Deep Ancestry–

The Journey of Humankind Based on Mitochondrial DNA and Y-Chromosome DNA Data

Ian McFarlane

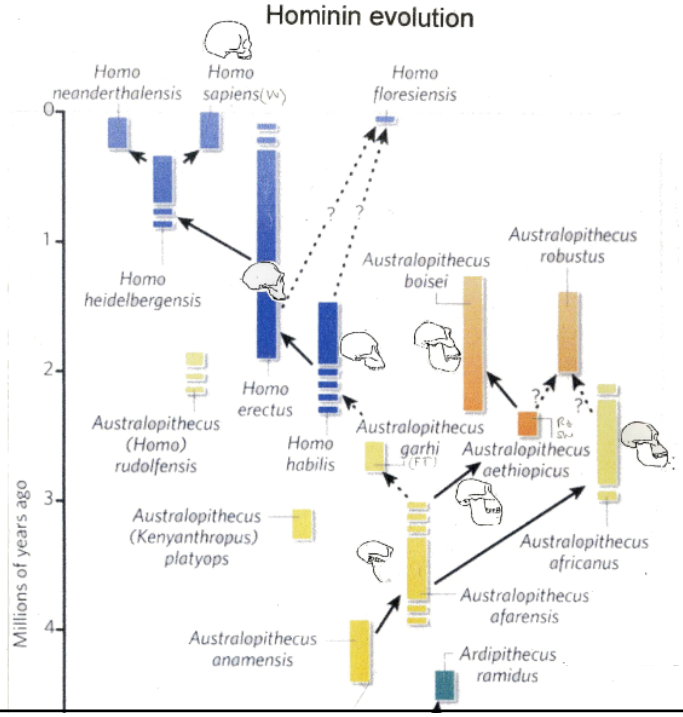
School of Biotechnology and Biomolecular Science

ISCAST Lecture New College UNSW 23 August 2010

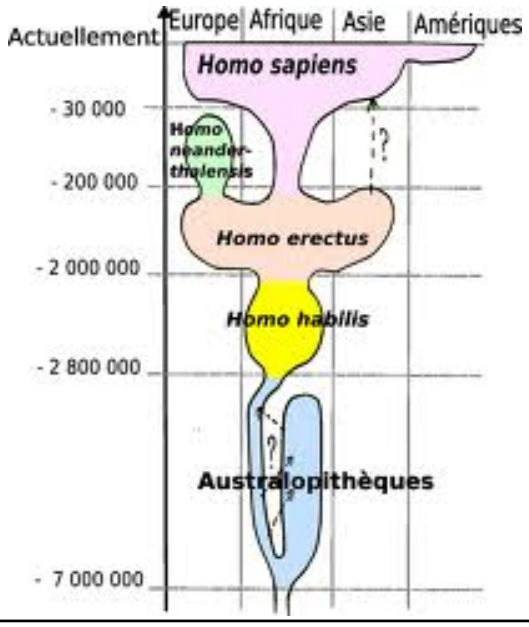
Lecture Outline

- Human Evolution and Migration
- Human DNA
- Mitochondrial DNA
  - Nature
- Y-Chromosome DNA
  - Nature
- Working With DNA
- Population Studies and Human Migration
- Genetic ‘Adam & Eve’ and/or Biblical ‘Adam & Eve’

The Primate Family Tree



Hominoid Origins and Migration



Evidence to Infer Human Migration

- Fossils (bones)
- Archaeological Sites (stones=tools)
- Geochronology
- Radiometric Dating
- Paleoclimatology
- Linguistics
- Genetics (DNA studies)

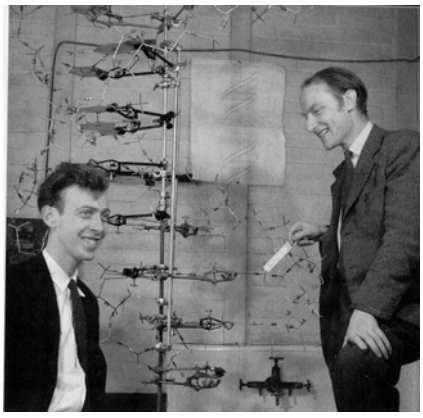
Humans are composed of many cell types

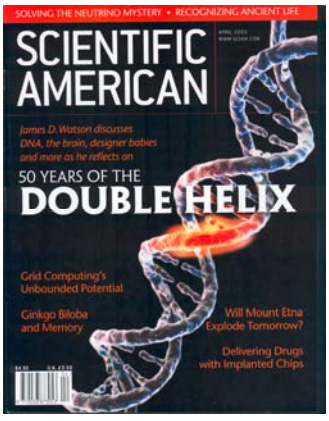
•All human cell types contain DNA except mature red blood cells

•DNA is found in the nucleus and the sub-cellular organelles called mitochondrion

The Biology of DNA

"This structure has novel features which are of considerable biological interest…" Watson and Crick, *Nature*, 25 April, 1953.



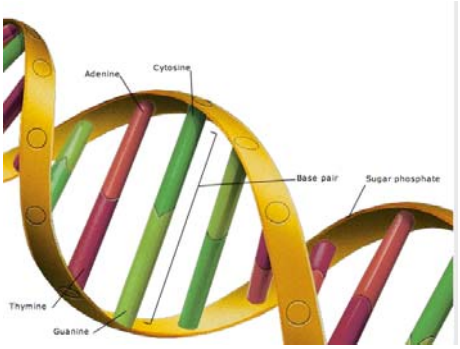


The Biology of DNA

DNA — deoxyribo nucleic acid

A polymer of;
A or *T* or *G* or *C* and
a *sugar* (deoxyribose) and
phosphoric acid

