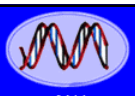

DNA
Genetic Code of Life


Entire Genetic Code of a Bacteria


DNA Fingerprinting


Cloning: Ethical Issues and Future Consequences

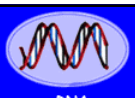

Plants of Tomorrow

HC70A
Spring 2021
Genetic Engineering in Medicine, Agriculture, and Law

Professor Bob Goldberg

Lecture 7
The Age of Genomics: Three-Parent Babies, Human Origins, & Race

1


DNA
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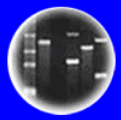

DNA Fingerprinting

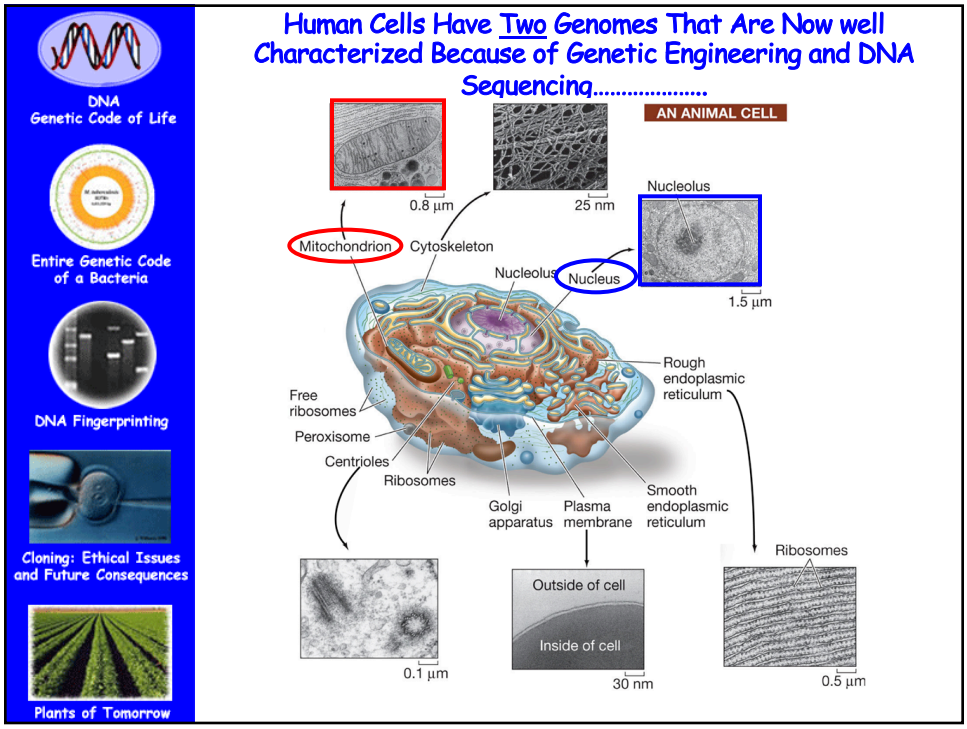

Cloning: Ethical Issues and Future Consequences


Plants of Tomorrow

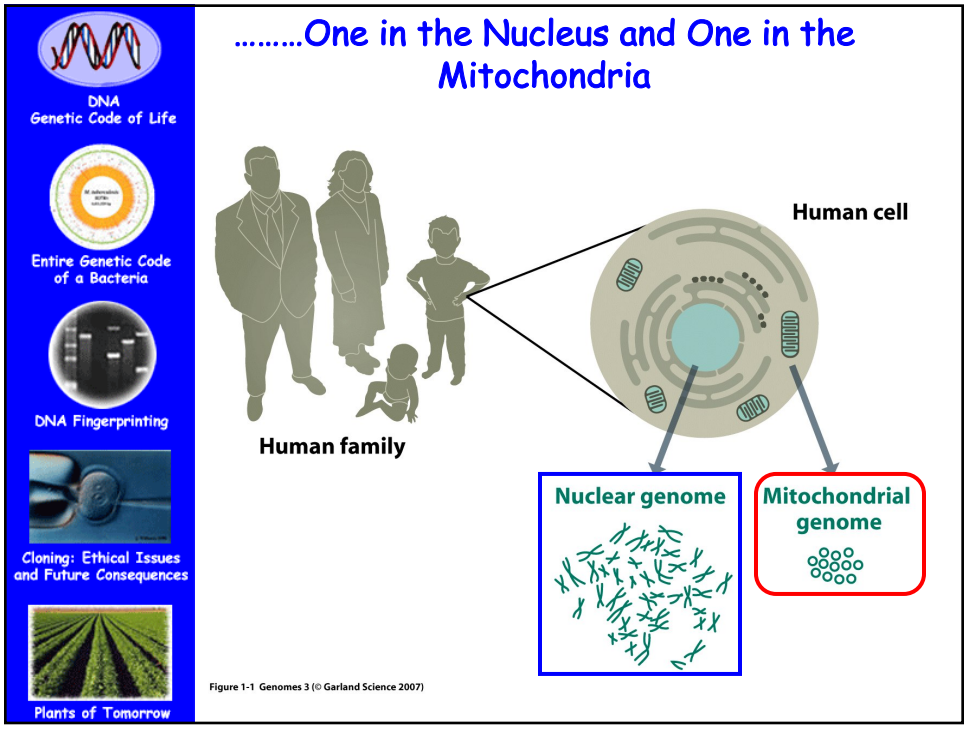
Themes

- The Human Genome – Two!
- Mitochondrial Genome, Diseases, & Ancestry
- Mitochondrial Replacement Therapy – Science, Ethics, & Politics
- CRISPR Editing Mitochondrial Genes?
- The Human Genome
- Human Disease Genes
- Correcting Human Gene Disorders
- Using Ancient DNA To Trace Human Ancestry
- Human Genetic Diversity & 1000 Genome Project
- Using Human Genetic Diversity to Unravel Our Recent Human History
- Using Human Genetic Diversity to Unravel the Concept of "Race"
- Knowledge vs. Certainty – Dogma in Science

2


DNA
Genetic Code of Life
Entire Genetic Code of a Bacteria
DNA Fingerprinting
Cloning: Ethical Issues and Future Consequences
Plants of Tomorrow
Human Cells Have Two Genomes That Are Now well Characterized Because of Genetic Engineering and DNA Sequencing.....
AN ANIMAL CELL
0.8 µm
25 nm
Nucleolus
Mitochondrion
Cytoskeleton
Nucleolus
Nucleus
1.5 µm
Rough endoplasmic reticulum
Free ribosomes
Peroxisome
Centrioles
Ribosomes
Golgi apparatus
Plasma membrane
Smooth endoplasmic reticulum
Ribosomes
Outside of cell
Inside of cell
0.1 µm
30 nm
0.5 µm

3


DNA
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Plants of Tomorrow
.....One in the Nucleus and One in the Mitochondria
Human cell
Human family
Nuclear genome
Mitochondrial genome
Figure 1-1 Genomes 3 (© Garland Science 2007)

4

Human Nuclear and Mitochondrial Genomes Differ in Size & Shape

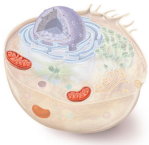
Characteristic	Nuclear Genome	Mitochondrial Genome
Size	3.3 x 10^9 bp	16,500 bp
DNA Molecules Per Cell	23 in Haploid Cells 46 in Diploid Cells	100 to >1,000 Per Cell (e.g., 50,000 in Egg Cell)
Number of Genes	25,000	37
Gene Density	1 per 40,000 bp	1 per 450 bp
Presence of Introns	In Most Genes	Absent
% Coding DNA	3%	93%
Codon Usage	Universal Code	AUA – Methionine UGA – Tyrosine AGG – Stop
Mode of Inheritance	Mendelian	Maternal
Repetitive Sequences (e.g., VNTR)	50%	Almost None

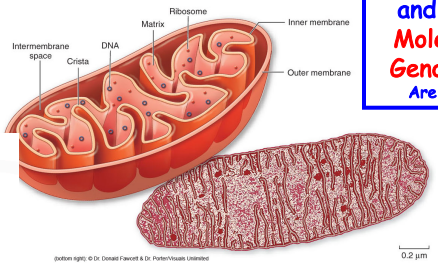
What Are the Consequences of Many Mitochondrial Genomes Per Cell For Human Mt Diseases?

5

Mitochondria are Semi-Autonomous, Power Human Cells (Makes ATP), and Contain a Circular Genome

Each Cell Has Many Mitochondria
Red Blood Cells: 0
Liver Cells: 2000
Egg Cell: 50,000
Sperm Cell: 50





Mitochondria Have Between 5 and 15 DNA Molecules or Genomes (They Are Polyploid)!!

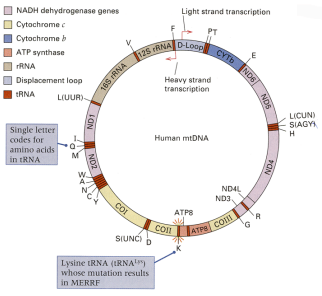


Figure 16.3 Genes in human mitochondrial DNA. The tRNA genes are indicated by the one-letter amino acid symbols; hence tRNA^{Lys} is denoted K. The positions of these and other genes in the mitochondrial DNA are indicated by color according to the key at the upper left. The arrows indicate the promoters for transcription of the heavy and light strands. [Courtesy of N-G. Larsson and D. A. Clayton. With permission, from the *Annual Review of Genetics* 29: 151. Copyright 1995 by Annual Reviews, www.AnnualReviews.org.]

