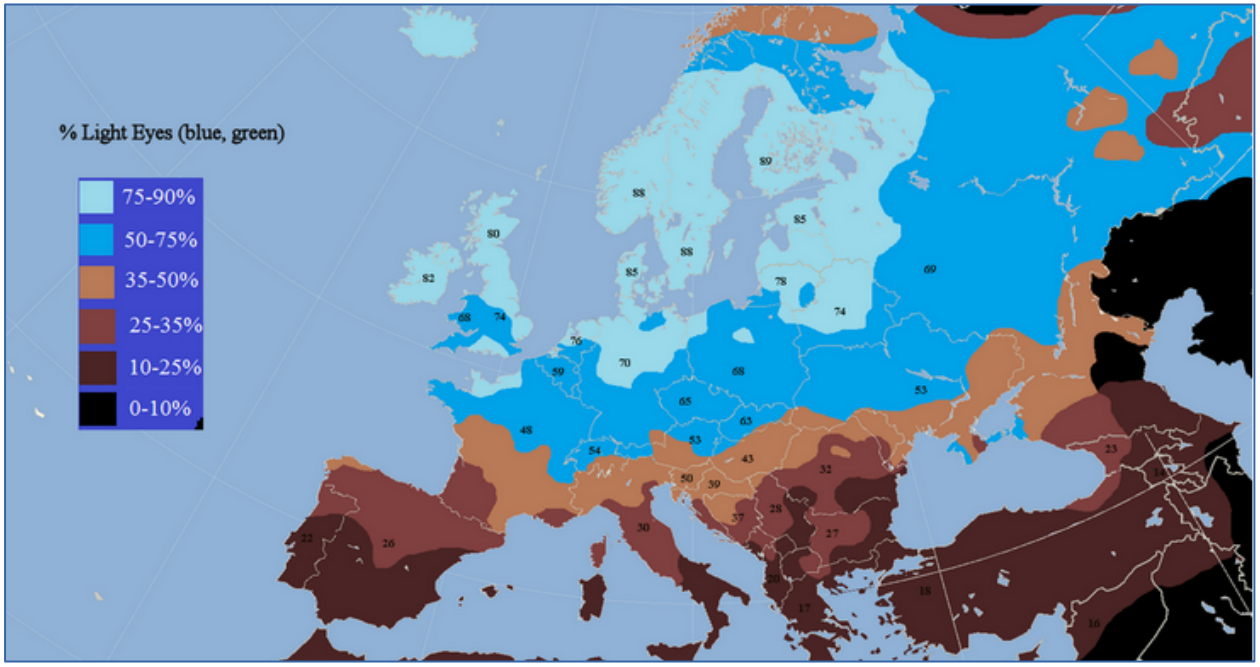
10% of modern Britons are related to him

Brace et al.
BioRxiv 2018

Modern Indian

Γαλάζια Μάτια

Πριν 8000 έτη
Βόρεια Ευρώπη



Eiberg et al.
Human Genetics
2008

Homo sapiens

Πατρική Κληρονομικότητα
(Y chr. DNA)

Μητρική Κληρονομικότητα
(mt DNA)

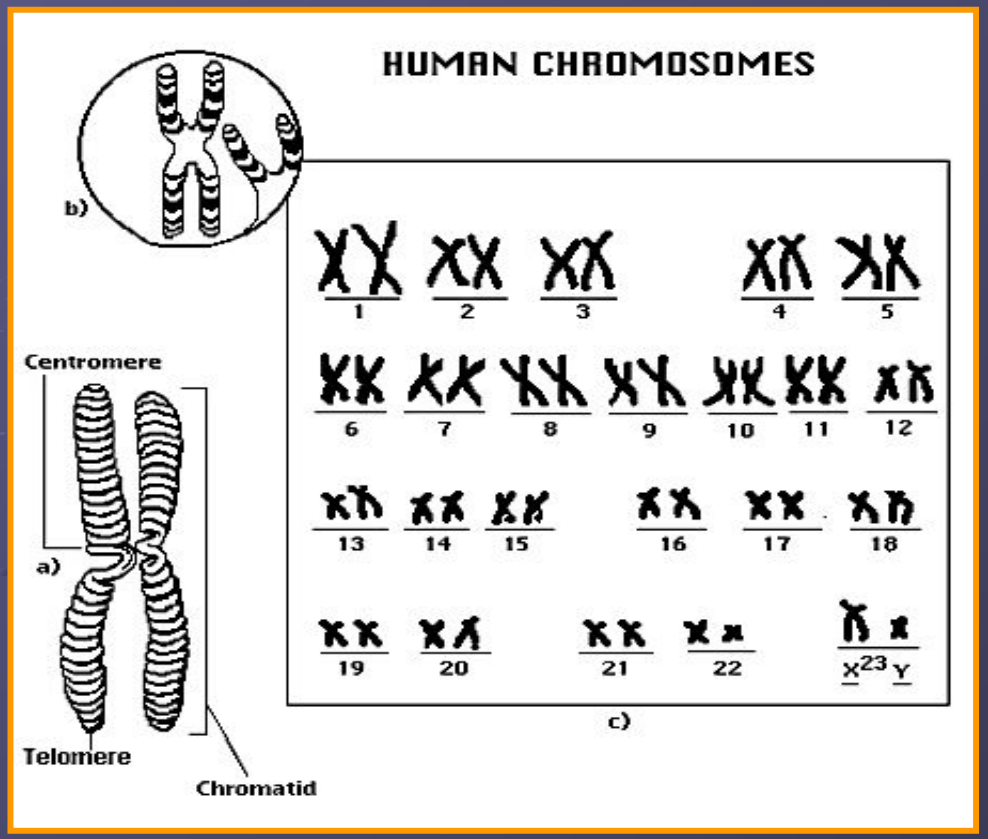
46 χρωμοσώματα (23 ζεύγη)