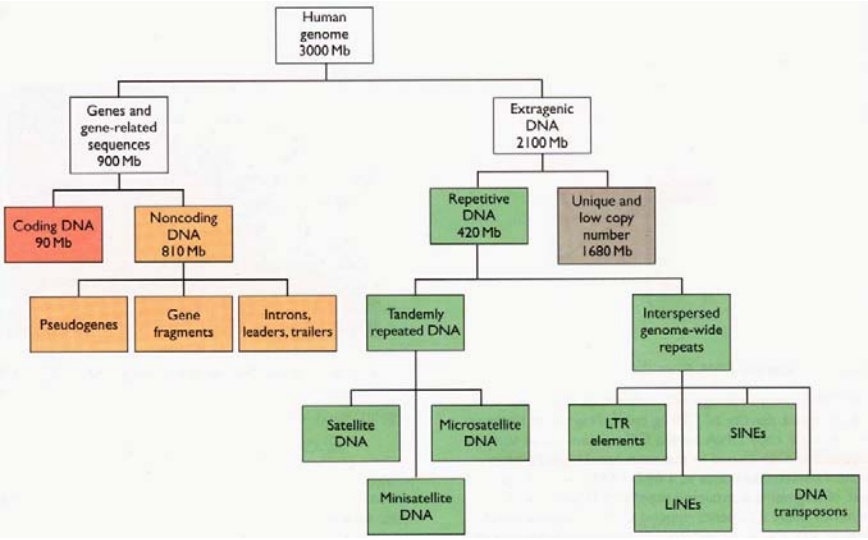
An information carrying molecule coded in the sequence of A, T, G & C



Organisation of Human Genetic Information

- A nucleotide — A letter
- A gene — A paragraph
- A chromosome — One volume
- A genome — A set of volumes
  - ~ 3.3 billion letters
  - ~ 30,000 genes
  - 100,000 proteins
  - 46 chromosomes (23 pairs)

Organisation of Human Genetic Information



Organisation of Human Genetic Information
Four Types of DNA?

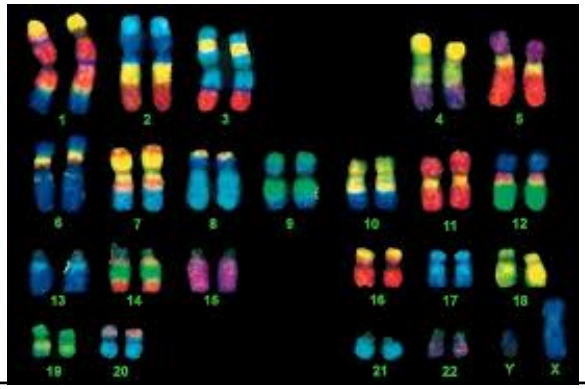
- Autosomal chromosomes
- X chromosome
- Y chromosome

Cell Nucleus

- Mitochondrial DNA (mtDNA)

Human Nuclear DNA

- 22 pairs of autosomal chromosomes (numbered 1 to 22)
- 1 ‘pair’ of sex chromosomes (either XX [female] or XY [male]
- Each chromosome is one long DNA molecule and genes are functional regions of this DNA
- We have two copies of each gene on the *autosomal* chromosomes, one on each of the paired chromosomes

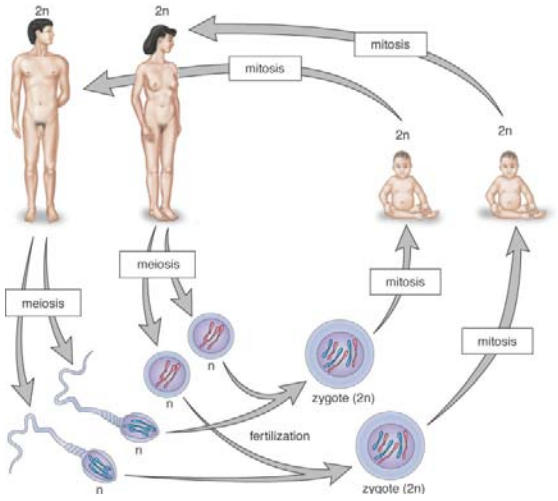


Inheritance of Nuclear DNA

Each child inherits one of each autosomal chromosome from the mother and another one of each autosomal chromosome from the father (22 +22 = 44 chromosomes)

Females receive an X from their father and an X from their mother
(1 + 1 = 2)

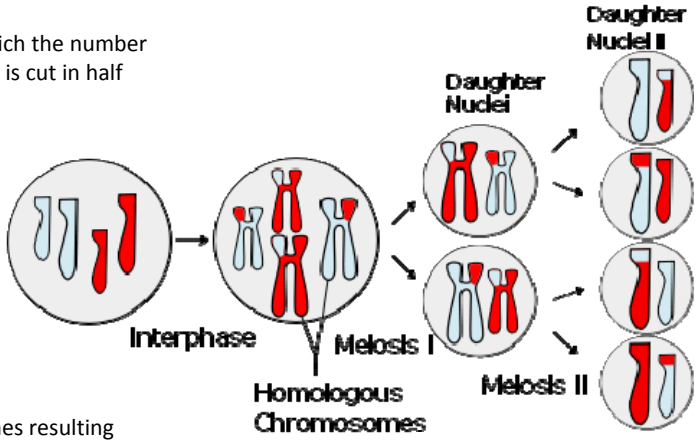
Males receive an X from their mother and a Y from their father
(1 + 1 = 2)



Inheritance of Nuclear DNA
Meiosis and Recombination

Meiosis
Reduction division in which the number of chromosomes per cell is cut in half

Diploid germ cell with 4 chromosomes (2 pairs)



Recombination
Physical exchange of genes resulting In new combinations of DNA within each chromosome

Chromosomal Crossover (Homologous Recombination)

Gametes (egg or sperm) 2 chromosomes (no pairs)

Inheritance of Nuclear DNA
Y–Chromosome

About 58 million bp (the X-chromosome has more than 153 million bp)

About 86 genes (the X-chromosome has about 2,000 genes)

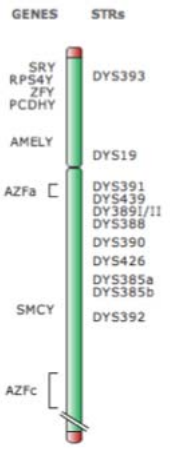
One gene, called SRY, triggers testis development, and hence 'maleness'