Semi-Autonomous
- DNA Genome
- Divides
- Transcription
- Translation

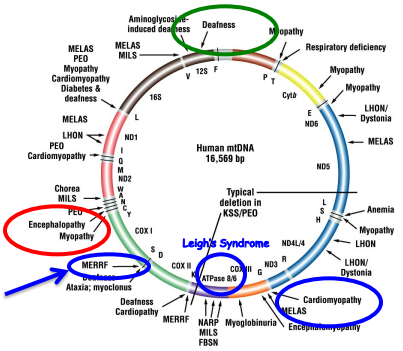
→ Mitochondrial Proteins

Mutations Lead to Mitochondrial Diseases

6

Mutant Mitochondria Mitochondrial Genomes Are Inherited Maternally

One in Five People Have Mutations in One Mitochondrial Genome *But They Do Not Have Disease Symptoms.* Why?



Disease Genes Present on the Mitochondrial Genome

Many Affect Muscles Because Mitochondria Produce Energy Needed For Muscle Activity

Provide a Hypothesis For the Variation in Disease Symptoms

Diseases:

MERRF	Myoclonic epilepsy and ragged red fiber disease	MMC	Maternally inherited myopathy and cardiomyopathy
LHON	Leber hereditary optic neuropathy	PEO	Progressive external opthalmoplegia
NARP	Neurogenic muscle weakness, ataxia, and retinitis pigmentosum	KSS	Kearns-Sayre syndrome
MELAS	Mitochondrial encephalomyopathy, lactic acidosis, and strokelike symptoms	MILS	Maternally inherited Leigh syndrome

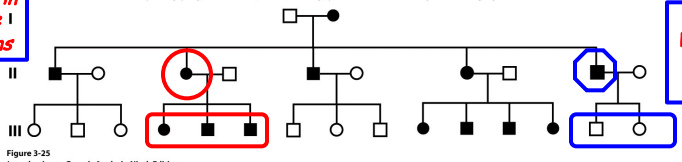


Figure 3-25
Introduction to Genetic Analysis, Ninth Edition
© 2008 W.H. Freeman and Company

Note: Passed on From Mother to All Children

7

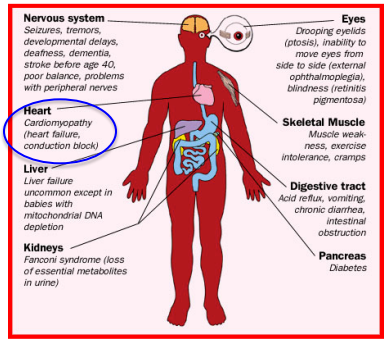
UNITED MITOCHONDRIAL DISEASE FOUNDATION®
HOPE. ENERGY. LIFE.

Mitochondrial DNA Diseases

Defects in Energy Production (ATP)

Affect 1/4000 People

- Alpers Disease
- Barth syndrome
- Beta-oxidation Defects
- Carnitine-Acyl-Carnitine Deficiency
- Carnitine Deficiency
- Creatine Deficiency Syndromes
- Co-Enzyme Q10 Deficiency
- Complex I Deficiency
- Complex II Deficiency
- Complex III Deficiency
- Complex IV Deficiency
- Complex V Deficiency
- COX Deficiency
- CPEO
- CPT I Deficiency
- CPT II Deficiency
- Glutaric Aciduria Type II
- KSS
- Lactic Acidosis
- LCAD
- LCHAD
- Leigh Disease or Syndrome
- LHON
- LIC (Lethal Infantile Cardiomyopathy)
- Luft Disease
- MAD
- MCAD
- MELAS
- MERRF
- MIRAS
- Mitochondrial Cytopathy
- Mitochondrial DNA Depletion
- Mitochondrial Encephalopathy
- Mitochondrial Myopathy
- MNGIE
- NARP
- Pearson Syndrome
- Pyruvate Carboxylase Deficiency
- Pyruvate Dehydrogenase Deficiency
- POLG Mutations
- Respiratory Chain
- SCAD
- SCHAD
- VLCAD



Treatment
At this time, there are no cures for these disorders.

8

9

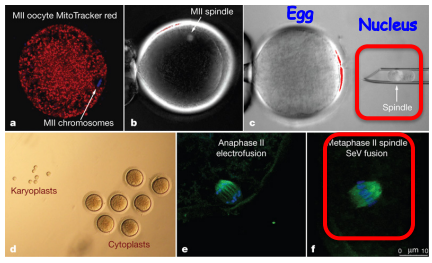
Mitochondrial Replacement Can Be Used to "Cure" Mitochondrial Gene Defects!

Replace "Bad" Mitochondria with "Good" Mitochondria

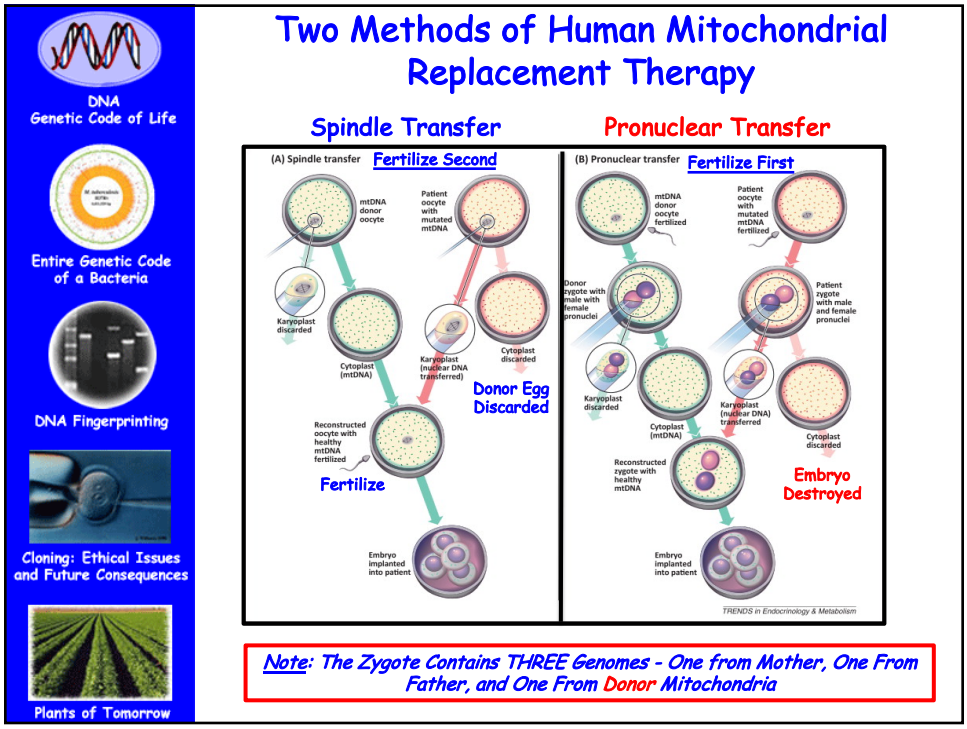
NUCLEAR TRANSPLANTATION Nature 2009 (Mitalapov)

Researchers Prevent Inheritance of Faulty Mitochondria in Monkeys

Mitochondrial replacement in human oocytes carrying pathogenic mitochondrial DNA mutations Nature 2016



10



11

Ethics of mitochondrial gene replacement: from bench to bedside

The prospect of using mitochondrial gene replacement to conceive children free of mitochondrial disease highlights the need for a sound ethical framework for reproductive genetic technology, say **Annelien Bredenoord** and **Peter Braude**

- How to Test Whether It Works? (Mt DNA Markers)
- Testing on Live Human Embryos
- When To Test Its Effectiveness
- Safety & Long-Term Potential Problems
- Nuclear-Mitochondrial Genome Incompatibility?
- Heteroplasmy?
- Approved Research Protocols
- IRB (Institutional Review Board) Oversight
- Informed Consent of Parents

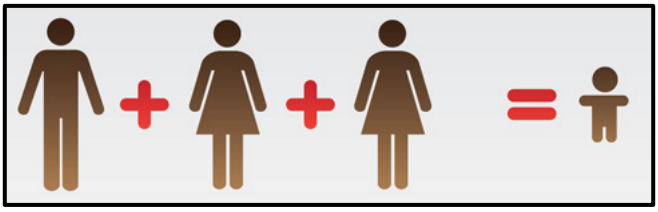
British Medical Journal, January 8, 2011,342, 87-89

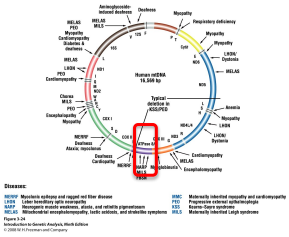
12

UK Becomes First Country to Approve 'Three-Parent Babies'