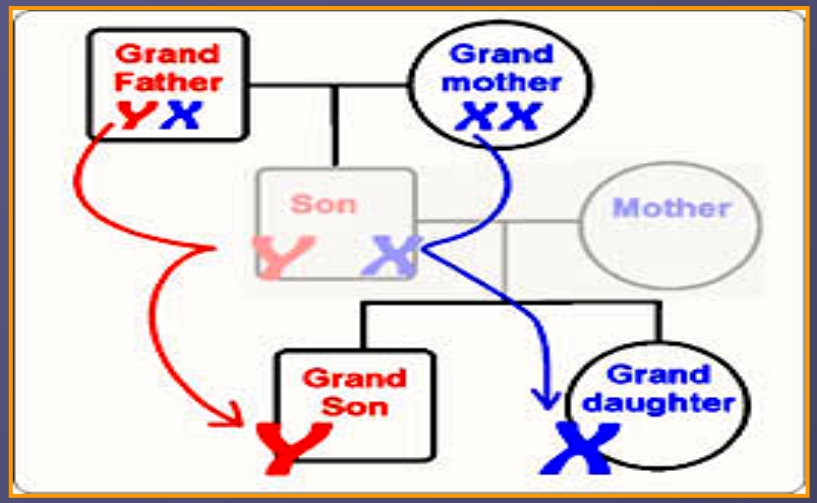
44 αυτοσώματα

+ 2 φύλου Χ,Υ

ΧΥ άνδρας

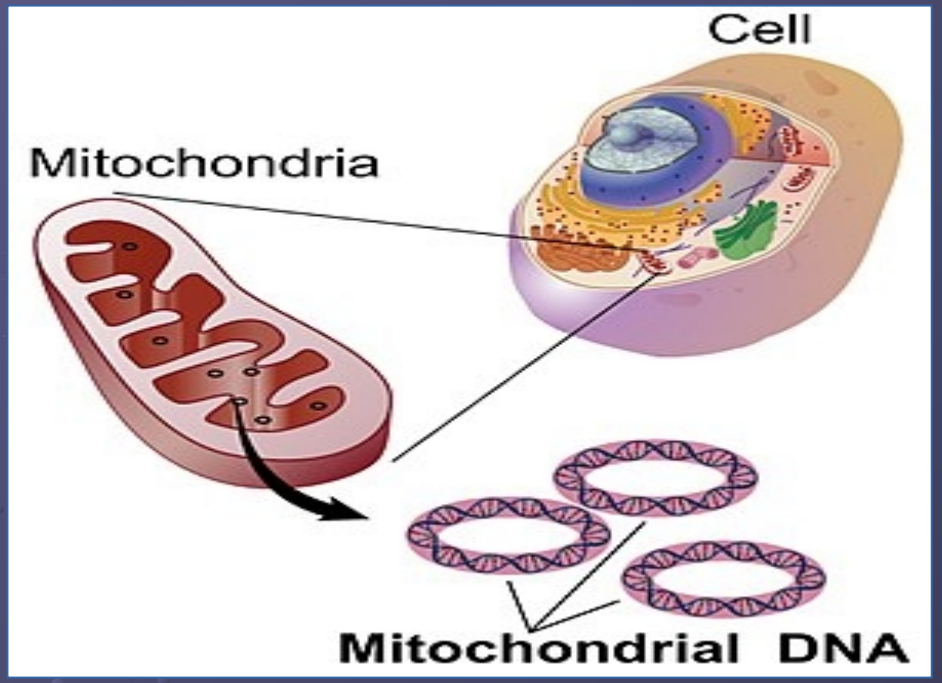
ΧΧ γυναίκα

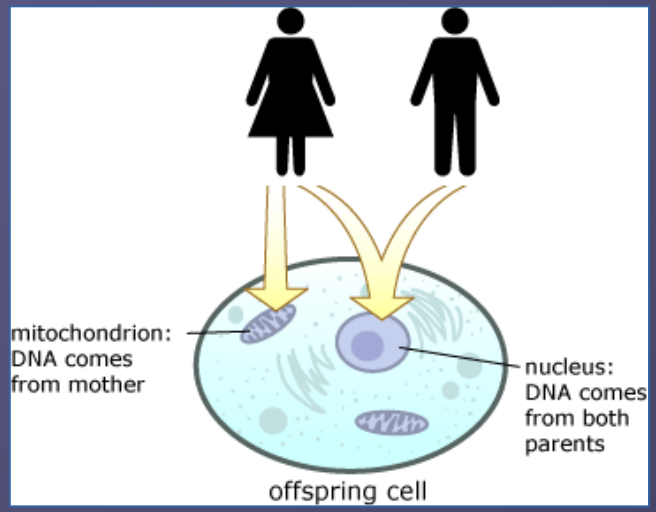


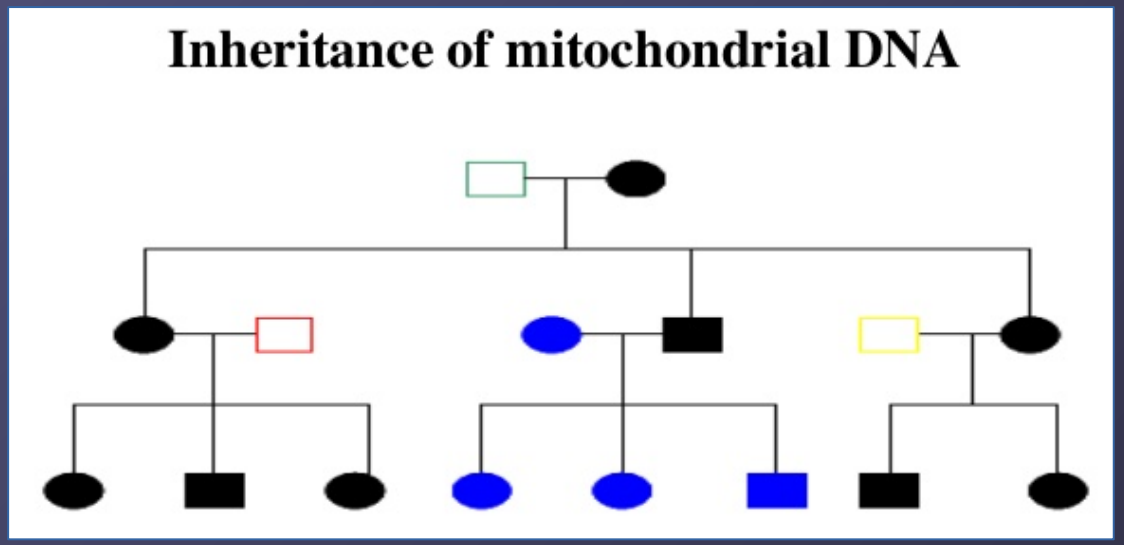


Μιτοχονδριακό DNA

Ωάριο γυναίκας







Homo sapiens

Paternal Y chromosome inheritance

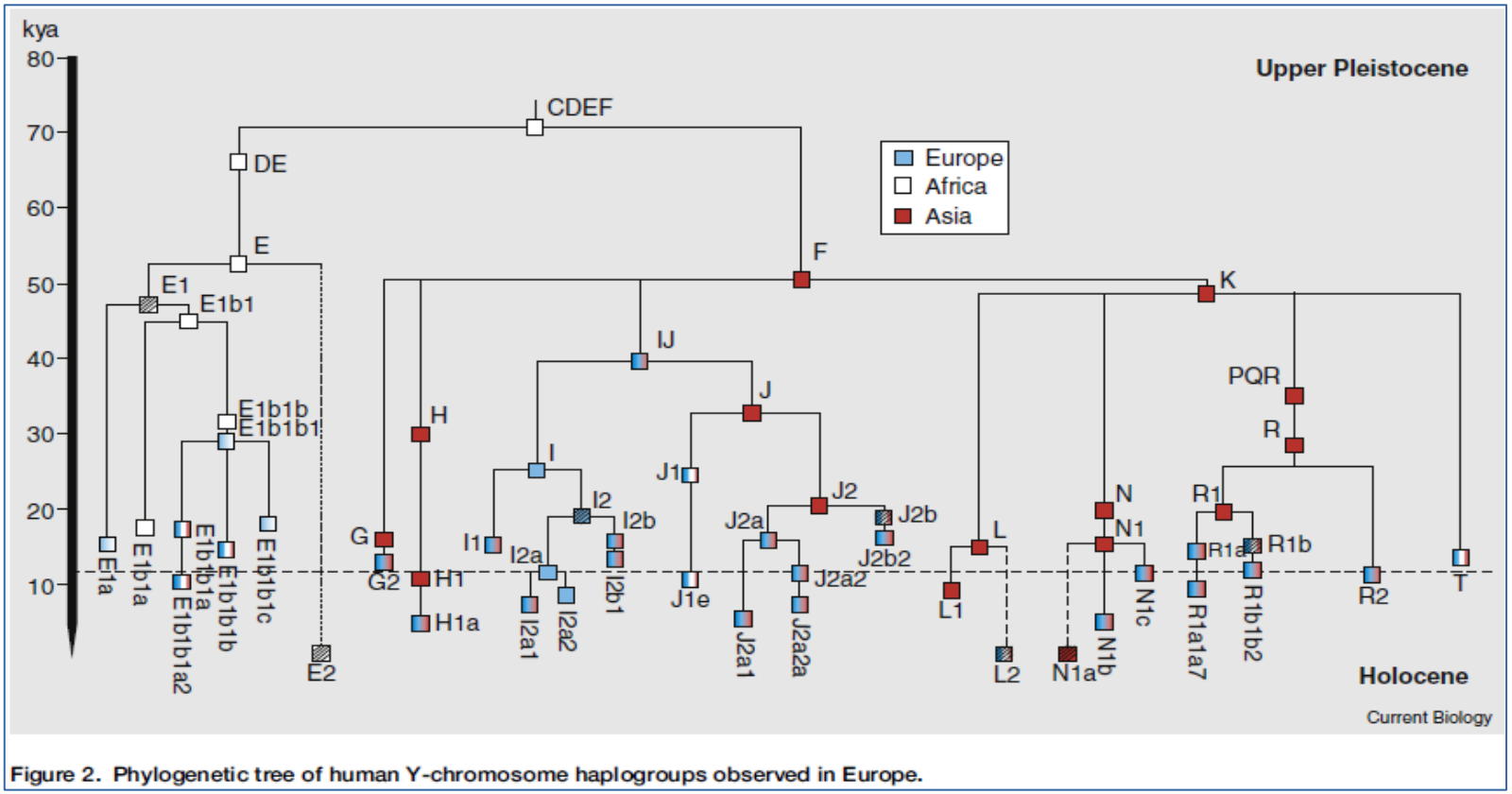


Figure 2. Phylogenetic tree of human Y-chromosome haplogroups observed in Europe.

Soares et al.
Current Biology 2010

Homo sapiens

Soares et al.
Current Biology 2010

Maternal mitochondrial inheritance

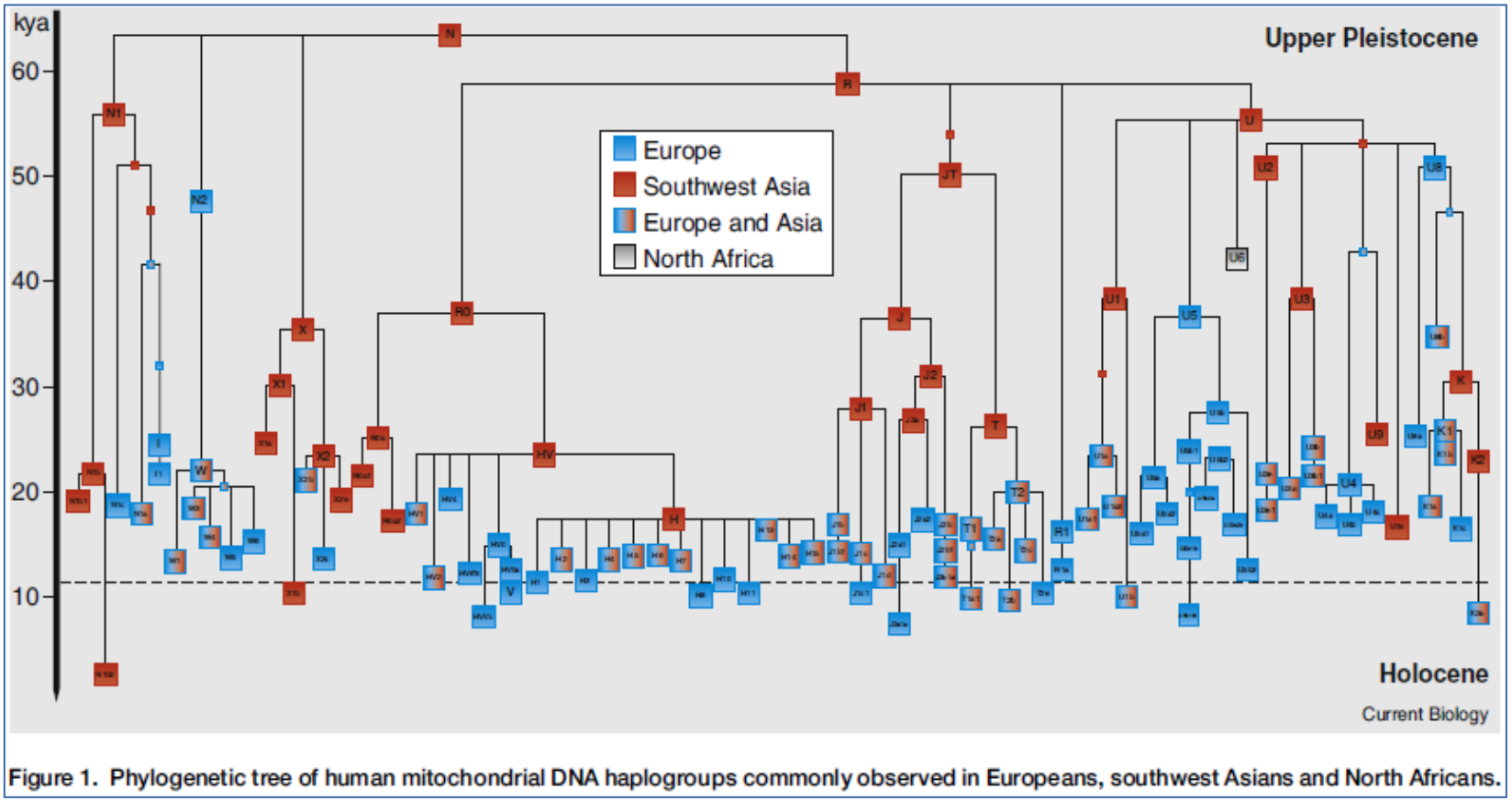
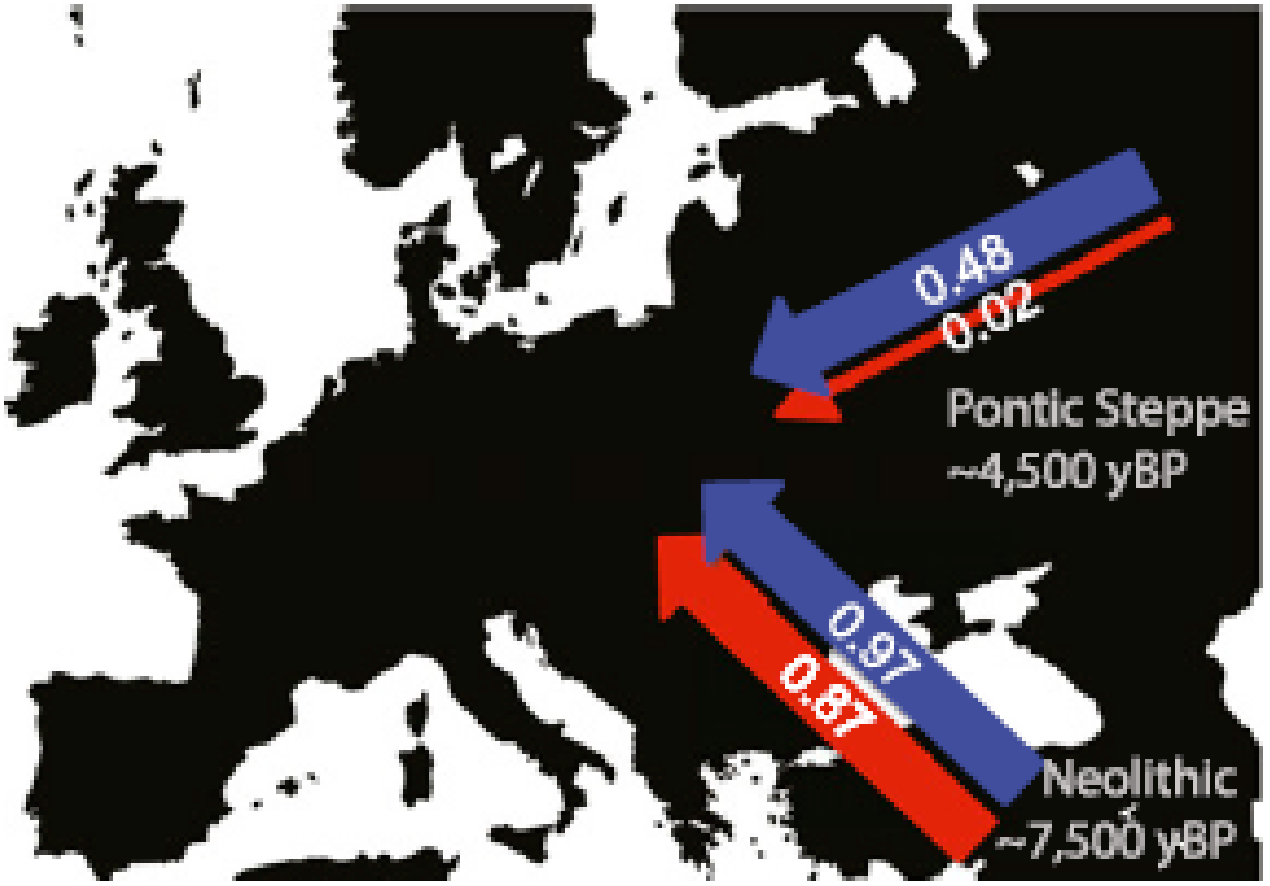


Figure 1. Phylogenetic tree of human mitochondrial DNA haplogroups commonly observed in Europeans, southwest Asians and North Africans.