23 distinct proteins

Since only males contain a Y-chromosome it is Inherited through the paternal line

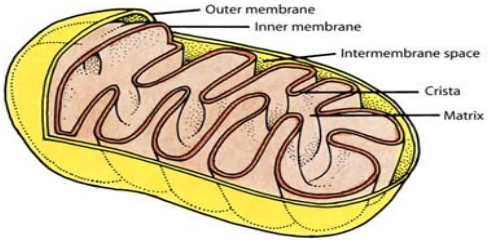
It is unable to recombine with its 'paired' X-chromosome and therefore no confounding effect of gene exchange with the X-chromosome occurs

Therefore the Y-chromosome is inherited intact over thousands of generations

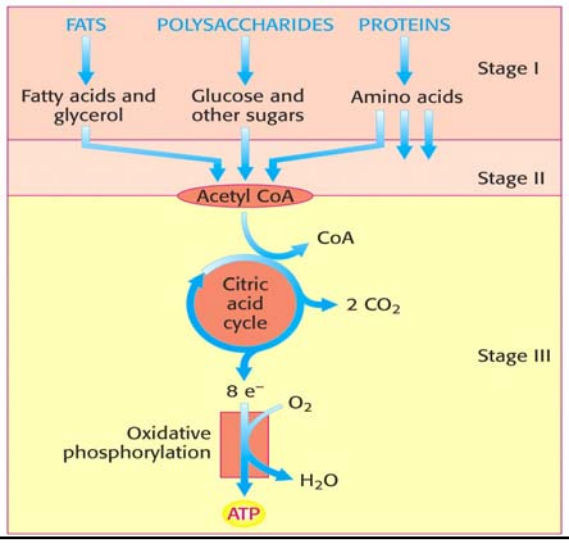


Human Mitochondrial DNA
Structure of a Mitochondrion

- Variable number and shape per tissue
- Similar in size to bacteria
- Double-membrane system
- "Powerhouse" of the cell by producing ATP from food molecules
- These reactions require oxygen

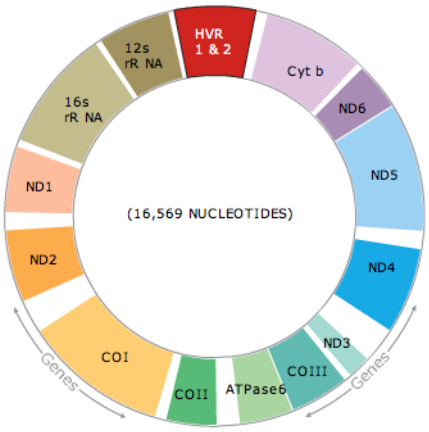


Human Mitochondrial DNA
Function of a Mitochondrion
(Oxidation of Foods in Aerobic Cells)



Mitochondrial DNA (mtDNA)

- Composition
  - 16,569 base pairs (bp)
  - Double stranded circular loop
  - 13 protein genes
  - 2 ribosomal RNA genes
  - 22 transfer RNA genes
  - Replication control region
- Function
  - Genes for the synthesis of some of the protein components of the electron transport chain (most mitochondrial proteins are encoded by nuclear genes
- Replication Control Region
  - HRV region or D-Loop
  - About 1,200 bp
  - Controls DNA and RNA synthesis
  - Accumulates point mutations about 10x the rate for nuclear DNA
  - Poor repair of mtDNA mutations

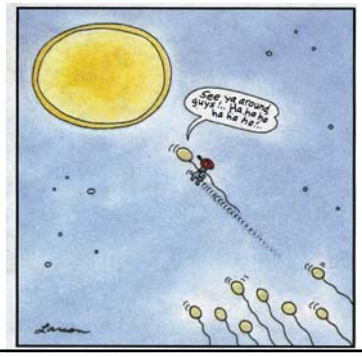


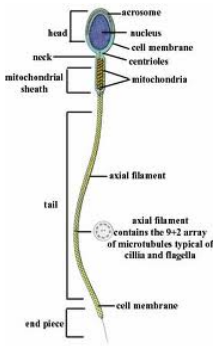
Inheritance of Mitochondrial DNA

Inherited through the maternal line. No sperm mitochondria enter the egg at fertilization.

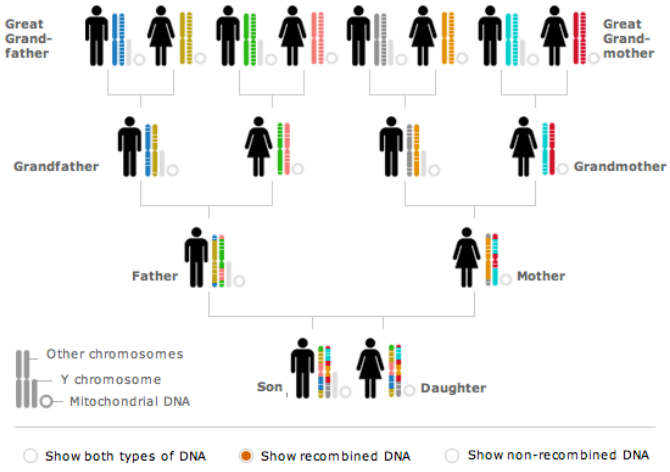
The large egg may have 100,000 mitochondria, the tiny sperm may have 50–100 concentrated in the base of the tail.