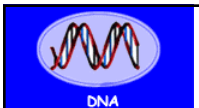
By Carl Engelking | February 3, 2015 1:58 pm

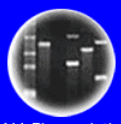
UK doctors select first women to have 'three-person babies' February 2, 2018



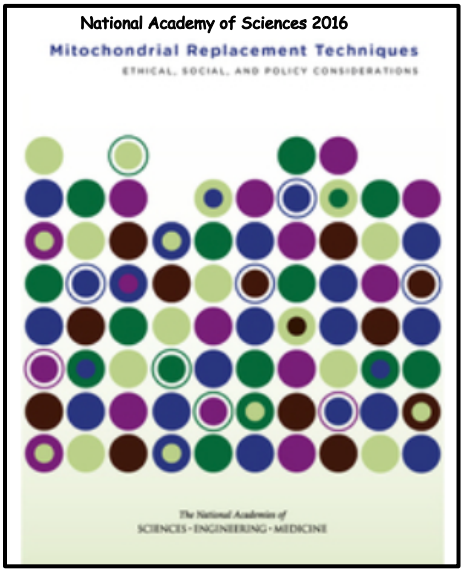


13





What About The United States? Recommendations to the FDA



14


DNA
Genetic Code of Life
Entire Genetic Code of a Bacteria
DNA Fingerprinting
Cloning: Ethical Issues and Future Consequences
Plants of Tomorrow
Finding an ethical path forward for mitochondrial replacement
NRC Report Summary - Science, February 3, 2016
Anne B. Claiborne[1*†], Rebecca A. English[1*], Jeffrey P. Kahn[2*†]
It is Ethically Permissible to Initiate Clinical Investigations of Mt Replacement Therapy in Humans So Long as Significant Conditions and Restrictions Are in Place
1. Initial Restriction to Transfer Only Male Embryos
2. No Transfer of Females Until Robust Evidence is Obtained of the Safety & Efficacy of Technique By Following Children Long Term
3. Public Discussion Should Be Held to Determine If Female Transfer Should Ever Be Permitted as This Results in a Heritable Genetic Modification
4. Limit Clinical Investigations to Women Who Are At Risk of Transmitting a Serious Mt Disease
5. Primary Concern in Assessing the Benefits & Risks in Clinical Investigation is Minimizaiton of Risk of Harm to the Resulting Child

15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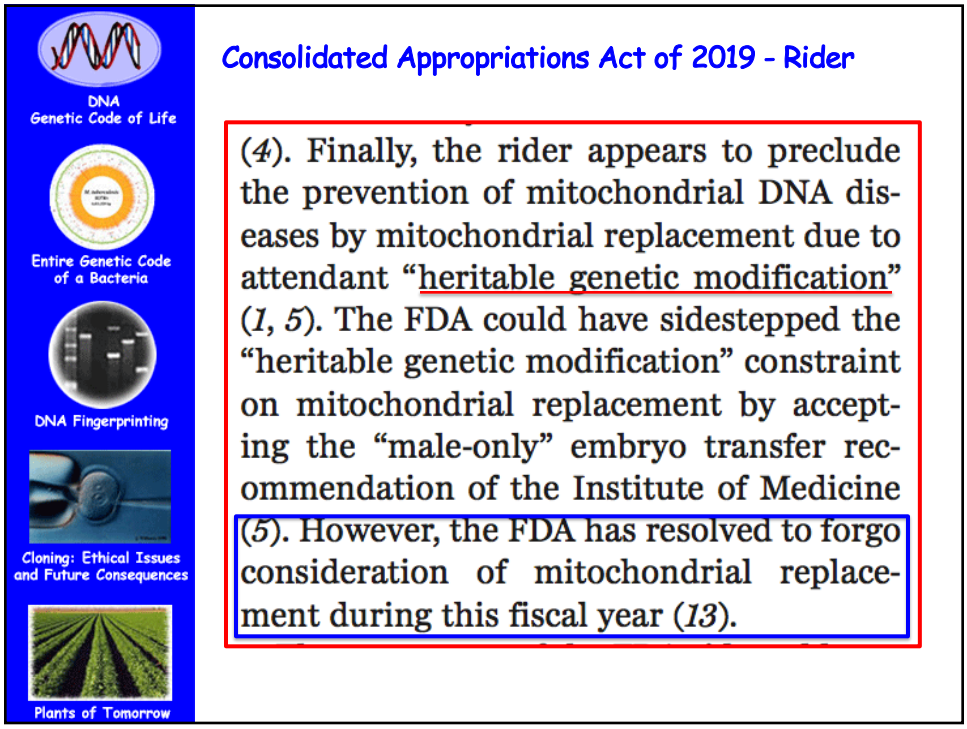
Road Blocks
Dickey-Wiker Amendment-1995
Federal Funds Cannot Be Used To:
• Create Human Embryos For Research Purposes
• Fund Research in Which a Human Embryo Will Be Destroyed, Discarded, or Knowingly Subjected to Risk or Injury of Death
2019 Congressional Budget (Expires 9/30/21)
• FDA Cannot Spend Any Money to Review Applications For Clinical Trials That Involve Human Embryos With Heritable Genetic Modifications (But...Male Mt Replacement Not Inherited & Egg Spindle Transfer Doesn't Destroy Embryo)

16


DNA
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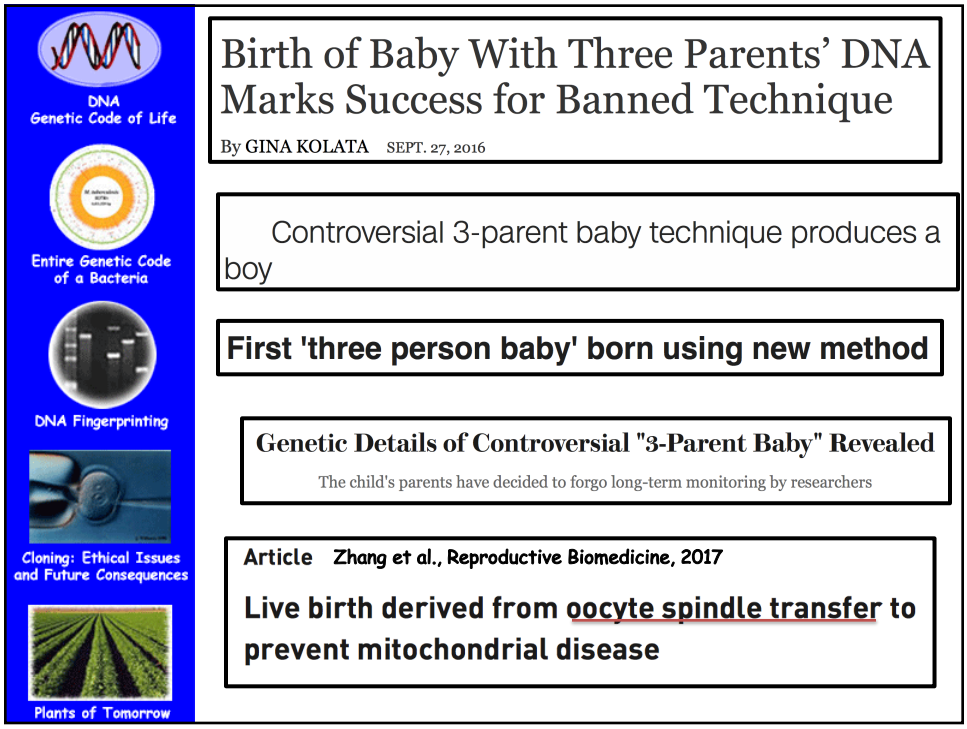
Plants of Tomorrow
Consolidated Appropriations Act of 2019 - Rider
(4). Finally, the rider appears to preclude the prevention of mitochondrial DNA diseases by mitochondrial replacement due to attendant "heritable genetic modification" (1, 5). The FDA could have sidestepped the "heritable genetic modification" constraint on mitochondrial replacement by accepting the "male-only" embryo transfer recommendation of the Institute of Medicine (5). However, the FDA has resolved to forgo consideration of mitochondrial replacement during this fiscal year (13).