ΓΕΝΕΤΙΚΗ ΣΥΝΕΙΣΦΟΡΑ ΔΥΟ ΦΥΛΩΝ ΣΤΗΝ ΕΥΡΩΠΗ ΔΥΟ ΜΕΤΑΚΙΝΗΣΕΩΝ

ΜΠΛΕ
Άνδρες

ΚΟΚΚΙΝΟ
Γυναίκες



Goldberg et al.
PNAS 2017

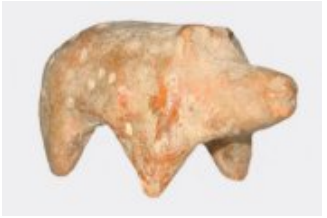
Mathieson et al.
Nature 2018

ΠΑΡΑΓΩΓΗ ΦΑΓΗΤΟΥ Αγροτική-Κτηνοτροφική





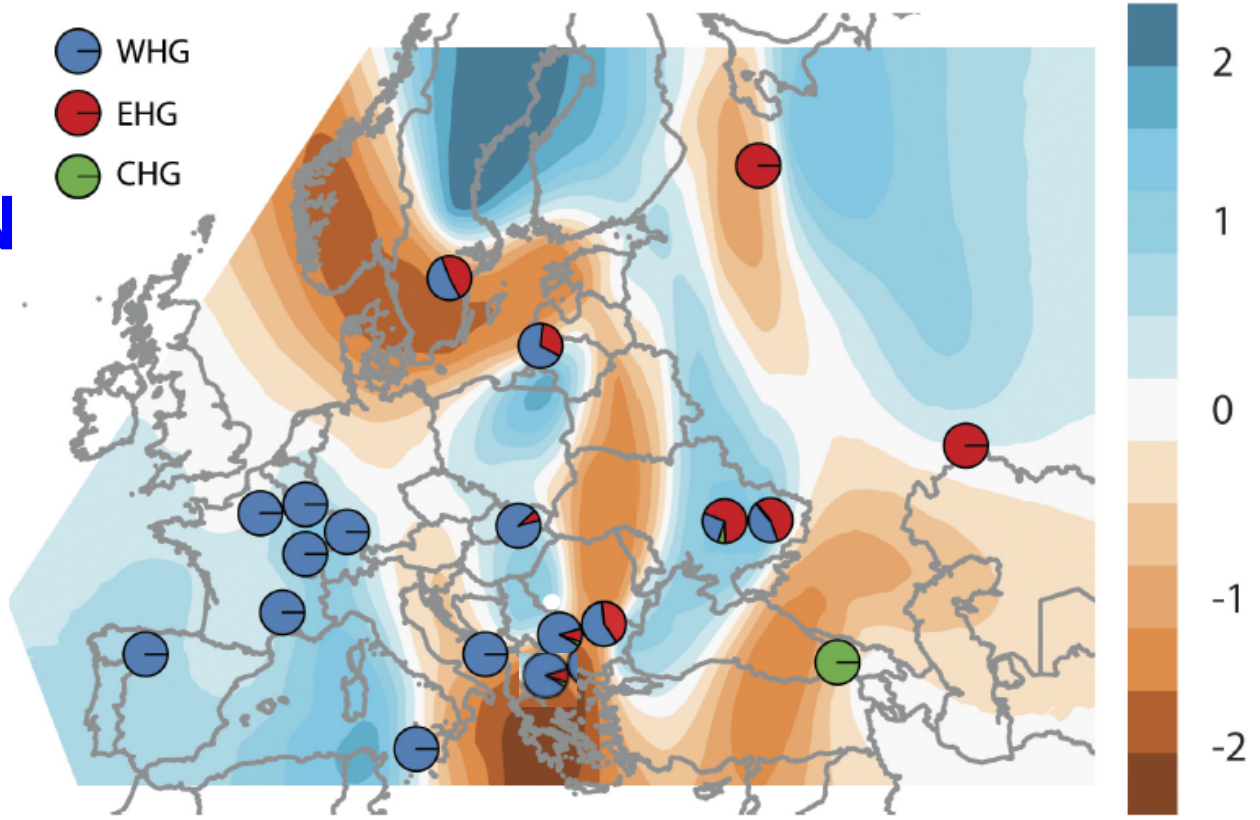


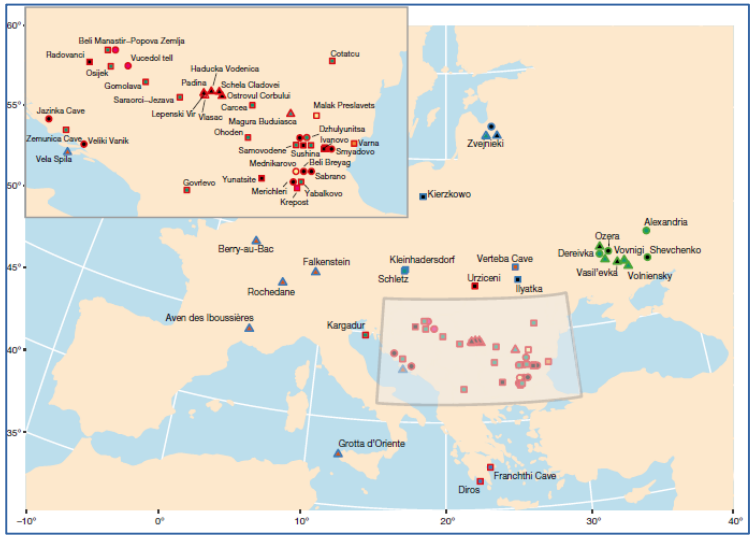


- Τοπική εξέλιξη με επιρροές από Μέση Ανατολή
- Ταυτόχρονη περίπου εξημέρωση ζώων και φυτών
- Πειραματισμός
- Σταθεροί αγροτικοί οικισμοί
- 7000 πΧ: βόδι, πρόβατο, χοίρος, σιτάρι, κριθάρι - Άργισσα Μαγούλα (Θεσσαλία)
- 6000 πΧ: κατσίκα – Σπήλαιο Φράχθι (Αργολίδα, Πελοπόννησος)
- Σημαντικές ενδείξεις ότι η αγροκαλλιέργεια και κτηνοτροφία είχαν καθιερωθεί στην Ελλάδα το 6000-5500 πΧ, στην Νότια/Κεντρική/Ανατολική Ευρώπη το 5000 πΧ, στην Βόρεια/Δυτική Ευρώπη το 5300-4000 πΧ
- Η χρήση αλετριού ξεκίνησε το 3600 και καθιερώθηκε έως 2600 πΧ

Munro and Stiner
Current Anthropology 2015

ΓΕΝΕΤΙΚΗ ΕΥΡΩΠΑΙΩΝ





Mathieson et al.
Nature 2018

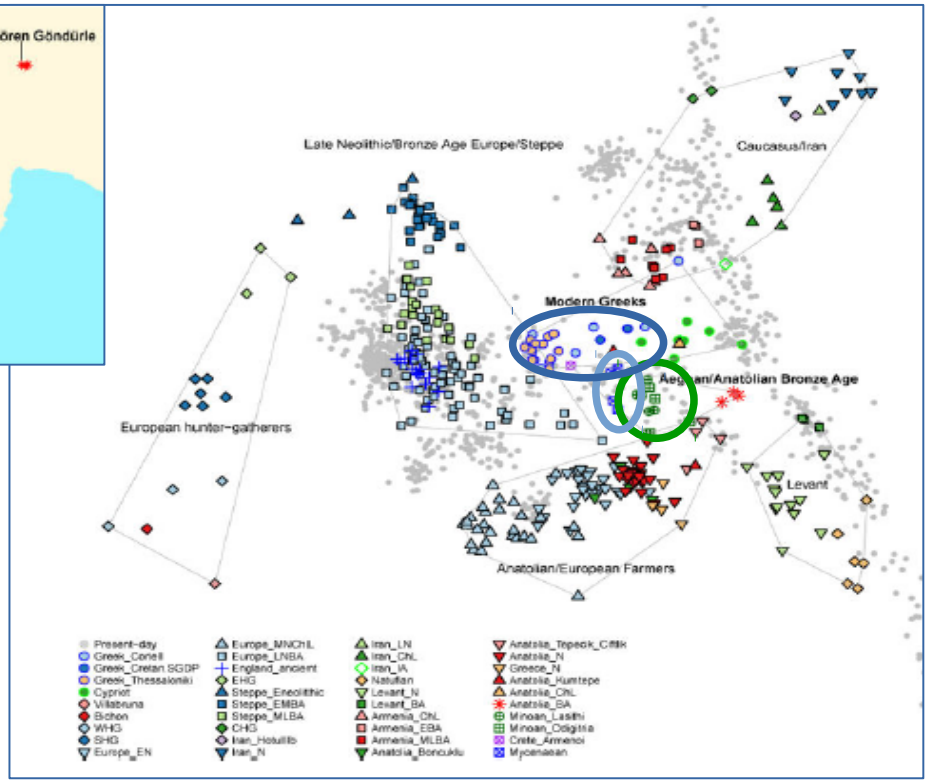
ΓΕΝΕΤΙΚΗ ΜΙΝΩΙΤΩΝ

Lazaridis et al.
Nature 2017

Nature. 2017 August 10; 548(7666): 214–218. doi:10.1038/nature23310.

Genetic origins of the Minoans and Mycenaeans

Iosif Lazaridis[1,2,*,†], Alissa Mittnik[3,4,*], Nick Patterson[2,5], Swapan Mallick[1,2,6], Nadin Rohland[1], Saskia Pfrengle[4], Anja Furtwängler[4], Alexander Peltzer[3,7], Cosimo Posth[3,4], Andonis Vasilakis[8], P.J.P. McGeorge[9], Eleni Konsolaki-Yannopoulou[10], George Korres[11], Holley Martlew[12], Manolis Michalodimitrakis[13], Mehmet Özsait[14], Nesrin Özsait[14], Anastasia Papathanasiou[15], Michael Richards[16], Songül Alpaslan Roodenberg[1], Yannis Tzedakis[17], Robert Arnott[18], Daniel M. Fernandes[19,20], Jeffery R. Hughey[21], Dimitra M. Lotakis[22], Patrick A. Navas[22], Yannis Maniatis[23], John A. Stamatoyannopoulos[24,25,26], Kristin Stewardson[1,6], Philipp Stockhammer[3,27], Ron Pinhasi[19,28], David Reich[1,2,6,†], Johannes Krause[3,4,†], and George Stamatoyannopoulos[22,25,†]