Therefore, like the Y-chromosome, mtDNA is inherited intact over thousands of generations

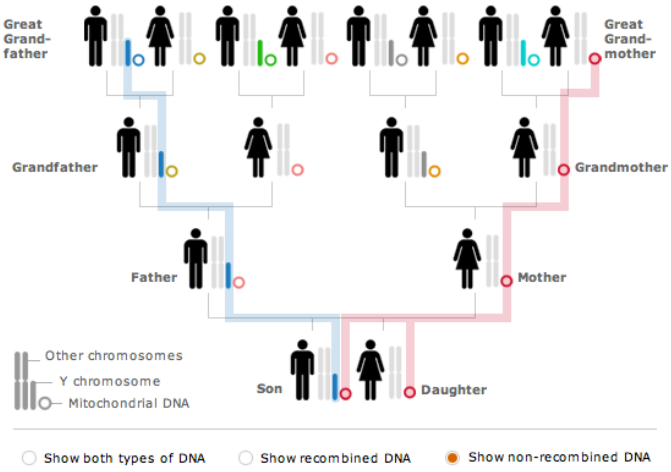




Summary of Autosomal Chromosome Inheritance



Summary of Y-Chromosome and mtDNA Inheritance



Working With DNA

- Isolation
  - Source
- Purification
  - Contamination
- Amplification
  - Polymerase Chain Reaction (PCR)
- Sequencing
  - Automated Dideoxy Sequencing

Working With DNA

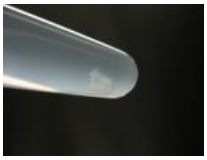
- Isolation
  - Buccal swab

  - Bones

  - Teeth

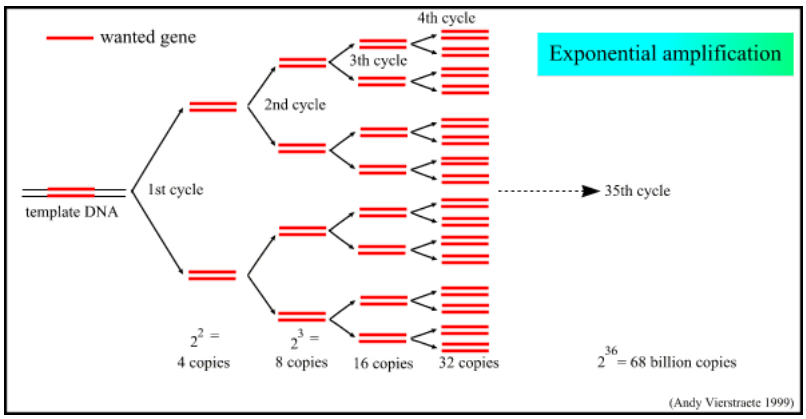
Working With DNA

- Purification
  - Contamination



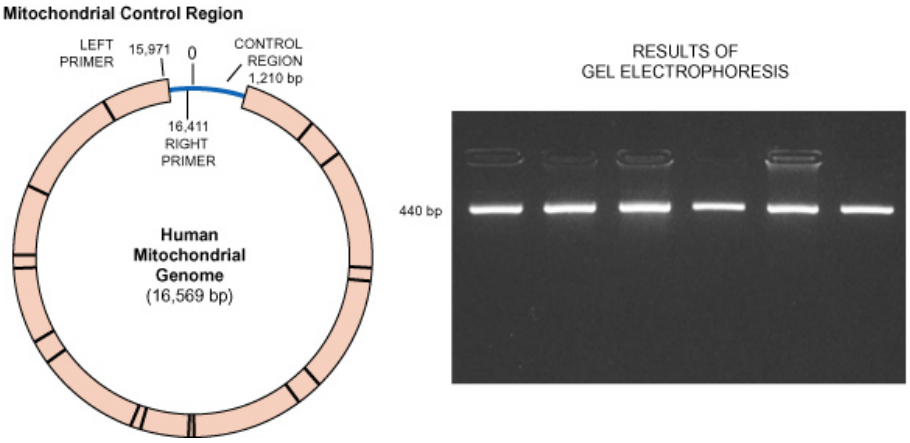
Working With DNA

- Amplification
  - Polymerase Chain Reaction (PCR)Multiplication of a targeted segment of DNA



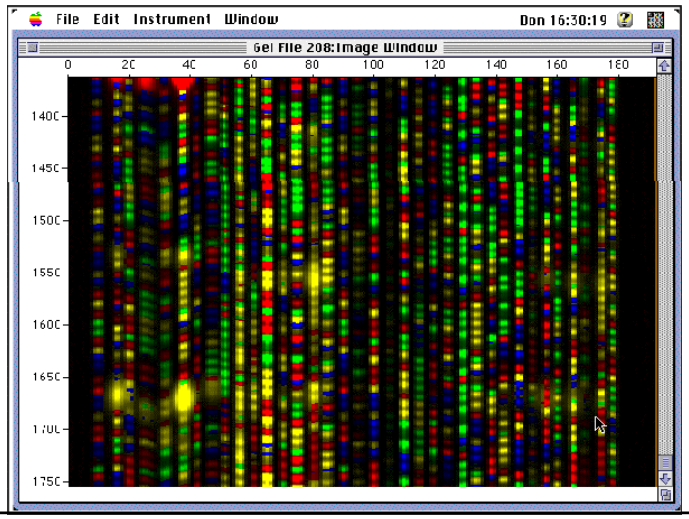
Working With DNA

- Amplification
  - Polymerase Chain Reaction (PCR)



Working With DNA

- Sequencing
  - Automated Dideoxysequencing

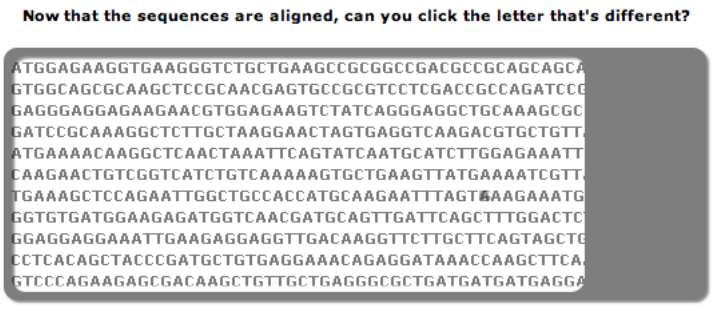


Working With DNA

- Alignment (or spotting the differences)