17


DNA
Genetic Code of Life
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Plants of Tomorrow
Birth of Baby With Three Parents' DNA Marks Success for Banned Technique
By GINA KOLATA SEPT. 27, 2016
Controversial 3-parent baby technique produces a boy
First 'three person baby' born using new method
Genetic Details of Controversial "3-Parent Baby" Revealed
The child's parents have decided to forgo long-term monitoring by researchers
Article Zhang et al., Reproductive Biomedicine, 2017
Live birth derived from oocyte spindle transfer to prevent mitochondrial disease

18


DNA
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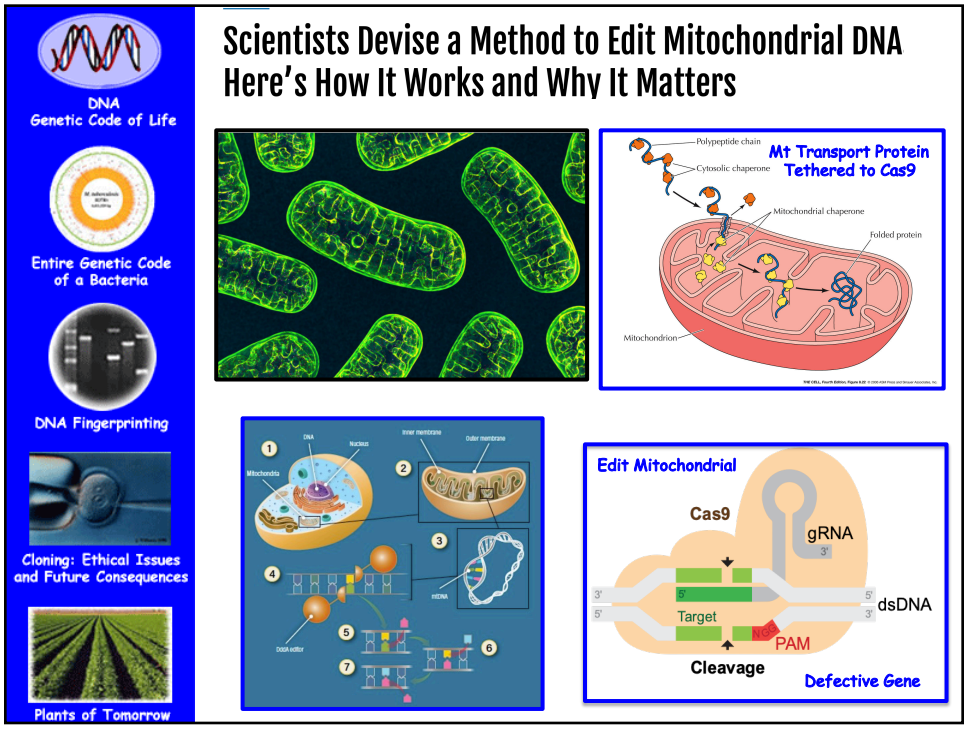
and Future Consequences
Plants of Tomorrow
Can Direct Editing of Mitochondrial
Genes Be Used Correct
Mitochondrial Diseases?

19


DNA
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and Future Consequences
Plants of Tomorrow
Scientists Devise a Method to Edit Mitochondrial DNA
Here's How It Works and Why It Matters
Polypeptide chain
Cytosolic chaperone
Mt Transport Protein
Tethered to Cas9
Mitochondrial chaperone
Folded protein
Mitochondrion
Edit Mitochondrial
Cas9
gRNA
3'
5'
Target
dsDNA
PAM
Cleavage
Defective Gene

20

Mitochondrial DNA SNPs As Markers in Human Populations

What is an ancestral marker?

mtDNA is a circular chain consisting of 16,569 pairs of nucleotides. Let's unwind the DNA double helix and take a closer look at its genetic code.

DNA consists of two chains of nucleotides, designated A, C, T, and G. "A" is always linked to "T", and "C" is always linked to "G" on the opposite chain. In this diagram, we will take a closer look at a short segment of mtDNA, namely locations 1 to 45. The unique combination of nucleotides in the chain is called a "genetic code" and holds genetic information.

DNA Sequence
(locations 1 to 45 of the mtDNA)

Location 1 — Location 45

GATCACAGGTCTATCACCCTATTAACCACTCACGGGAGCTCTCCA
CTAGTGTCCAGATAGTGGGATAATTGGTGAGTGCCCTCGAGAGGT

Ancestral markers are "mutations", little changes or "hiccups" that occur in the genetic code of the mtDNA. There are many types of mutations, but the type of mutation most commonly found in mtDNA is called a "SNP" (single nucleotide polymorphism). A SNP mutation occurs when a single nucleotide is replaced with a different nucleotide. For example, in this diagram, the "T" at location 40 is replaced by a "G".

DNA Sequence
(locations 1 to 45 of the mtDNA)

Location 1 — Location 45

GATCACAGGTCTATCACCCTATTAACCACTCACGGGAGGCTCTCCA
CTAGTGTCCAGATAGTGGGATAATTGGTGAGTGCCCTCCGAGAGGT

TA to GC SNP @ NT 45 Becomes a MARKER!

SNP mutation at Location 40

This mutation is documented as follows:
- Location: 40
- Nucleotide Change: T>g (also indicated as T40G)

21

How Trace Ancestry Using Mitochondrial DNA SNPs
Oldest Populations Contain the Most Diversity

Analysis of human mtDNA led to the Mitochondrial Eve Hypothesis

In the 1980s, Allan Wilson pioneered the use of mtDNA to study human evolution.

In two papers published in 1987 and 1991, he and his colleagues at Cal proposed that we all come from a population of humans that lived in Africa approximately 200,000 years ago.

Here's the logic behind the hypothesis.

DNA molecule — Geographic region — Start with A.

Original Geographic Region

Time

Detected By Using Specific Markers (RFLPs or SNPs)

Mutation generates B from A; now have individuals with both A and B DNAs in population.

Additional mutations generate diversity; now have individuals with both A, B, C and D DNAs.

Subset of "Old" Variants + New Variants

Newest Population

Lots of "Old" Variants

Oldest Population

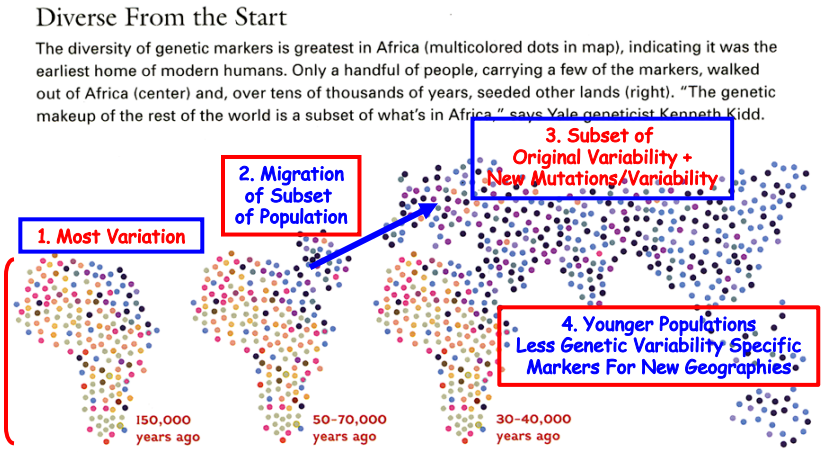
Migrates to form separate population.

Additional mutations diversify DNAs in populations: original population more diverse (A, B, C, D, F, G, H, I) than newer population (C, E).

Old Variants Trace Ancient Lineage. New Variants Mark New Populations SPECIFICALLY

22

Most Genetic Diversity Originated in the Founder Populations to Modern Humans!

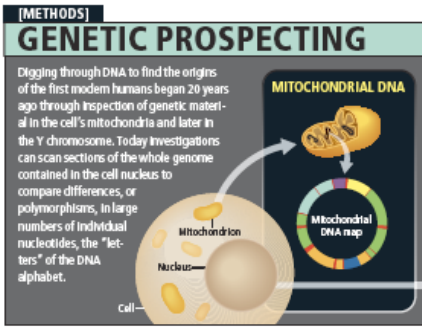


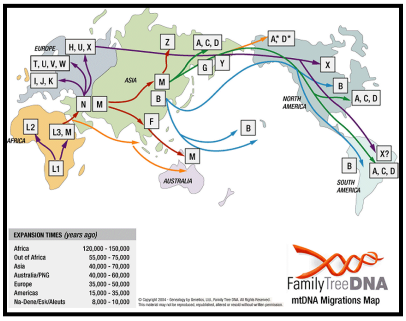
Genetic Variation Proportional to Population Age

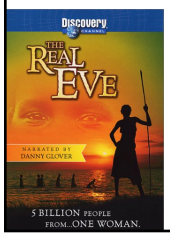
Markers From Original Population + New Markers For "New" Population

23

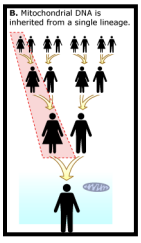
Tracing Human Migrations Using Mitochondrial DNA Polymorphisms (SNPs) - Back to Eve!