Μινωίτες
~2,900–1,700 πΧ

Μυκηναίοι
~1,700–1,200 πΧ

ΓΕΝΕΤΙΚΗ ΜΙΝΩΙΤΩΝ

nature COMMUNICATIONS

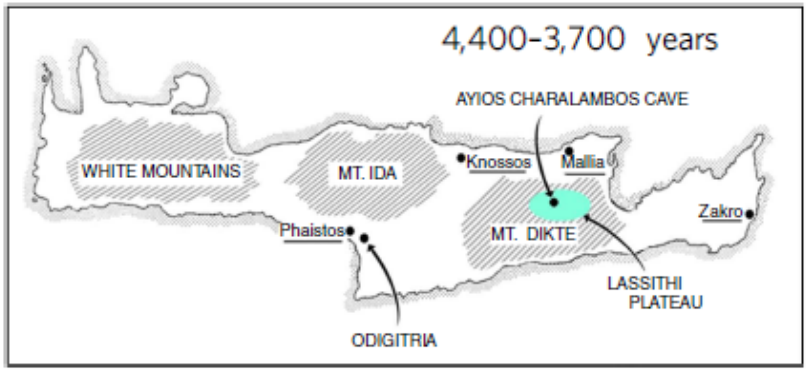
ARTICLE

Received 31 Dec 2012 | Accepted 12 Apr 2013 | Published 14 May 2013

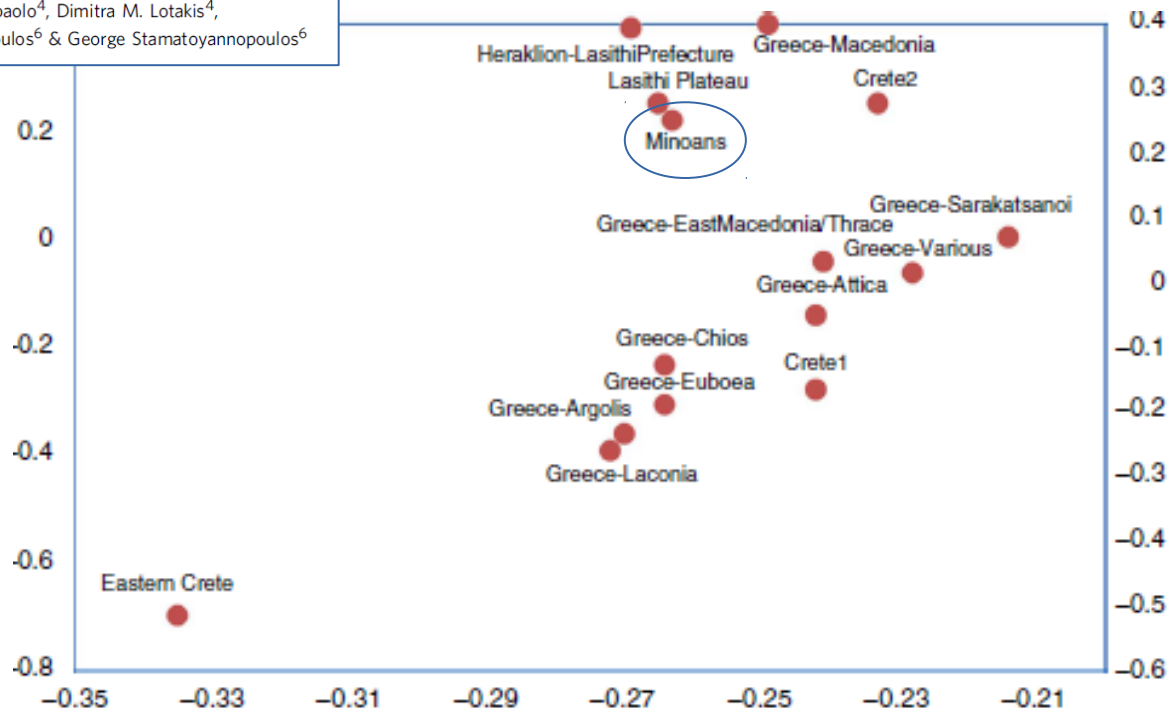
DOI: 10.1038/ncomms2871 OPEN

A European population in Minoan Bronze Age Crete

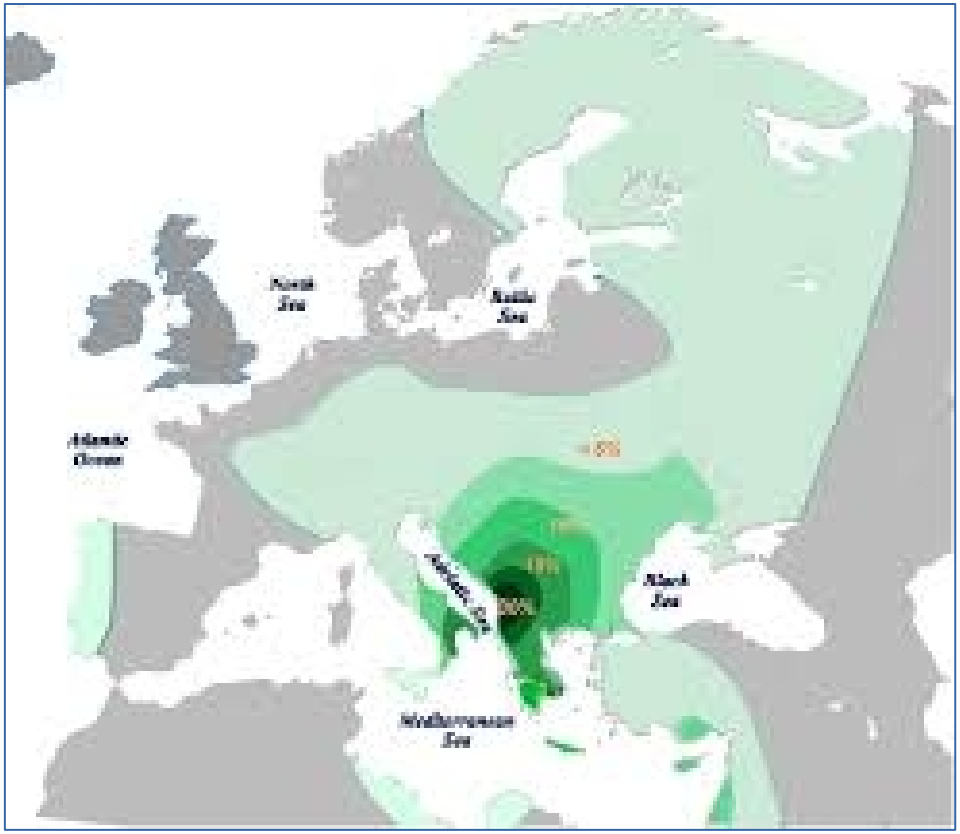
Jeffery R. Hughey[1], Peristera Paschou[2], Petros Drineas[3], Donald Mastropaolo[4], Dimitra M. Lotakis[4], Patrick A. Navas[4], Manolis Michalodimitrakis[5], John A. Stamatoyannopoulos[6] & George Stamatoyannopoulos[6]



Hughey et al. *Nature Communications* 2013



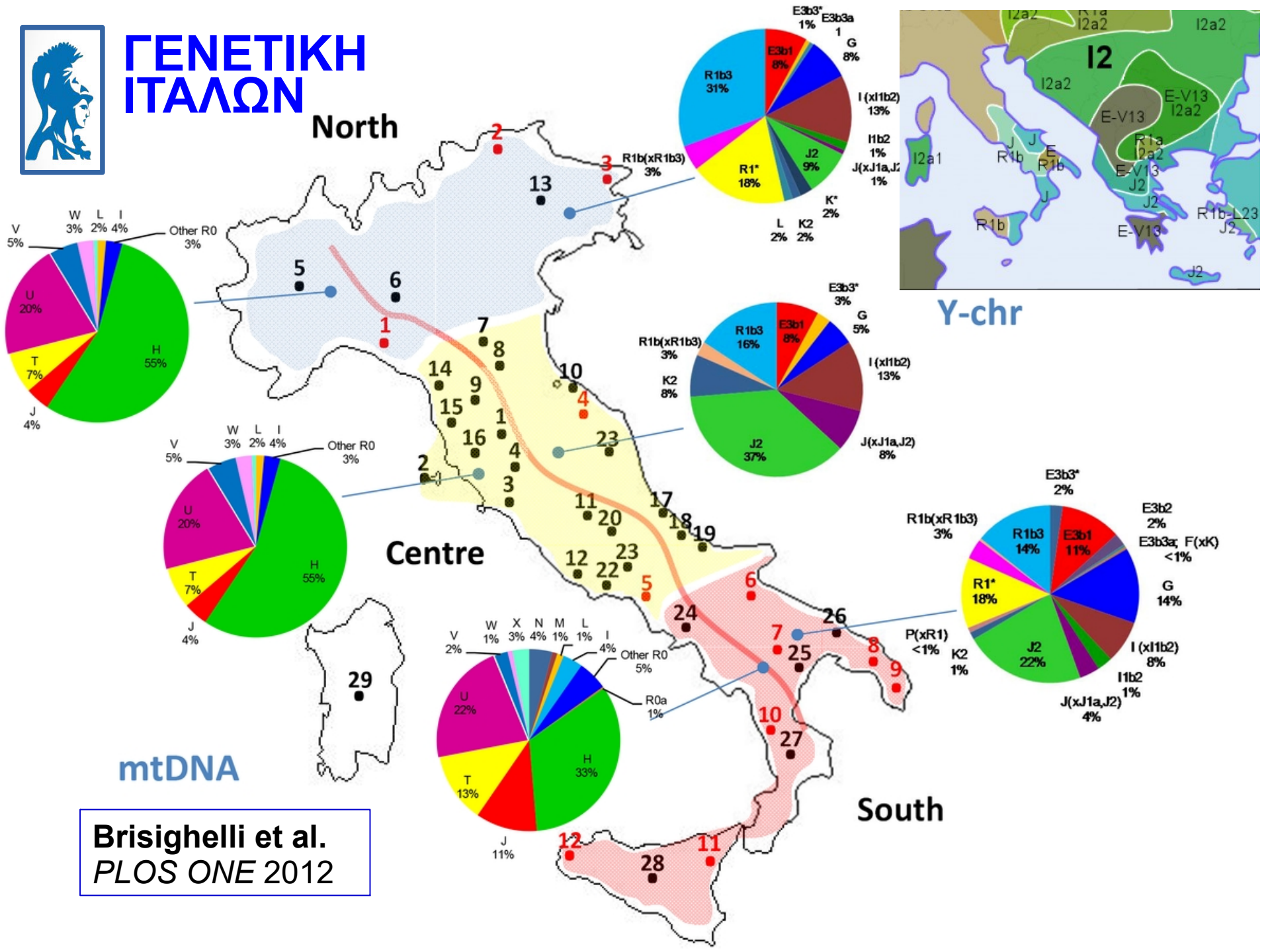
“Ελληνικό” Y haplogroup E1b1b1a2 (E-V13)



King, Di Cristofaro, Kouvatsi, Triantaphyllidis et al.
(Corsica) *BMC Evol Biol* 2011

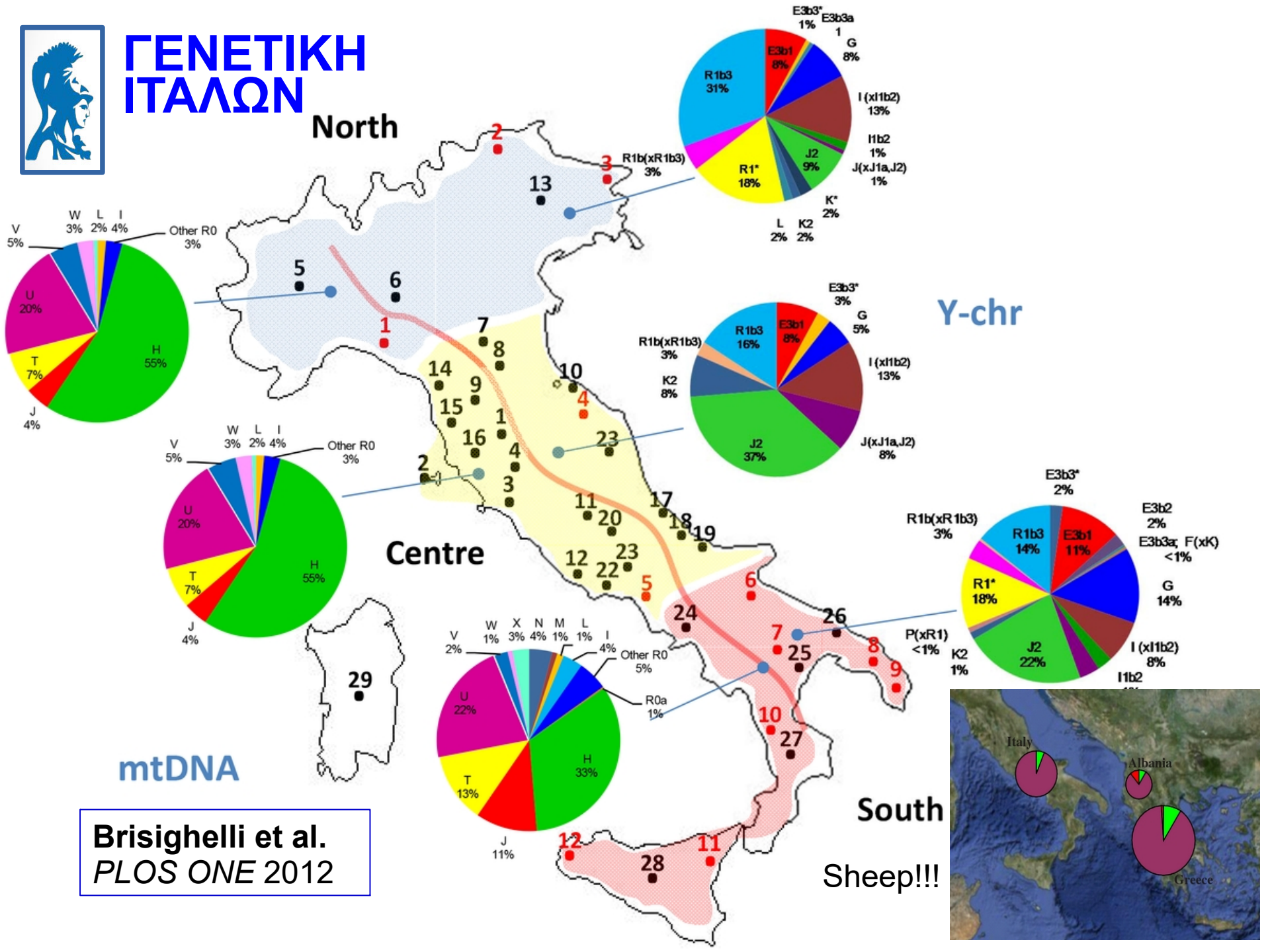
Gunther, Jakobsson
Current Opinion in Genetics & Development 2016