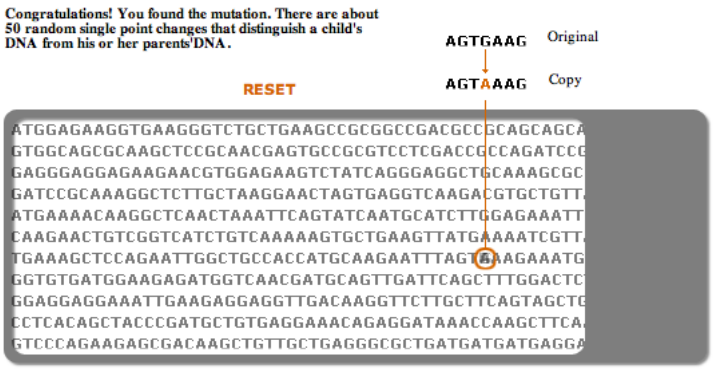
Working With DNA

- Alignment (or spotting the differences)



Working With DNA

- Alignment (or spotting the differences)



Working With DNA

- Analysis of Data
  - Computer Algorithms
  - Statistical analysis
  - Phylogenetic trees

DNA Mutations and Molecular Markers

- Mutations
  - Changes in genetic sequence
  - Causes
    - Radiation, mutagenic chemicals, etc
    - Errors that occur during meiosis or DNA replication
  - Inherited if they occur in the germ line (gametes)

- Molecular Markers
  - A DNA sequence with a known location on a chromosome (or mtDNA) that can be used to identify individuals or species.
  - Many types
    - SNP (Single Nucleotide Polymorphism)
    - VNTR (Variable Number of Tandem Repeats)
    - SSR (Simple Sequence Repeats)
  - Passed on from generation to generation

The Inheritance of Genetic Markers

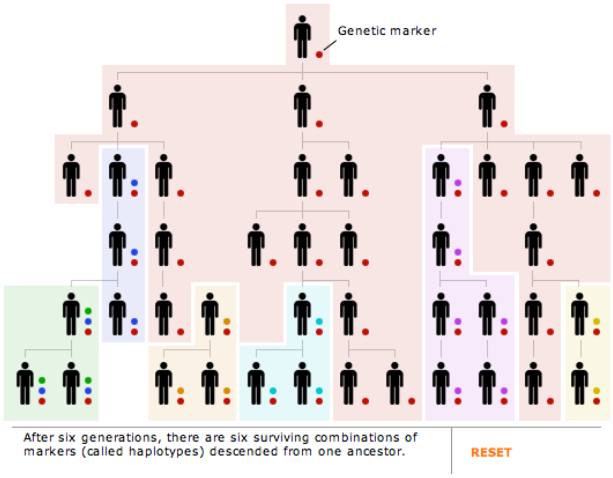


Illustration of Genetic Drift of a Y-Chromosome Marker

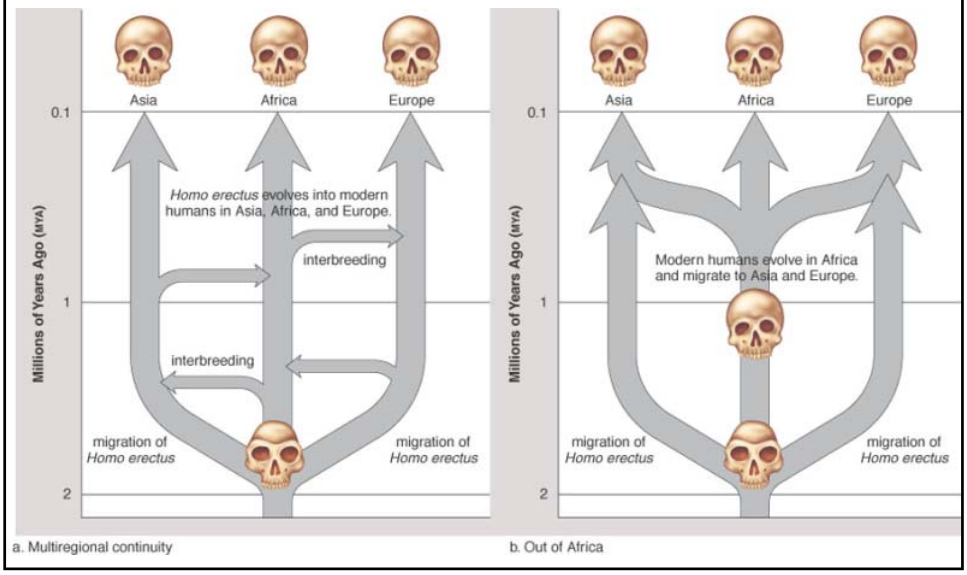
The Molecular Clock and Anthropology

- Oldest intact DNA yet isolated dates back only about 40,000 years
- DNA of any individual bears the accumulated genetic history of its species
- Common ancestor
  - Accumulation of a unique set of random DNA mutations in each branch
  - Assumes mutations accumulate at a constant rate (debated and differs between autosomal, Y- and mitochondrial DNA)
  - Number of mutations is proportional to the length of time that the two groups have been separated
  - A time scale is attached by linking an event that has been independently established by anatomical, anthropological, or geochronological data, eg. humans and chimps (5 to 6 million years ago)

Where Did *H. sapiens* Arise?

- Two hypotheses:
  - Multiregional continuity model
  - African emergence model
- Both attempt to address both biochemical and fossil evidence

Where Did *H. sapiens* Arise?



Where Did *H. sapiens* Arise?

- Africa appears to be the cradle of human evolution
- No human fossils older than 1.8 million years exist anywhere but Africa
- Mitochondrial Eve about 150,000 years ago in East Africa
- Y-Chromosome Adam about 70,000 years ago in East Africa

The Puzzle of the Pacific

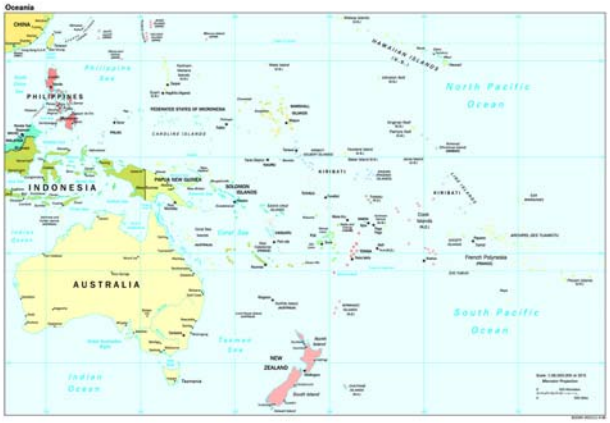
Population Movements in Polynesia

West to East or East to West?