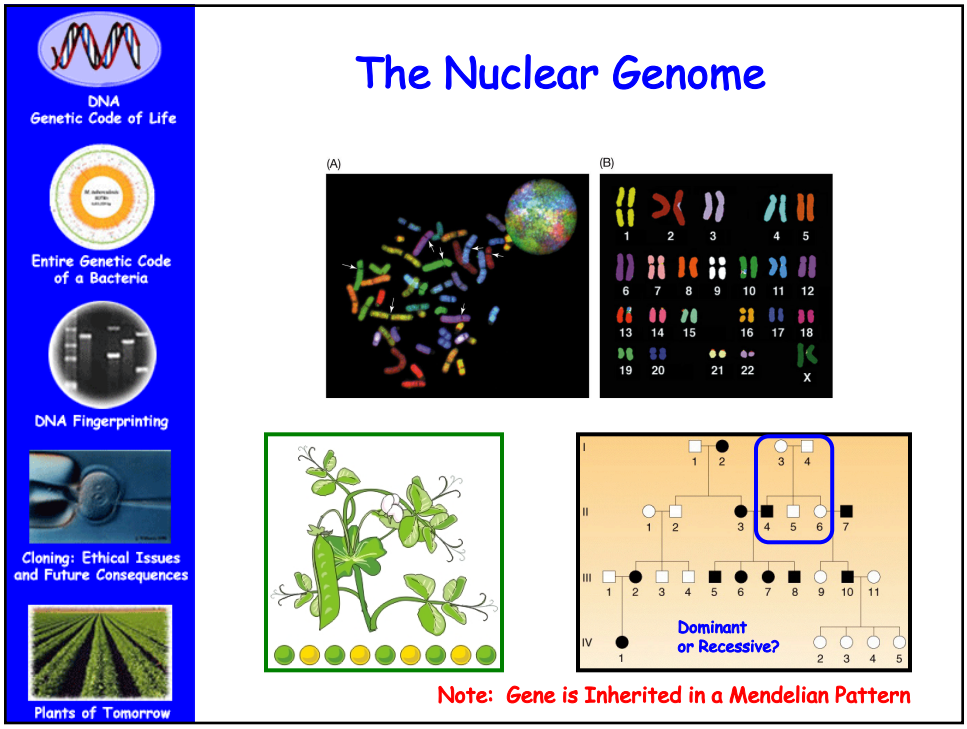
Eve Lived ~200,000 Years Ago!!



ancestry

23andMe

24


DNA
Genetic Code of Life
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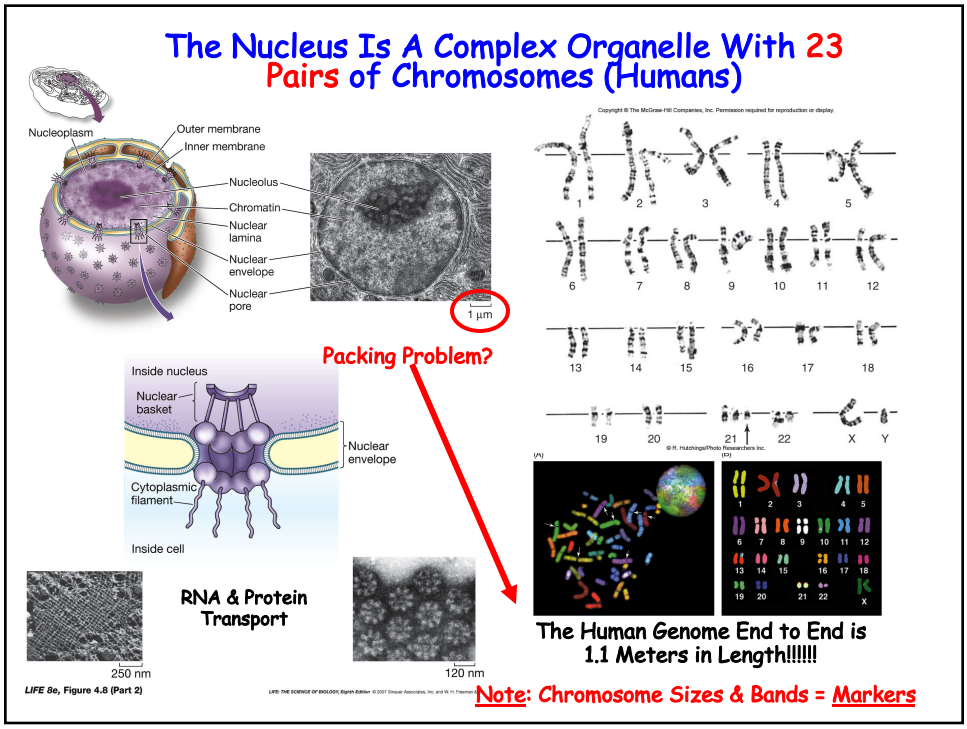
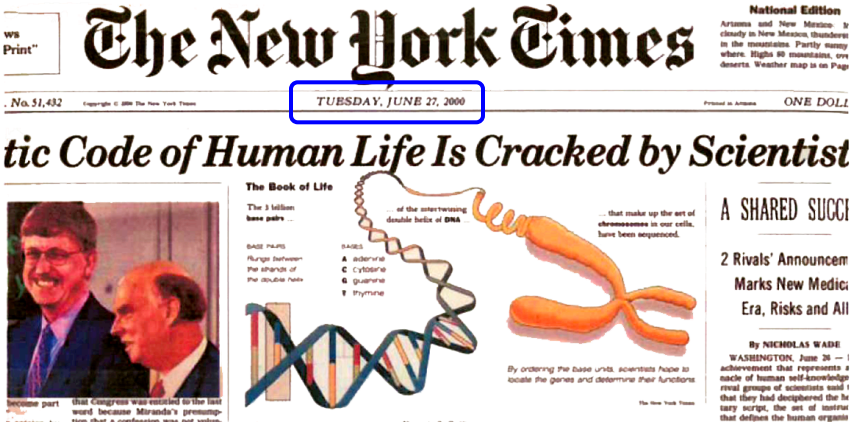
Plants of Tomorrow
The Nuclear Genome
(A)
(B)
Dominant or Recessive?
Note: Gene is Inherited in a Mendelian Pattern

25


The Nucleus Is A Complex Organelle With 23 Pairs of Chromosomes (Humans)
Nucleoplasm
Outer membrane
Inner membrane
Nucleolus
Chromatin
Nuclear lamina
Nuclear envelope
Nuclear pore
1 µm
Packing Problem?
Inside nucleus
Nuclear basket
Nuclear envelope
Cytoplasmic filament
Inside cell
250 nm
RNA & Protein Transport
120 nm
LIFE 8e, Figure 4.8 (Part 2)
The Human Genome End to End is 1.1 Meters in Length!!!!!!
Note: Chromosome Sizes & Bands = Markers

26

The Human Genome Was Sequenced Twenty Years Ago!
The Human Genome Project



The New York Times

National Edition

TUESDAY, JUNE 27, 2000

ONE DOLL

tic Code of Human Life Is Cracked by Scientist

The Book of Life

A SHARED SUCCI

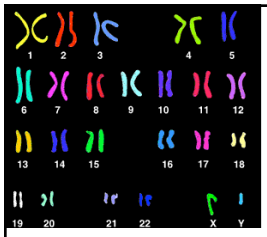
2 Rivals' Announcem
Marks New Medic
Era, Risks and All

By NICHOLAS WADE

Public & Private Effort Using Different Strategies - A Race!

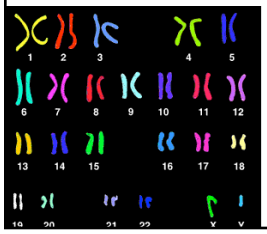
3 Billion Dollars & Took 15 Years

27



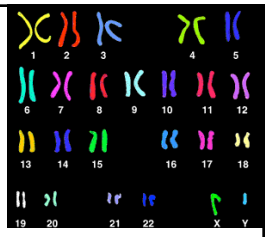
Chromosome Size
Large

Small

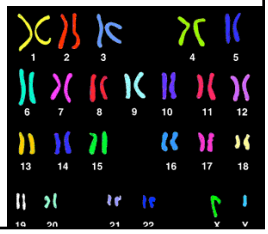


The Human Genome

Chromosome	Including gaps	Sequenced	Gaps
1	247,249,719	224,999,719	22,250,000
2	242,951,149	237,712,649	5,238,500
3	199,501,827	194,704,827	4,797,000
4	191,273,063	187,297,063	3,976,000
5	180,857,866	177,702,766	3,155,100
6	170,899,992	167,273,992	3,626,000
7	158,821,424	154,952,424	3,869,000
8	146,274,826	142,612,826	3,662,000
9	140,273,252	120,143,252	20,130,000
10	135,374,737	131,624,737	3,750,000
11	134,452,384	131,130,853	3,321,531
12	132,349,534	130,303,534	2,046,000
13	114,142,980	95,559,980	18,583,000
14	106,368,585	88,290,585	18,078,000
15	100,338,915	81,341,915	18,997,000
16	88,827,254	78,884,754	9,942,500
17	78,774,742	77,800,220	974,522
18	76,117,153	74,656,155	1,460,998
19	63,811,651	55,785,651	8,026,000
20	62,435,964	59,505,253	2,930,711
21	46,944,323	34,171,998	12,772,325
22	49,691,432	34,851,332	14,840,100
X	154,913,754	151,058,754	3,855,000
Y	57,772,954	25,652,954	32,120,000
M	16,571	16,571	0
Total genome	3,080,436,051	2,858,034,764	222,401,287



3.1 x 10^9 Base Pairs
Per Haploid Genome



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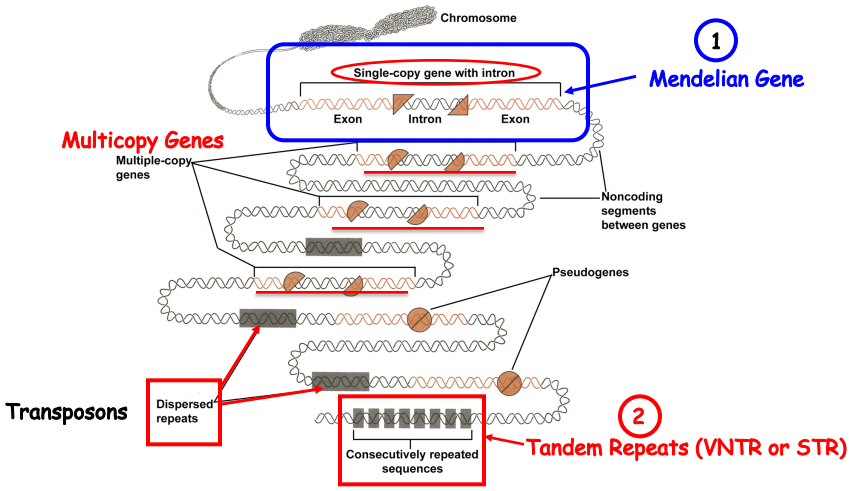
The Human Genome Landscape



Tandem Repeats or VNTRs are Useful for DNA Fingerprinting Studies!

e.g., DIS80 Locus For "Class" DNA Fingerprint on Chromosome 4 Core = 16bp

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A Small Fraction of the Human Genome Encodes Proteins and There Are 25,000 Different Genes!