ΓΕΝΕΤΙΚΗ ΙΤΑΛΩΝ



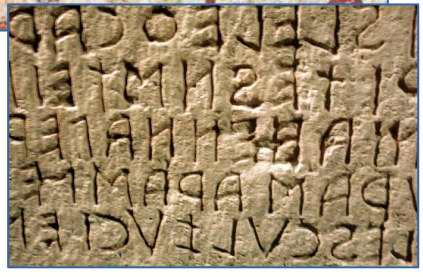
Brisighelli et al.
PLOS ONE 2012

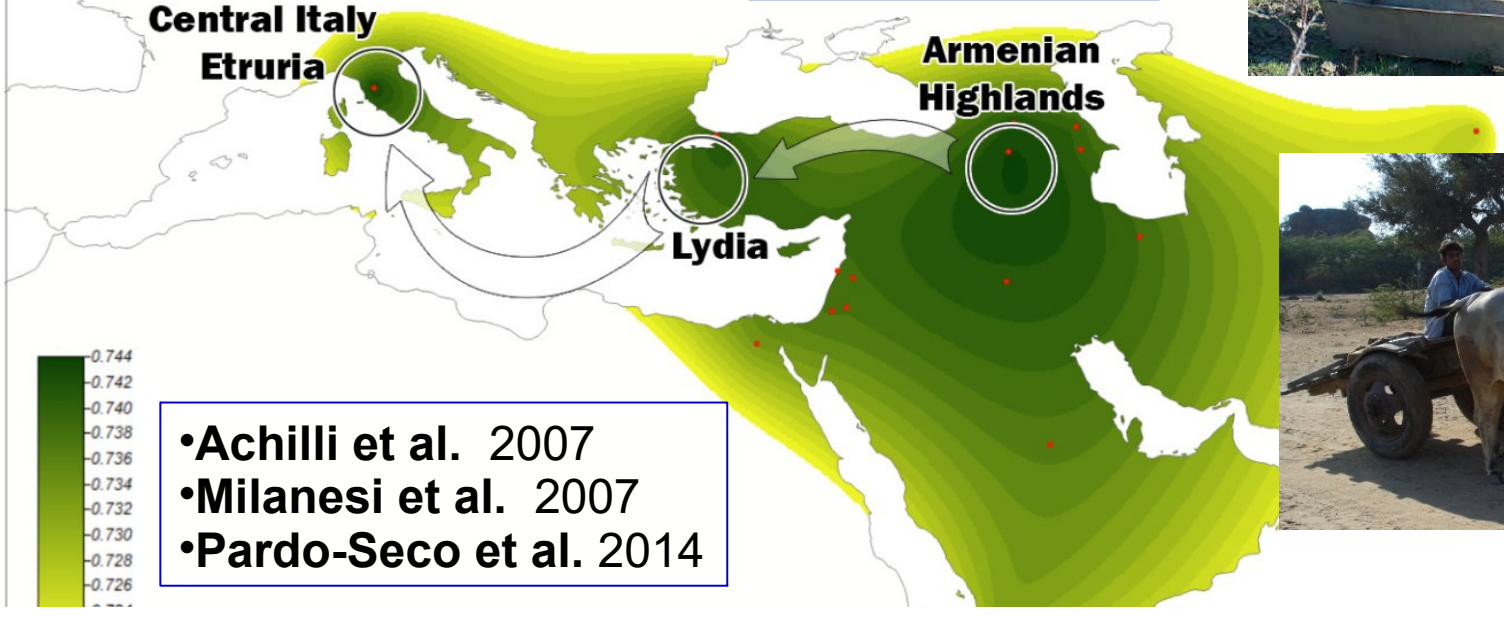
ΓΕΝΕΤΙΚΗ ΙΤΑΛΩΝ



Brisighelli et al.
PLOS ONE 2012

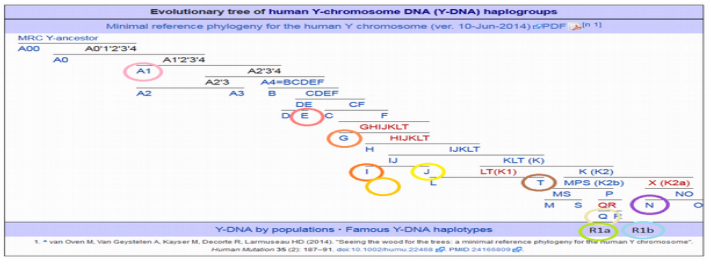
ΓΕΝΕΤΙΚΗ ΠΡΟΕΛΕΥΣΗ ΕΤΡΟΥΣΚΩΝ

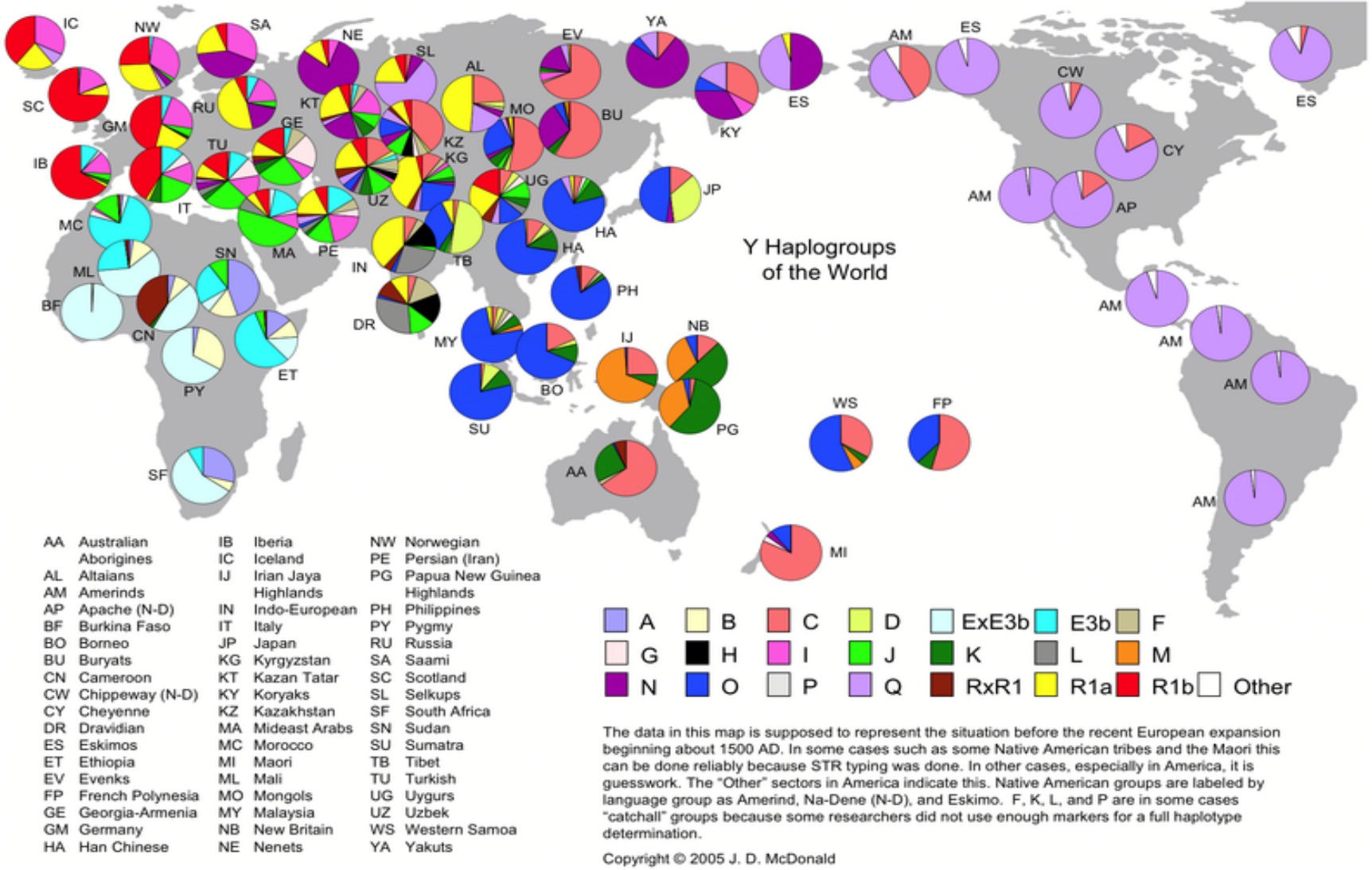




- **Achilli et al.** 2007
- **Milanesi et al.** 2007
- **Pardo-Seco et al.** 2014

Y haplogroups
Paternal Inheritance





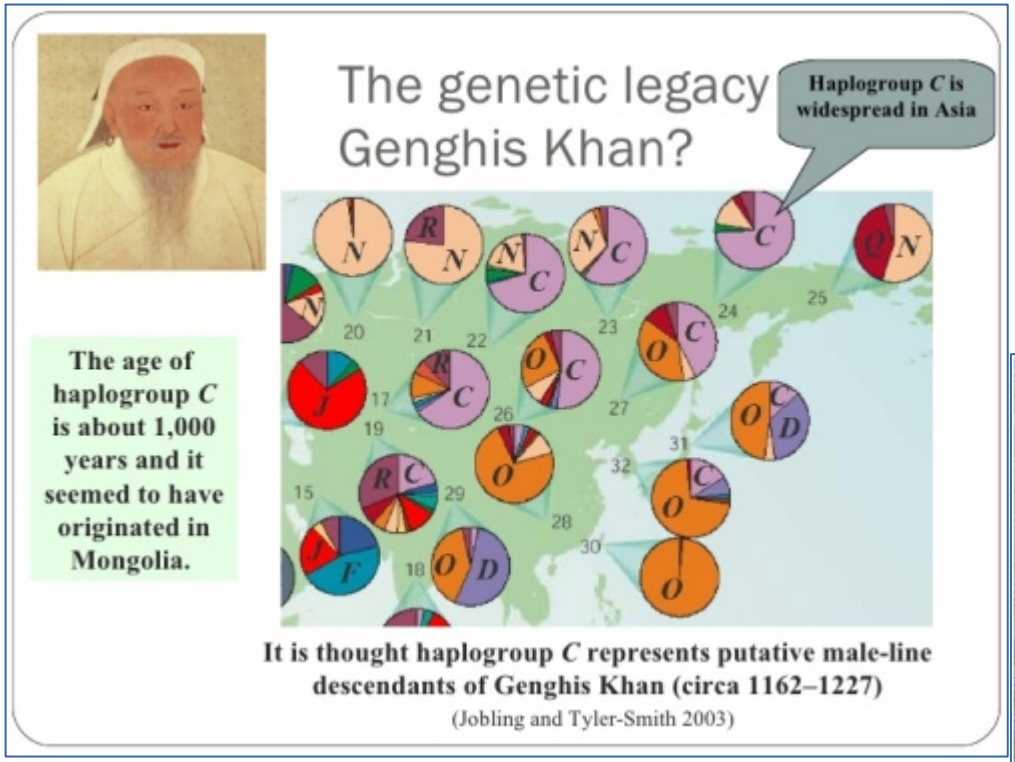
AA	Australian Aborigines	IB	Iberia	NW	Norwegian
AL	Altaians	IC	Iceland	PE	Persian (Iran)
AM	Amerinds	IJ	Irian Jaya Highlands	PG	Papua New Guinea Highlands
AP	Apache (N-D)	IN	Indo-European	PH	Philippines
BF	Burkina Faso	IT	Italy	PY	Pygmy
BO	Borneo	JP	Japan	RU	Russia
BU	Buryats	KG	Kyrgyzstan	SA	Saami
CN	Cameroon	KT	Kazan Tatar	SC	Scotland
CW	Chippeway (N-D)	KY	Koryaks	SL	Selkups
CY	Cheyenne	KZ	Kazakhstan	SF	South Africa
DR	Dravidian	MA	Mideast Arabs	SN	Sudan
ES	Eskimos	MC	Morocco	SU	Sumatra
ET	Ethiopia	MI	Maori	TB	Tibet
EV	Evenks	ML	Mali	TU	Turkish
FP	French Polynesia	MO	Mongols	UG	Uygurs
GE	Georgia-Armenia	MY	Malaysia	UZ	Uzbek
GM	Germany	NB	New Britain	WS	Western Samoa
HA	Han Chinese	NE	Nenets	YA	Yakuts

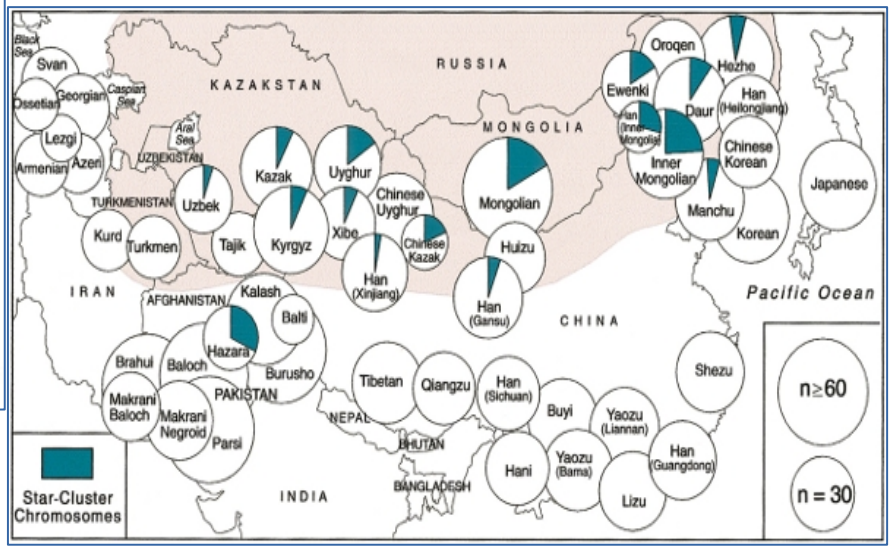
The data in this map is supposed to represent the situation before the recent European expansion beginning about 1500 AD. In some cases such as some Native American tribes and the Maori this can be done reliably because STR typing was done. In other cases, especially in America, it is guesswork. The "Other" sectors in America indicate this. Native American groups are labeled by language group as Amerind, Na-Dene (N-D), and Eskimo. F, K, L, and P are in some cases "catchall" groups because some researchers did not use enough markers for a full haplotype determination.

Copyright © 2005 J. D. McDonald

Y απλότυπος του Τζέγκις Χαν

- ~10% των ανδρών στην περιοχή της Μογγολικής εξάπλωσης
- ~0.5% των ανδρών παγκοσμίως, περίπου 16 εκατομμύρια σήμερα