Archaeology, language, domesticated animals and plants

Kon-Tiki, 1947

mtDNA, 1990s



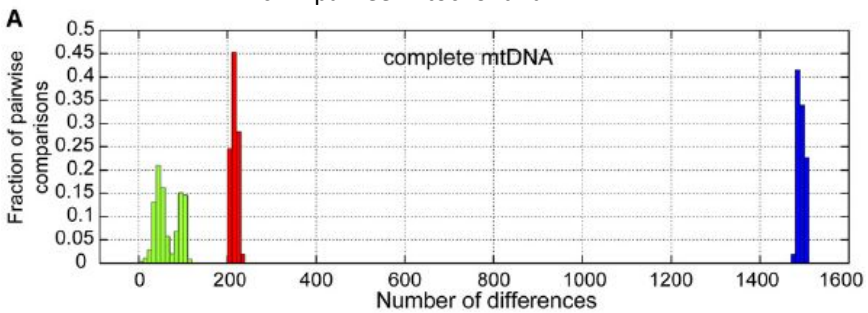
Conclusion:
Based on mtDNA, the movement of peoples was from West to East with a possible origin in Taiwan, but….?

Neanderthal Man

- Neanderthals (*H. neaderthalensis*)
  ca. 200,000 to 20,000 years ago
- Germany's Neader Valley
- Culturally advanced?
- Stone tools
- Buried dead
- Supplanted or assimilated by modern humans?

Neanderthal Man

Pairwise nucleotide base comparisons between modern human, Neanderthal and chimpanzee mitochondrial DNA

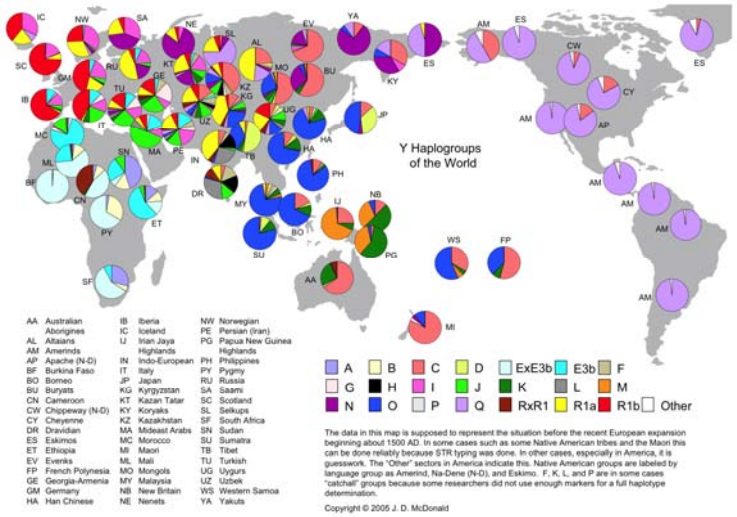


Green: human/human comparisons; Red: human/N'tal comparisons; Blue: human/chimp comparisons

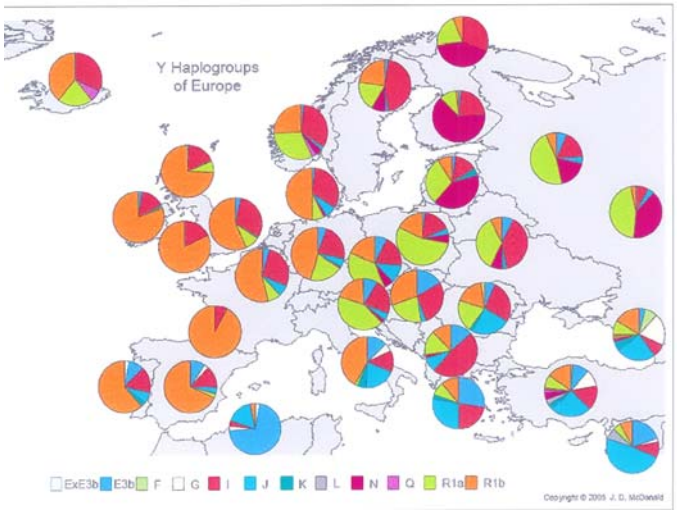
Conclusions:

- *Neanderthal mtDNA falls outside the variation of extant human mtDNAs*
- *Neanderthals as a species distinct from humans (Homo neanderthalensis)*
- *Strongly suggests that Neanderthals and modern humans did not form part of a single large interbreeding population (although it does not prove the absence of admixture of autosomal DNA*
- *Estimated divergence date between the two mtDNA lineages of 660,00 ± 140,000 years*