TABLE 18.1 Classes of DNA Sequences Found in the Human Genome

Class	Frequency (%)	Description
Protein-encoding genes	1.5	Translated portions of the 25,000 genes scattered about the chromosomes
Introns	24	Noncoding DNA that constitutes the great majority of each human gene
Segmental duplications	5	Regions of the genome that have been duplicated
Pseudogenes (inactive genes)	2	Sequence that has characteristics of a gene but is not a functional gene
Structural DNA	20	Constitutive heterochromatin, localized near centromeres and telomeres
Simple sequence repeats	3	Stuttering repeats of a few nucleotides such as CGG, repeated thousands of times
Transposable elements	45	21%: Long interspersed elements (LINEs), which are active transposons 13%: Short interspersed elements (SINEs), which are active transposons 8%: Retrotransposons, which contain long terminal repeats (LTRs) at each end 3%: DNA transposon fossils

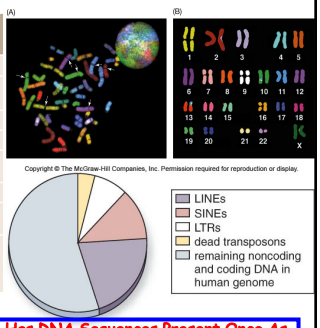
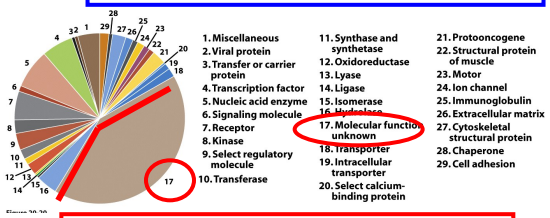


Table 20.6 Average characteristics of genes in the human genome

Characteristic	Average
Number of exons	8.8
Size of internal exon	145 bp
Size of intron	3,365 bp
Size of 5′ untranslated region	300 bp
Size of 3′ untranslated region	770 bp
Size of coding region	1,340 bp
Total length of gene	27,000 bp

Human Genes are Large but Contain Mostly Introns

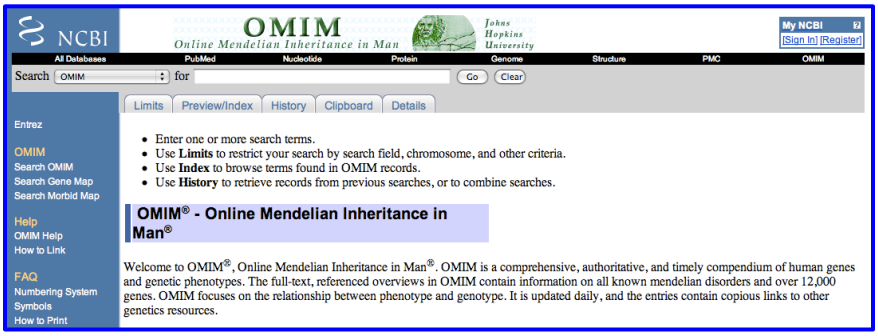
The Human Genome Has DNA Sequences Present Once As Well as Repeated Many Times



Do Not Know Functions of Most Human Genes!

30

How Many Human Disease Genes Have Been Identified?



There are ~25,000 Genes in The Human Genome

1. 6,873 Phenotypes For Which Molecular Basis Known (Single Gene Disorders & Traits)
2. 4,440 Genes With a Mutation Causing Phenotype.

OMIM 5/10/21 http://omim.org/statistics/entry

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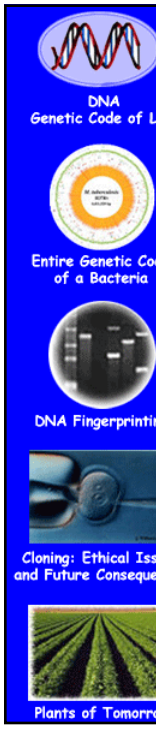
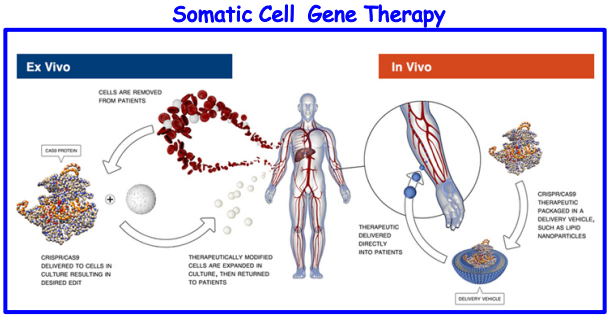
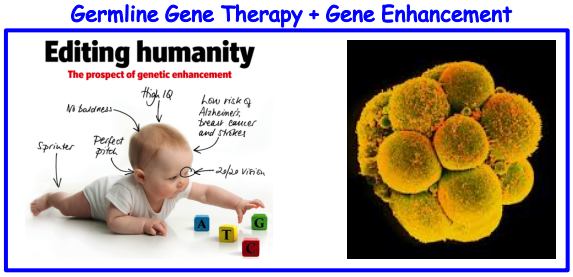


Some Day….Adding and Editing Genes May Be Used To Correct These Human Genetic Disorders

Somatic Cell Gene Therapy



Germline Gene Therapy + Gene Enhancement



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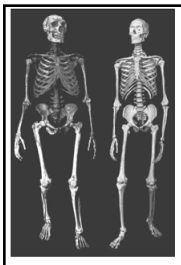
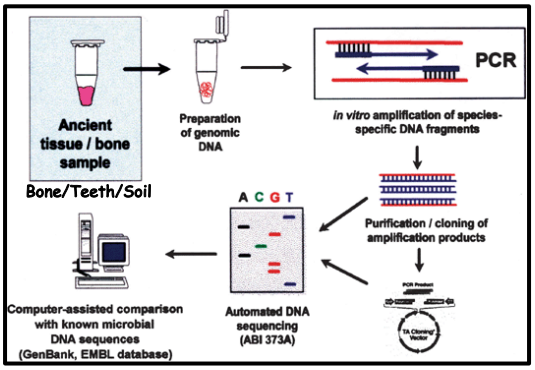
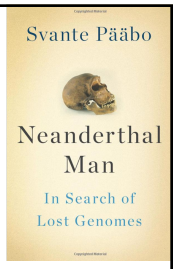
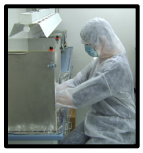


Using Ancient Genome Sequencing to Unravel Our Human Heritage



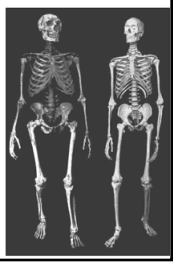


Neanderthals carb loaded, helping grow their big brains



DNA from cave soil reveals ancient human occupants Science April, 2017

Technique may help open a new era in paleoanthropology



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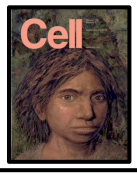
Ancient human genomes–keys to understanding our past

A Draft Sequence of the Neandertal Genome



A Crystal-Clear View Of an Extinct Girl's Genome

New DNA Analysis Shows Ancient Humans Interbred with Denisovans

A new high-coverage DNA sequencing method reconstructs the full genome of Denisovans--relatives to both Neandertals and humans--from genetic fragments in a single finger bone