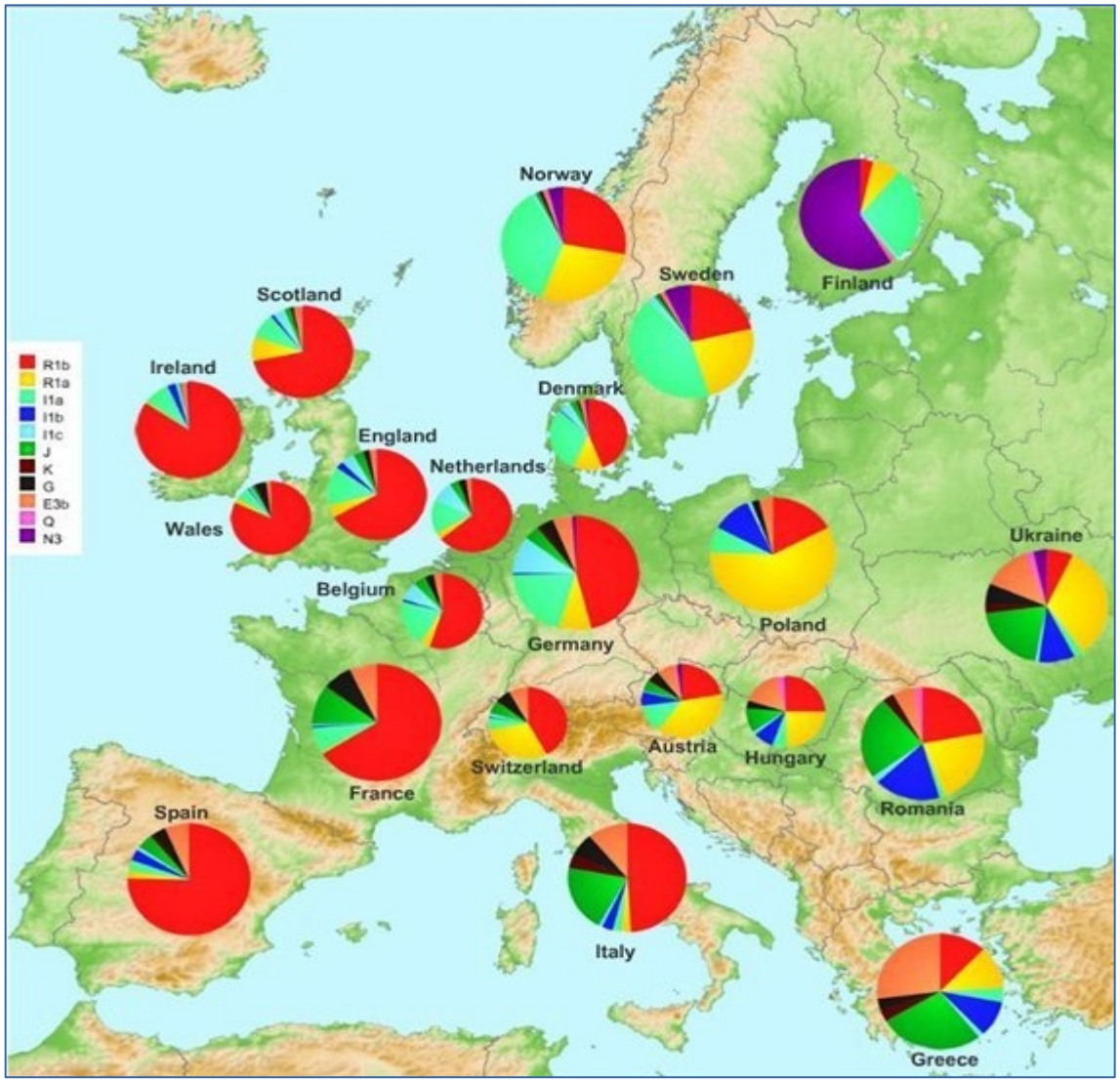


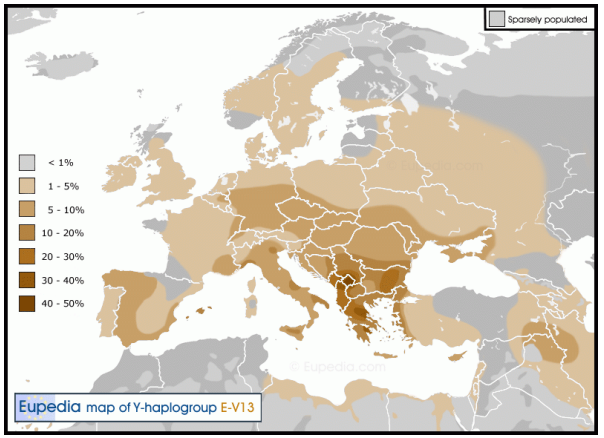


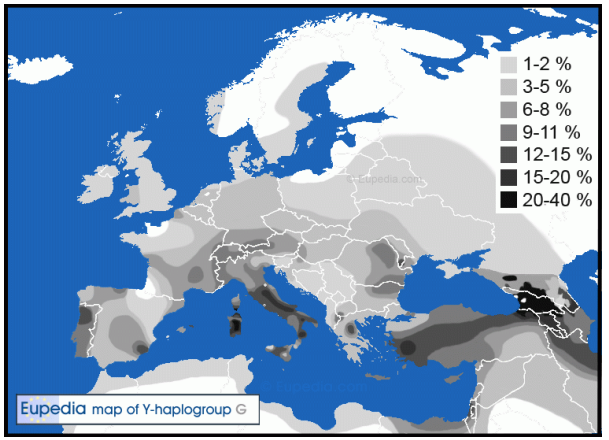
Zerjal et al.
The genetic legacy of the Mongols
Am J Hum Genet 2003