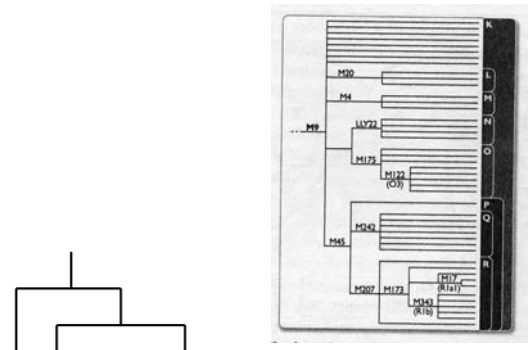
Y Haplogroups of the World



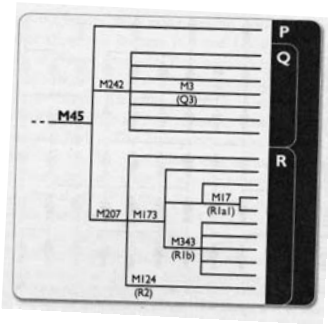
Y Haplogroups of Europe



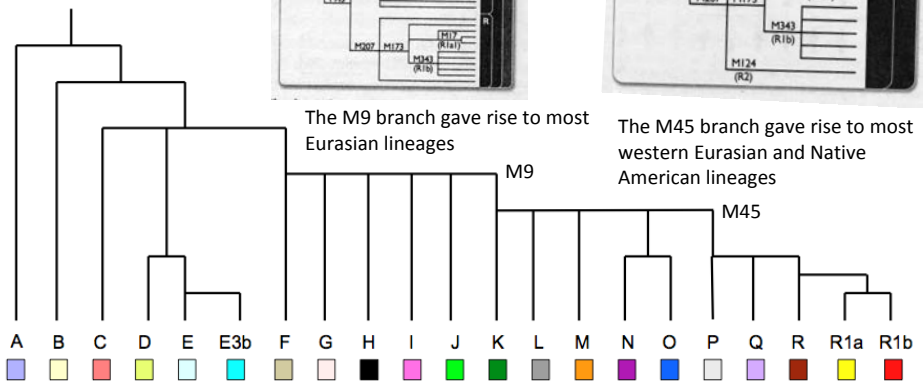
Simplified Tree of Y-Chromosome Haplogroups



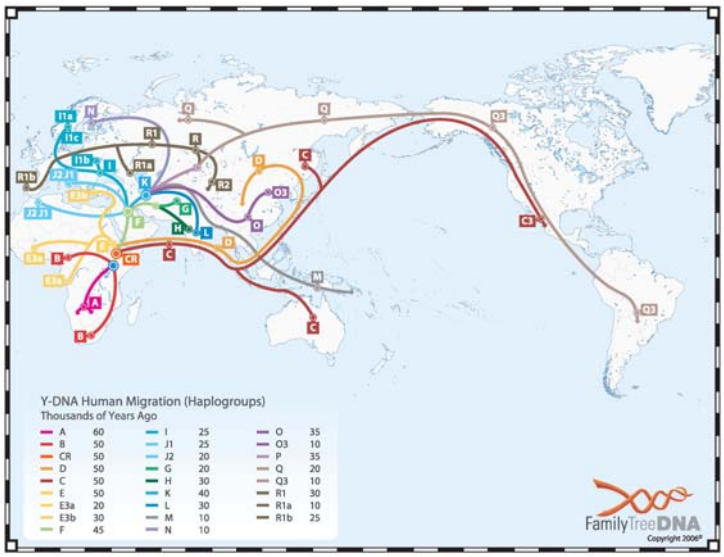
The M9 branch gave rise to most Eurasian lineages



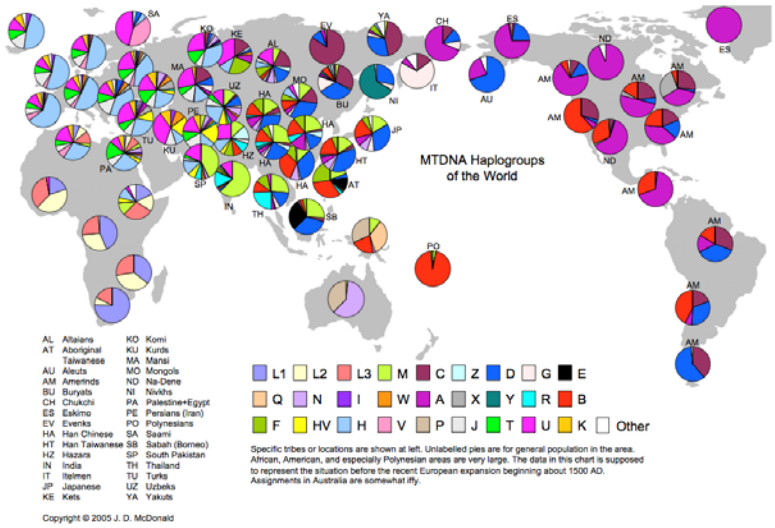
The M45 branch gave rise to most western Eurasian and Native American lineages