The genome of the offspring of a Neanderthal mother and a Denisovan father

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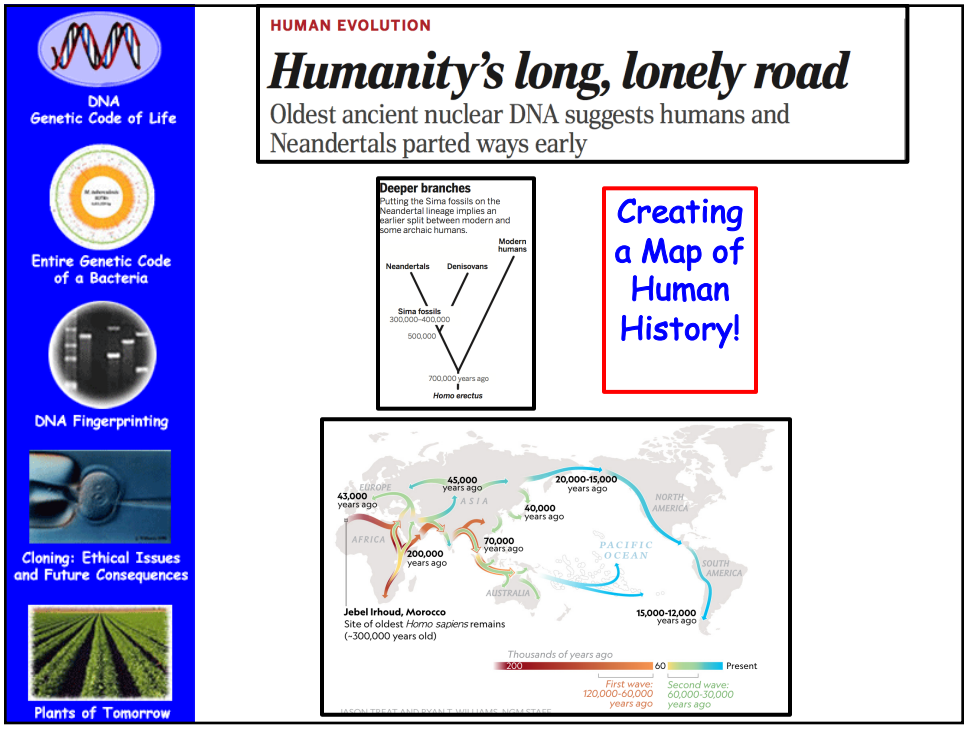

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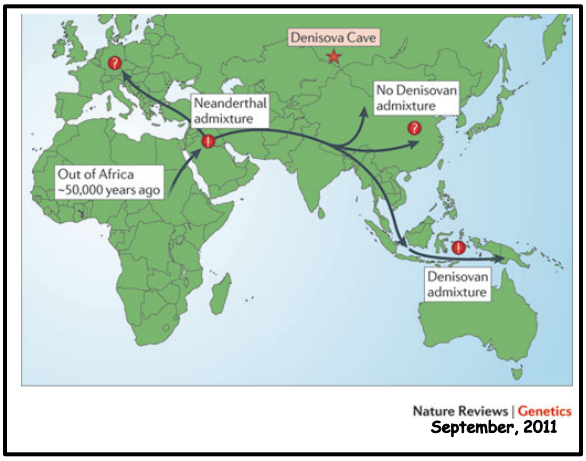
The Shaping of Modern Human Immune Systems by Multiregional Admixture with Archaic Humans

www.sciencemag.org **SCIENCE** VOL 334 7 OCTOBER 2011

Comparing 130,000 Year-Old Fossil Genomes to Our Genome Reveals Ancient "Matings" Between Different Human Ancestor Lineages!!



2-4% of Human Genome Consists of Neanderthal Sequences!

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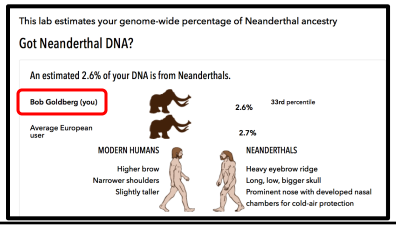
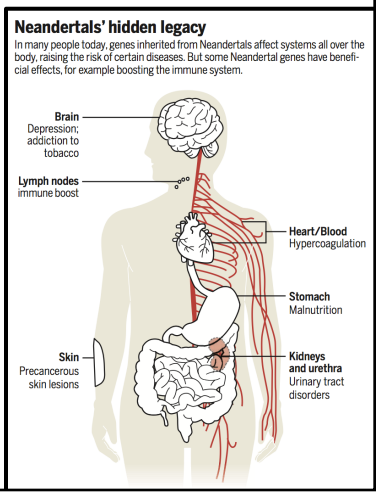
The genomic landscape of Neanderthal ancestry in present-day humans Nature, January 29, 2014

Neandertal genes linked to modern diseases

The phenotypic legacy of admixture between modern humans and Neandertals

Genomic Signatures of Selective Pressures and Introgression from Archaic Hominins at Human Innate Immunity Genes





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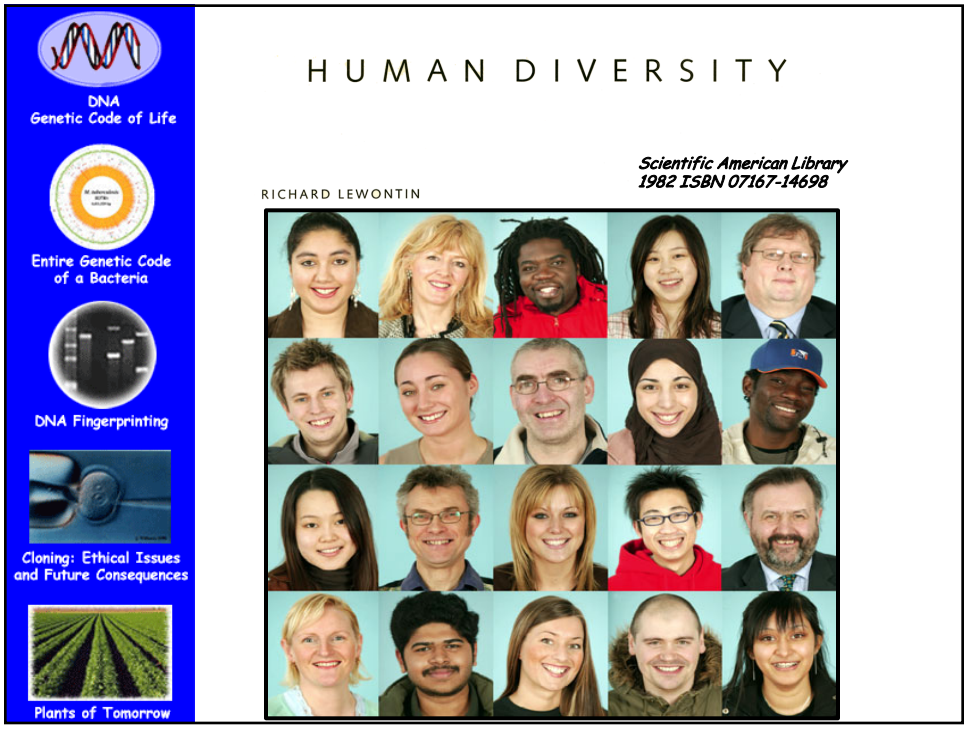

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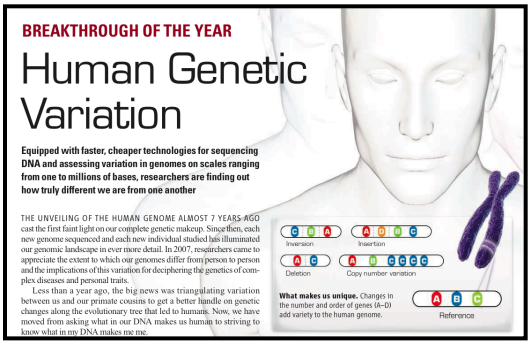
Using Nuclear DNA Variation (SNPs) Between Individuals (Living & Dead) Has Many Uses

1. Marking and Identifying Disease Genes
2. Paternity, Individual Identification, Ancestry
3. Human Population History and Origins
4. Identifying Ancient Hominid Alleles in Modern Human Populations
5. Forensics (Genealogical Searches)



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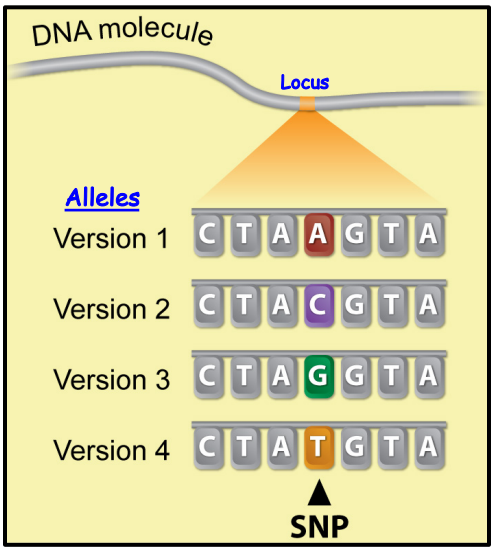
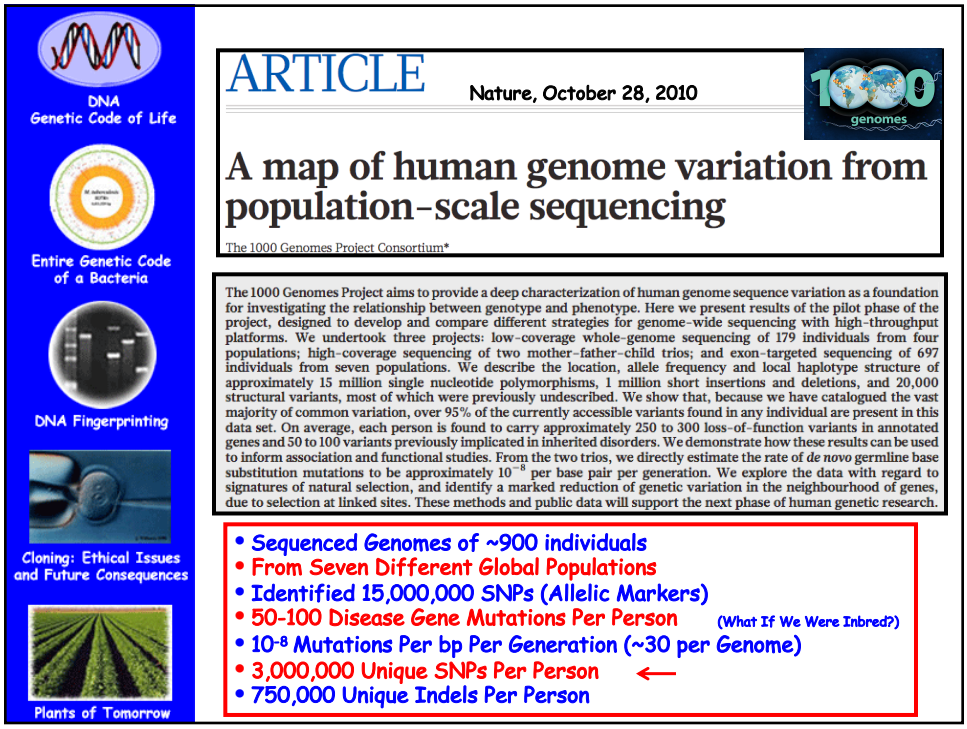
Genetic Diversity Refers to Allelic Variations Within a Population