Y απλότυποι στην Ευρώπη

Soares et al.
Current Biology 2010

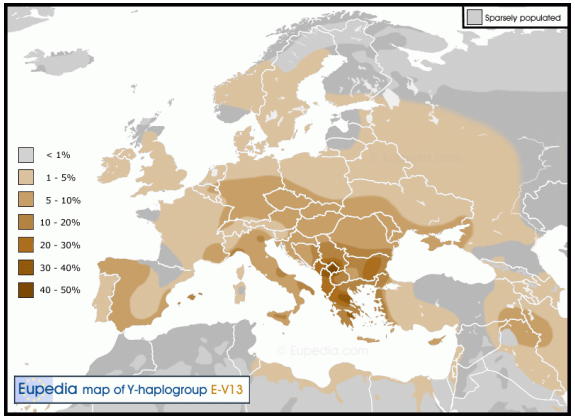


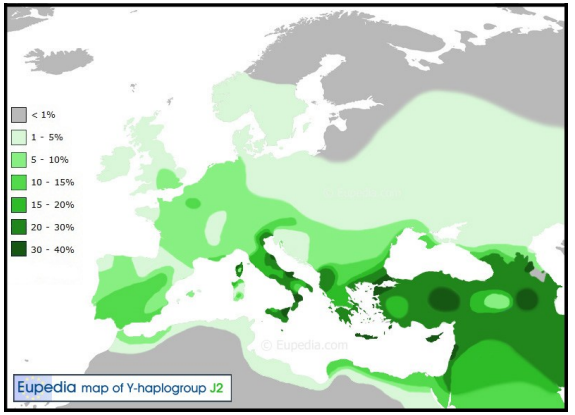


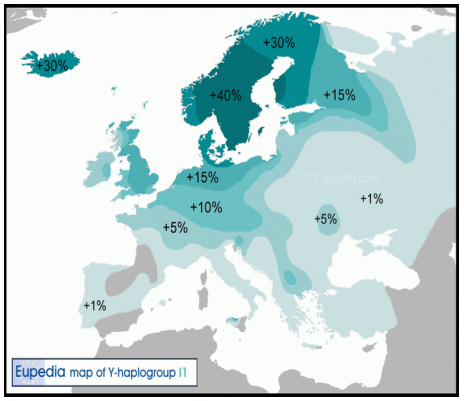


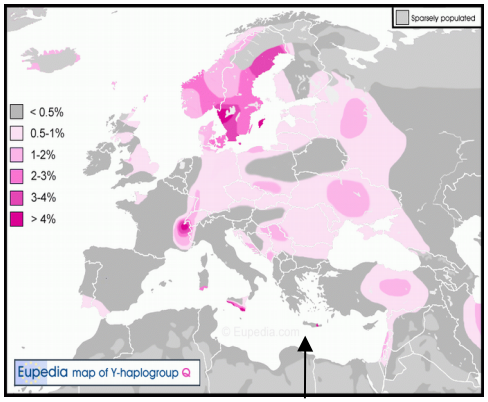
Y haplogroups In Europeans

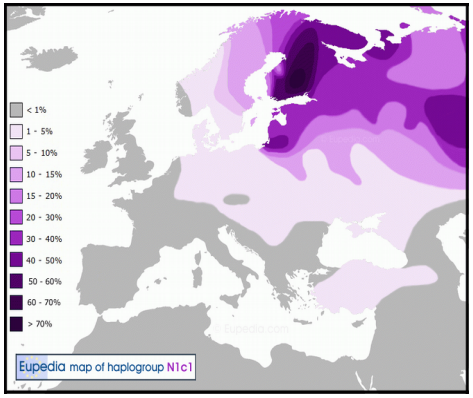
Soares et al.
Current Biology 2010

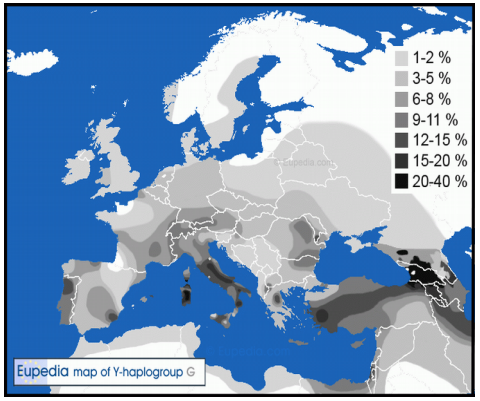


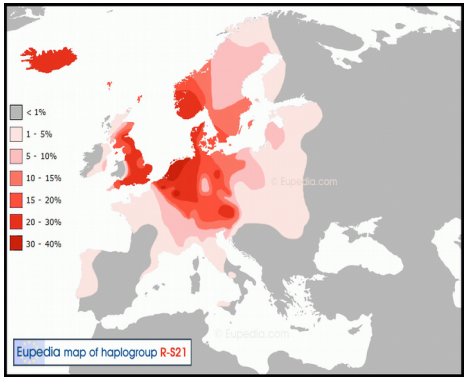


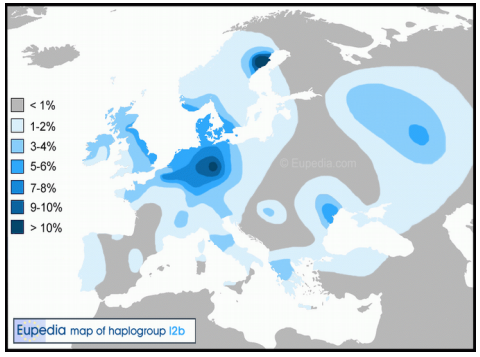


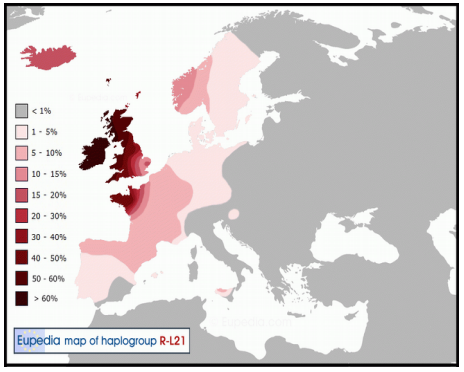


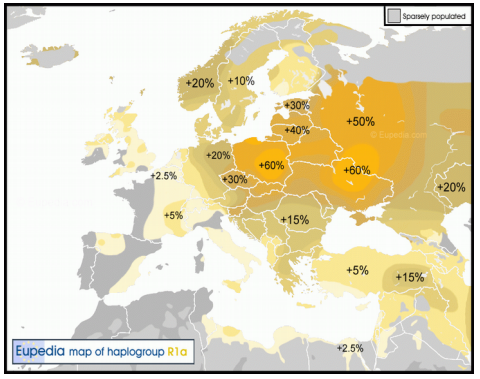




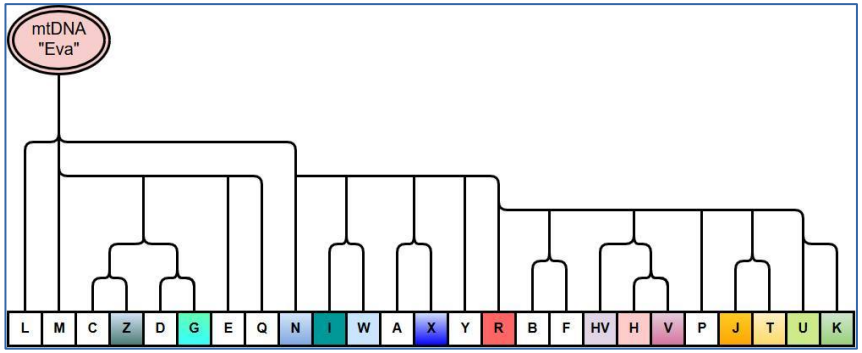


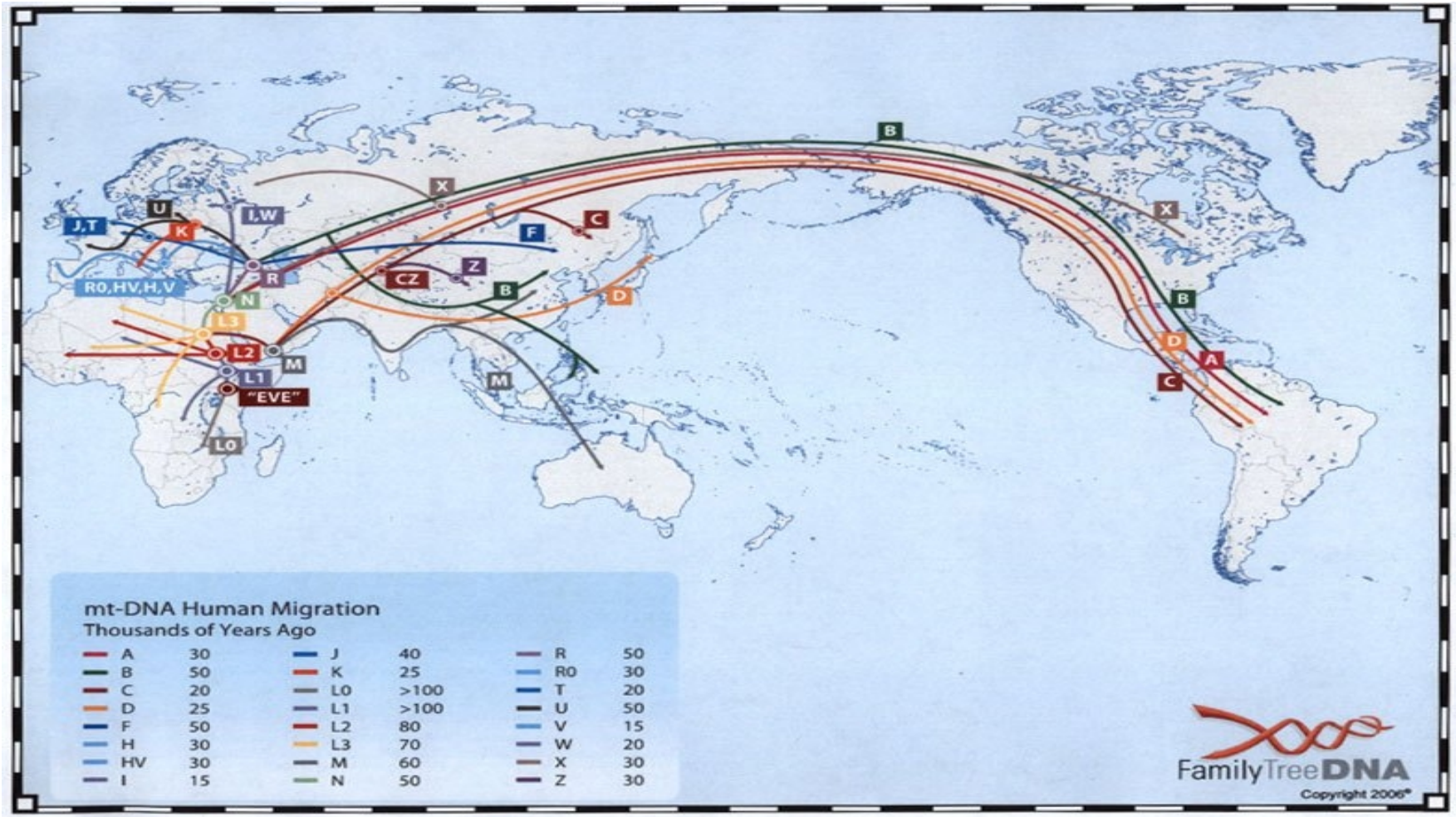






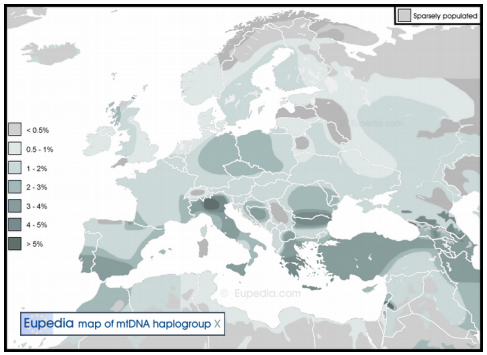
mt haplogroups
Maternal Inheritance

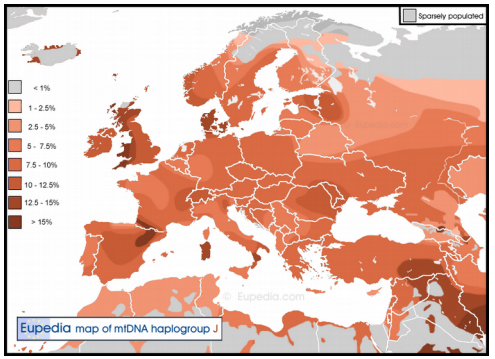


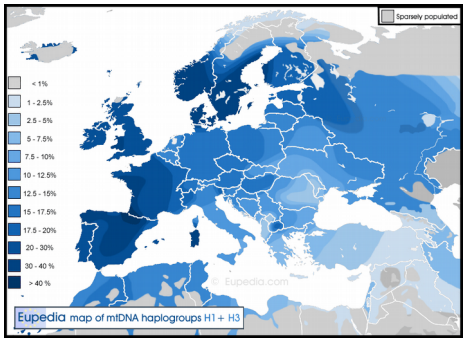


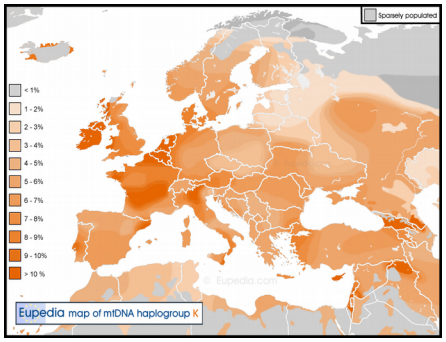
mt haplogroups in Europeans

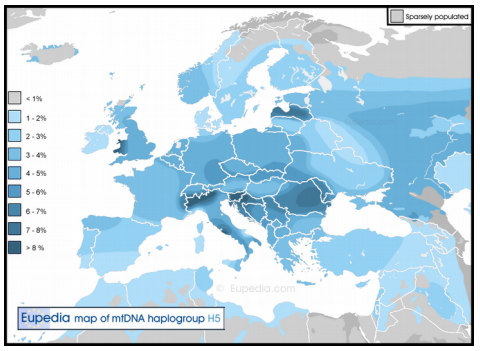
Soares et al.
Current Biology 2010

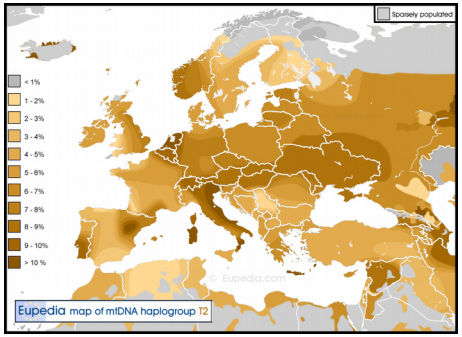


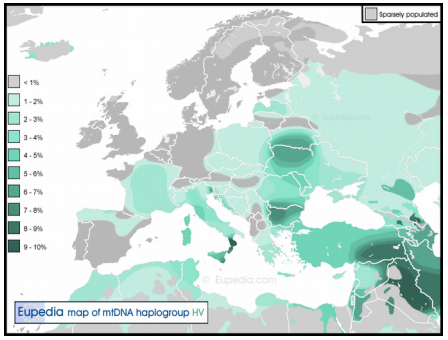


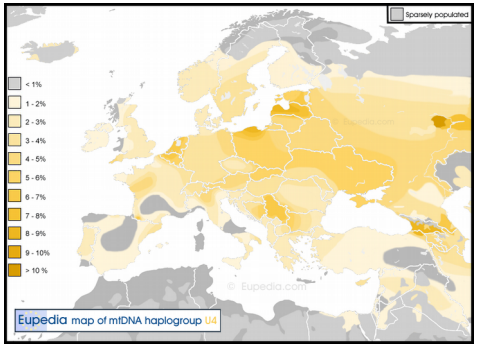


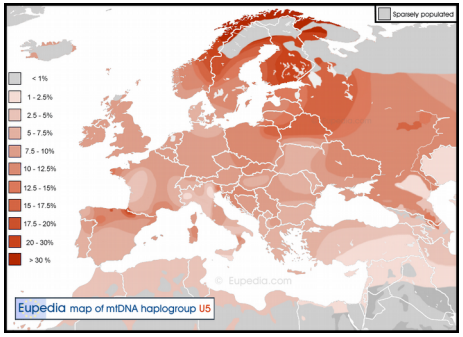


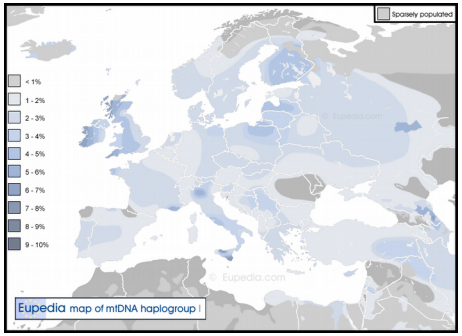


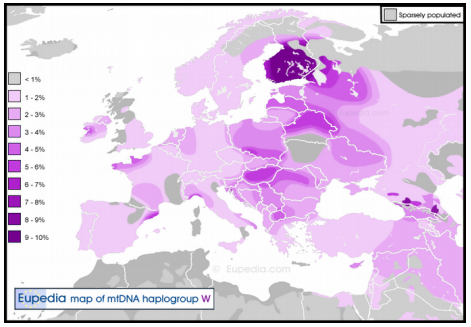






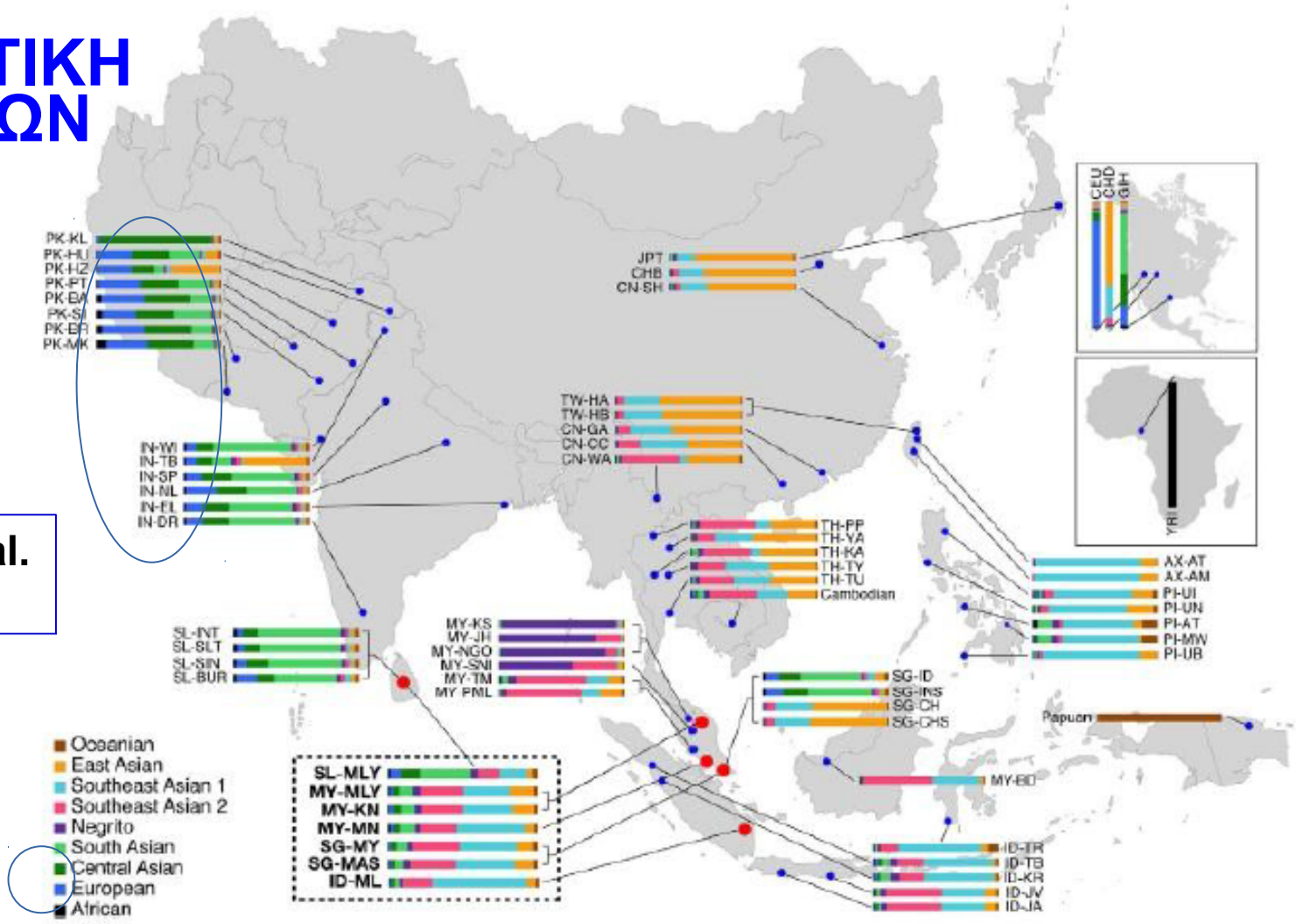




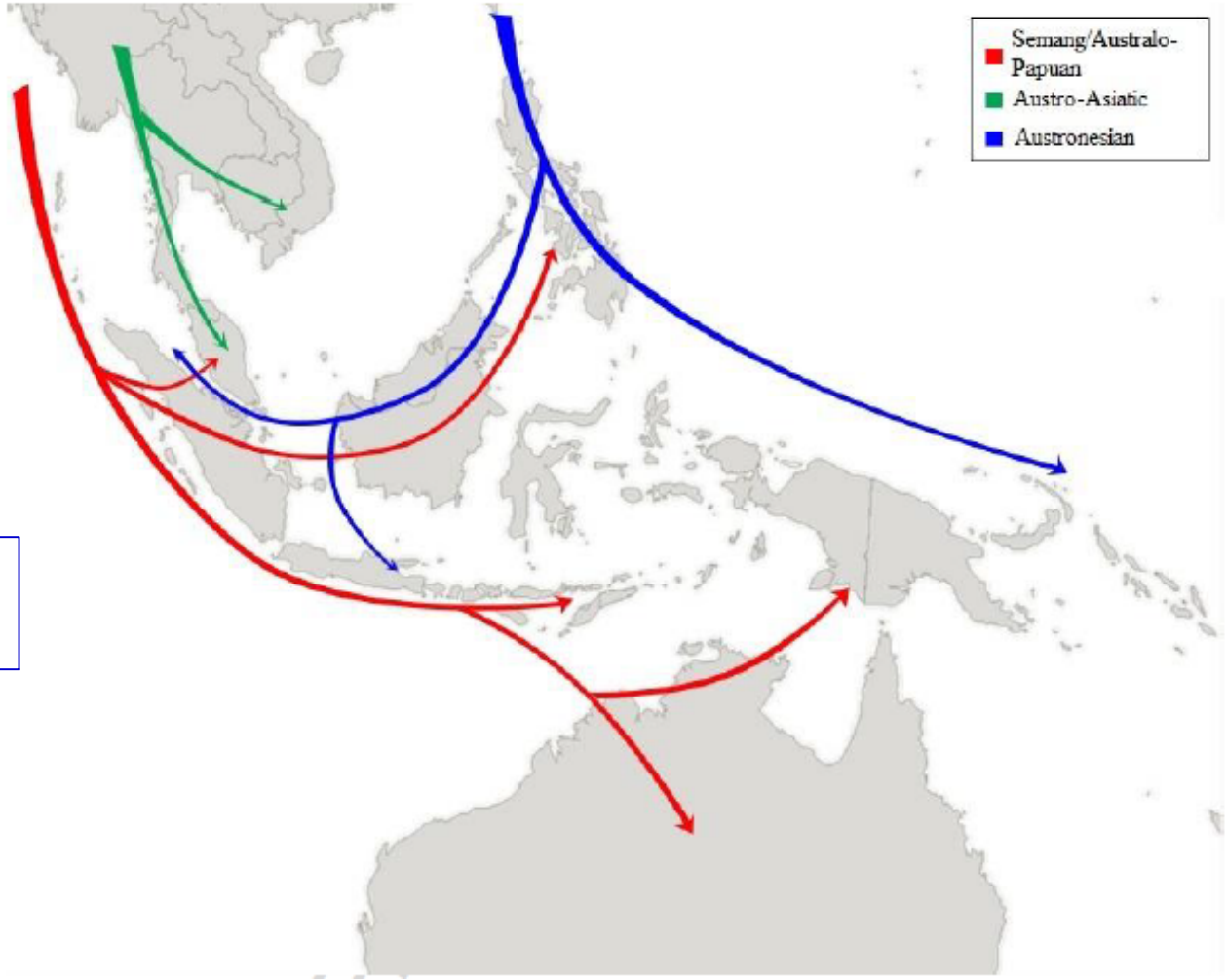


ΓΕΝΕΤΙΚΗ ΑΣΙΑΤΩΝ

Norhalifah et al.
Gene 2016

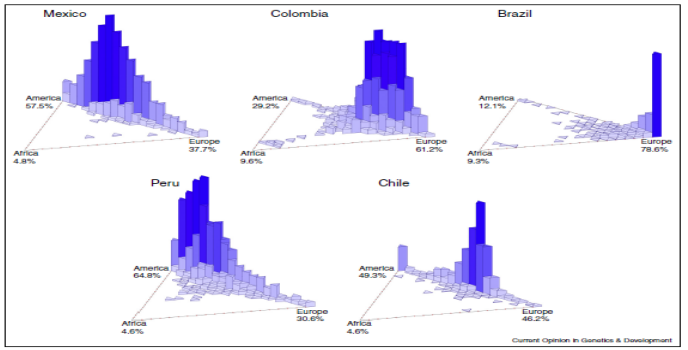


ΓΕΝΕΤΙΚΗ ΩΚΕΑΝΙΑΣ-ΠΟΛΥΝΗΣΙΑΣ

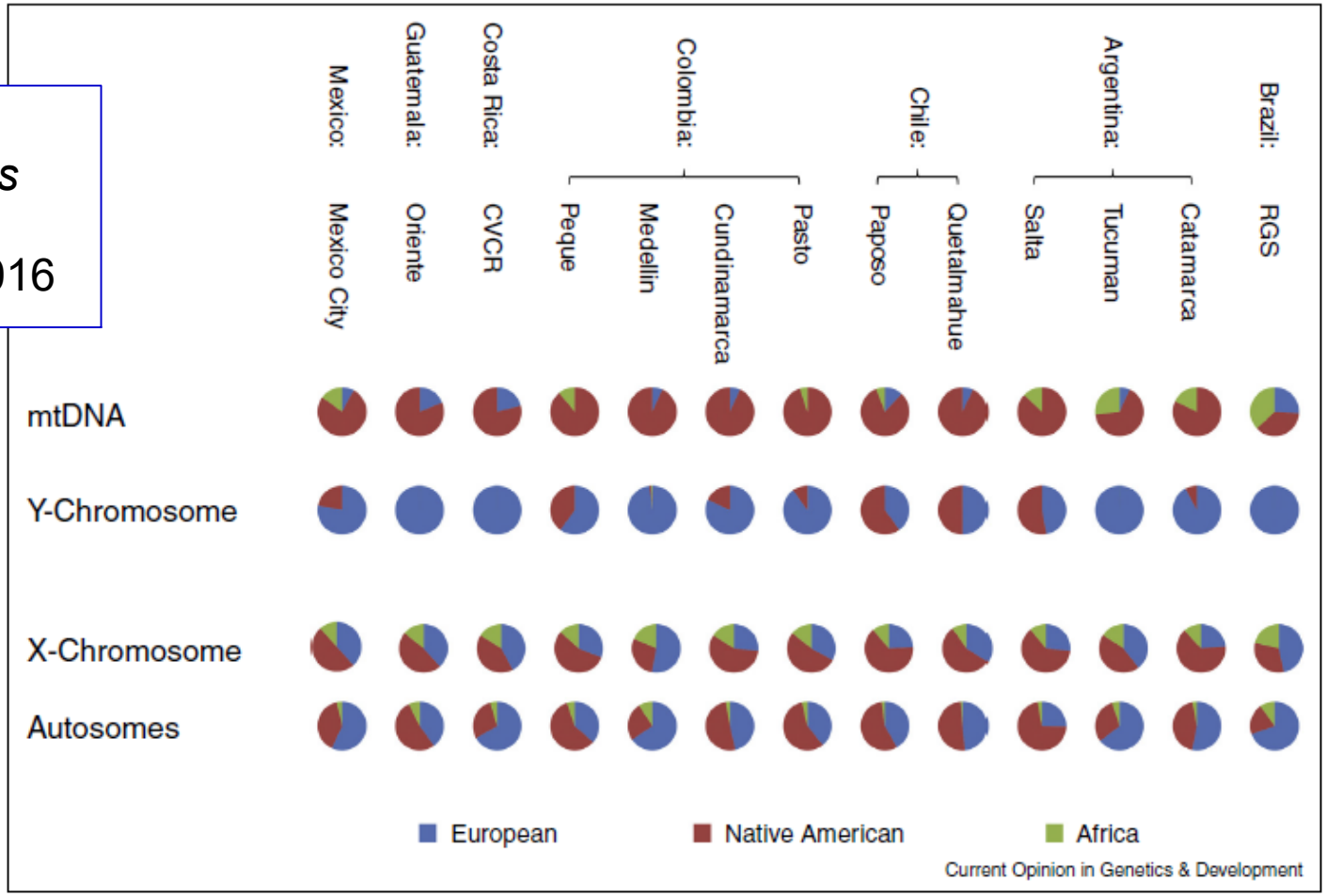


Norhalifah et al.
Gene 2016

ΓΕΝΕΤΙΚΗ ΛΑΤΙΝΟΑΜΕΡΙΚΑΝΩΝ



Adhikari et al.
Current Opinions in Genetics & Development 2016

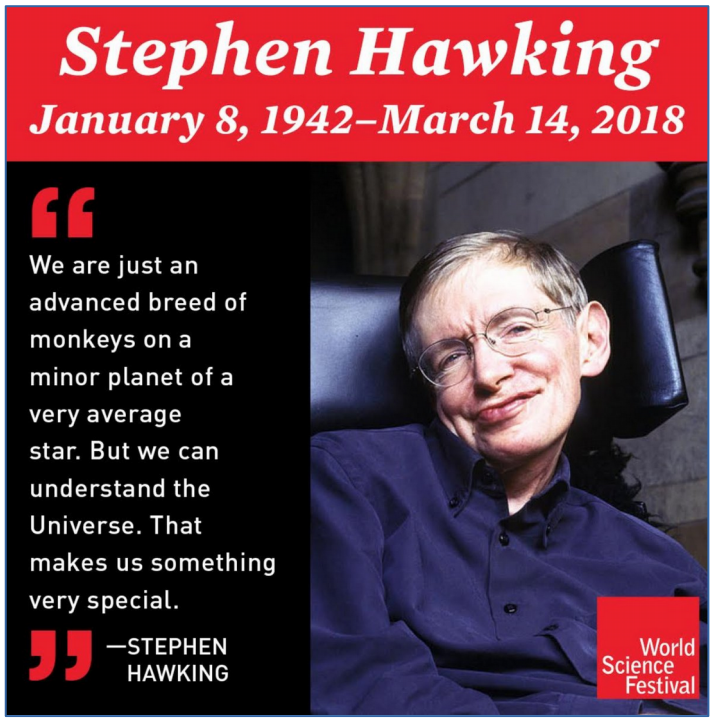


ΜΥΘΟΙ ΠΟΥ ΚΑΤΑΡΡΙΠΤΕΙ Η ΑΝΑΛΥΣΗ DNA

- Μύθος δημιουργίας ανθρώπου από χώμα