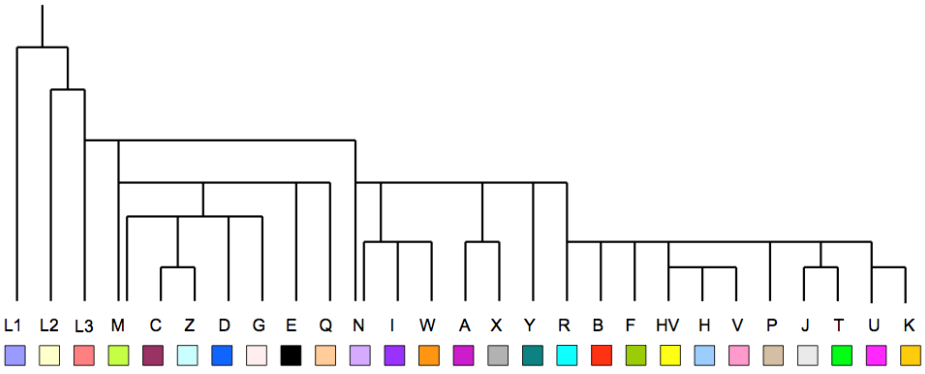
Y-Chromosome Human Migration



mtDNA Haplogroups of the World

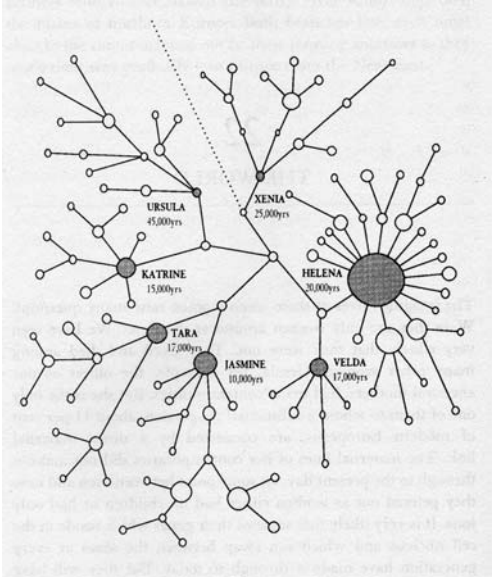


Simplified Tree of Mitochondrial Haplogroups

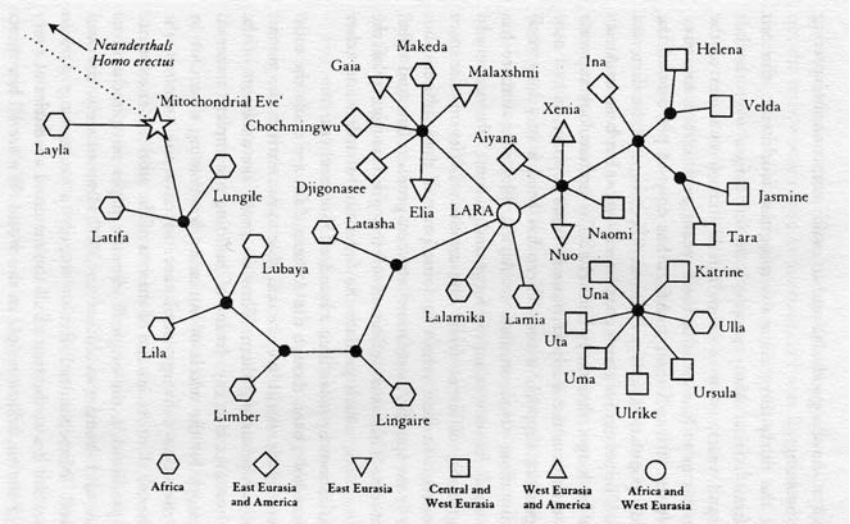


Note that unlike the Y-Chromosome Haplogroups, the ones for the Mitochondrial DNA are not related in a simple way to alphabetical order. This is due to the historical nature of their definition. The Native American groups A, B, C, and D were put together alphabetically. They are, as seen above, not closely related in the tree. M, N, and R are called "Superhaplogroups" as indicated. Note that M and N are in fact somewhat heterogeneous.

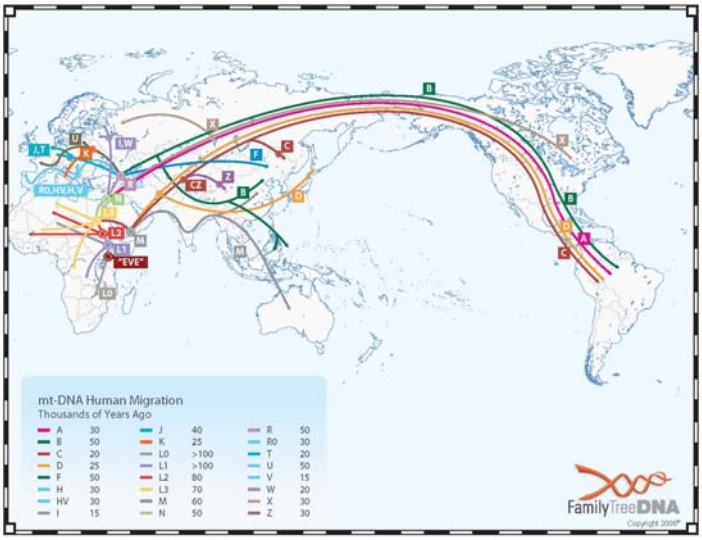
The Seven Daughters of Eve



World mtDNA Clans and Where They are Found



mtDNA Human Migration



Mitochondrial Eve/Y-Chromosome Adam
Biblical Eve/Biblical Adam

32 April 21, 2002 THE SUN-HERALD

Face to face with Eve

Mother of all humans traced to Africa

By SCOTT ELLIS

AFTER more than 150,000 years, scientists have pieced together the face of Eve, the mother of modern humans.

Dark skinned and with dark hair, she was brought back to life by researchers who cracked back in time following DNA carried on the female line.

Tracing female DNA through grandmama, the scientists created a "genetic map" they claim proves everyone on Earth comes from the same place in Africa and all humans living today are descended from a single woman who lived in East Africa about 150,000 years ago. She's our genetic Eve.

After establishing a common mother, the scientists then combined what they had learnt from their DNA research with modern forensic reconstruction techniques and Eve was born.

"It is probably very close to what Eve looked like," said Oxford University's Stephen Oppenheimer, a world authority on genetic research.

"There is every evidence which indicates she must have been black. To have lived in Africa, the protection of black skin was essential to survival.

"It's also reasonable to suppose she had frizzy hair rather than straight, long hair because remnant popu-

ART'S VIEW OF EVE: Michiel Cascie, 1530.

lations on the Indian Ocean must still have frizzy hair. She would also have been taller and larger than people living today."

Eve is believed to have emerged with the first modern humans in an area of Africa where the Ice Age had produced deserts dotted with fertile "islands".

Through the DNA tracks and with archeological evidence the scientists followed Eve's descendants out of East Africa to Indonesia and Australia about 80,000 years ago. They arrived in Europe about 50,000 years ago.

Dr Oppenheimer points out two possible routes out of Africa – one across the Sahara Desert, the other across a 18km stretch of ocean.

Locally, the straits where the first crossing out of Africa could have occurred are known as the "Gates of Grief" because of the strong currents.

But 80,000 years ago, the sea was 150ft (46m) lower and a number of islands and reefs appeared which let our ancestors travel across the world.

Eve, or at least as close to Eve as the scientists can get, and her descendants' exodus from Africa was recreated for a documentary, *The Real Eve*, which premieres worldwide on the Discovery Channel on pay TV today.

By giving a face to Eve, scientists hope people will recognise the similarities in humans.

"I hope people will begin to understand that the different races are relatively superficial," Dr Oppenheimer said. "If we all came from the same place and are related to the same woman, the fact that we look different is because we live in different environments. Our skin tone and culture changed over the years."

HOW THEY RECONSTRUCTED THE HEAD

■ The face of Eve was reconstructed from a female skull (known as Galilah 9) which was discovered in Israel. Forensic artist Richard Neave added muscle and flesh using modern reconstruction techniques based on the scientists' finding.

Thank you for your attention

Questions?