- Μύθος δημιουργίας άνδρα πρώτα (μύθος ανωτερότητας)
- Μύθος ύπαρξης Αδάμ και Εύας
- Μύθος ύπαρξης καθαρόαιμων φυλών
- Μύθος ανωτερότητας κάποιων φυλών
- Μύθος ανωτερότητας Άριας φυλής
- Μύθος ρατσισμού
- Ο ρατσισμός των Ναζιστών (“καθαρότητα Άριας φυλής”, “φυλετική εξυγίανση από τους “υπανθρώπους”) προέρχεται από τον μύθο του Πλάτωνα **περί ανθρώπων των οποίων η σύσταση περιέχει χρυσό, άργυρο, χαλκό και σίδηρο**, και περί της θεϊκής προφητείας ότι η πόλις θα καταστραφεί όταν κυβερνηθεί από ανθρώπους χάλκινου και σιδηρού γένους (Πλάτων *Πολιτεία* 3.415a-c

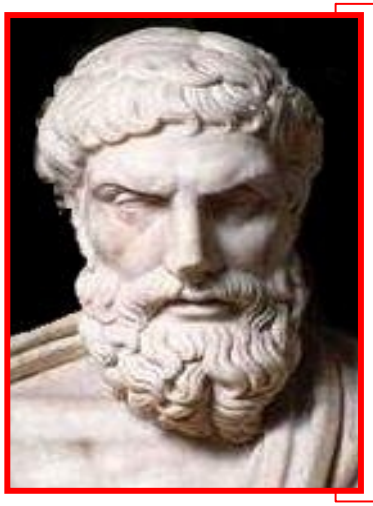
Bannes J. Hitlers Kampf und Platons Staat, 1933
Gabler A. Platon und der Führer, 1934)

Ἀμεινον επαίτην ἡ απαίδευτον είναι. Ο μεν γαρ χρημάτων, ο δε ανθρωπισμού δείται» (Δ.Λ, II70)
“Καλύτερα να είναι κάποιος ζητιάνος παρά απαίδευτος. Διότι ο ζητιάνος χρειάζεται πράγματα, ενώ ο απαίδευτος ανθρωπισμό”
(Αρίστιππος, Αθηναϊκή Δημοκρατία 400πΧ)



Stephen Hawking (1942-2018)

«Είμαστε, απλώς, ένα
εξελιγμένο είδος μαϊμούδων
σε έναν ασήμαντο πλανήτη
ενός πολύ μέτριου αστέρα.
Αλλά μπορούμε
να αντιληφθούμε το Σύμπαν.
Αυτό μας κάνει ιδιαίτερα
σημαντικούς».



Μέμνησο ὅτι θνητὸς ὢν τῇ φύσει καὶ λαβὼν χρόνον ὡρισμένον ἀνέβης τοῖς περὶ φύσεως διαλογισμοῖς ἐπὶ τὴν ἀπειρίαν καὶ τὸν αἰῶνα καὶ κατεῖδες τὸ τ’ ἐοντα τὰ τ’ ἐσσόμενα πρὸ τὰ ἐοντα. (Επικ. Προσφ. 10)

Επίκουρος ο Αθηναίος(341-270 πΧ)

“Να θυμάσαι ότι αν και είσαι θνητός σύμφωνα με τη Φύση και έχεις λάβει μια περιορισμένη διάρκεια ζωής, ανέβηκες με τους διαλογισμούς περί της Φύσης τόσο στην άπειρία της, όσο και στην αιωνιότητά της, και είδες καθαρά τα τωρινά, τα μελλούμενα και τα παρελθόντα”.*

*Παναγιωτόπουλος Τ. epicuros.gr

Ευχαριστώ για την προσοχή σας!