SNPs at a Given Locus Are Alleles!

Individuals Can Contain Only Two Alleles at a Given Locus, But Populations Can Contain Many!!

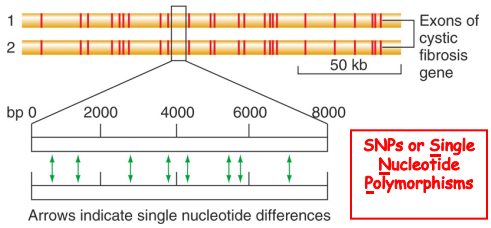
40



41

Most DNA Variations Between Individuals Occur Because of Base-Pair Changes in Non-Coding Regions of the Genome

Two cystic fibrosis (*CFTR*) alleles from two healthy individuals



SNPs or Single Nucleotide Polymorphisms

To Be on the safe side, suppose you assume that only 80% (0.8) of the 3 billion base pairs in the genome are noncoding, and on average only 1 base pair in 700 is polymorphic. With these assumptions, you can determine the frequency of polymorphism within a single individual by multiplying 3 billion by 0.8 and then multiplying that amount by 1/700:

(3x109) x 0.8 = 2.4 x 109, (2.4 x 109) x 1/700 = 3.4 million.

The result of 3.4 million is astonishing: It means that there are millions of differences between any two haploid sets of human chromosomes. Combined with differences in coding and regulatory sequences (which occur much less frequently), the millions of polymorphisms at anonymous loci contribute to an enormous pool of potential DNA markers.

Types of DNA Polymorphisms

TABLE 11.1 Classes of DNA Polymorphisms

Class	Size of Locus	Number of Alleles	Number of Loci in Population	Rate of Mutation	Use	Method of Detection
SNP	Single base pair	2	100 million	10^{-9}	Linkage and association mapping	PCR followed by ASO hybridization or primer extension
Microsatellite	30–300 bp	2–10	200,000	10^{-3}	Linkage and association mapping	PCR and gel electrophoresis
Multilocus minisatellite	1–20 kb	2–10	30,000	10^{-3}	DNA fingerprinting	Southern blot and hybridization
Indels (deletions and duplications)	1–100 bp	2	N/A	$<10^{-9}$	Linkage and association mapping	PCR and gel electrophoresis

Single nucleotide polymorphism (SNP) …GCAA T TCCCGATT…
…GCAA G TCCCGATT…

Simple sequence repeat (SSR) …GCATTATATATATATC…
…GCATTATAT[ ]C…

This is What Makes Us Unique Individuals!

There is ~1bp Change per 700bp in Human Genomes or ~3.4 Million bp Differences Between Individuals ~0.1% of Genome

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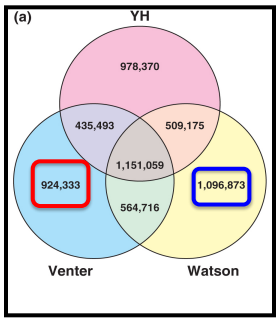
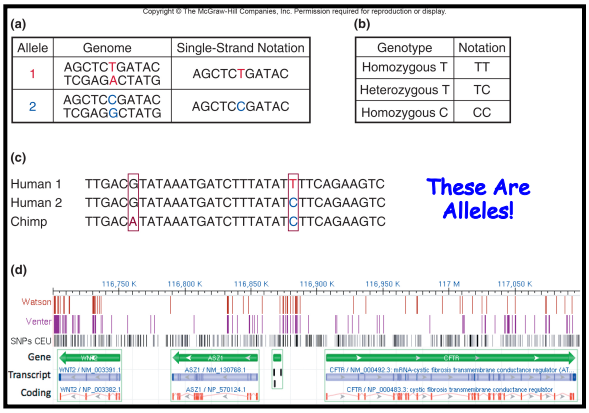
Comparison of Watson's and Ventner's Genomes Indicates That Individuals Have Unique SNPs!





Allele	Genome	Single-Strand Notation
1	AGCTCTGATAC TCGAGACTATG	AGCTCTGATAC
2	AGCTCCGATAC TCGAGGCTATG	AGCTCCGATAC

Genotype	Notation
Homozygous T	TT
Heterozygous T	TC
Homozygous C	CC

YH= Anonymous Chinese Man

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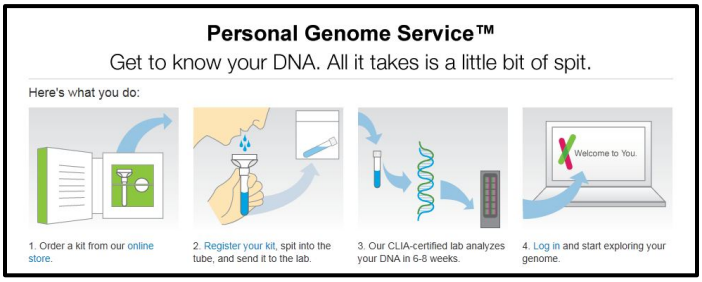

SNPs Used to Trace Ancestry & Individuality

SNPs That Have High Frequencies in Specific Populations

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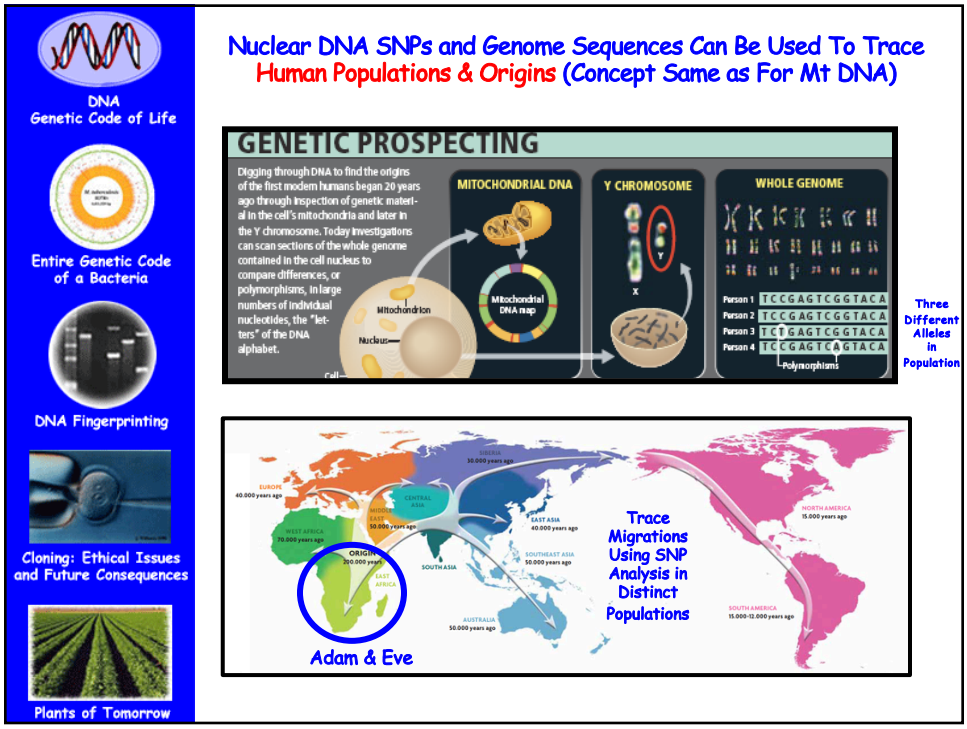
DNA
Genetic Code of Life
Entire Genetic Code of a Bacteria
DNA Fingerprinting
Cloning: Ethical Issues and Future Consequences
Plants of Tomorrow
Nuclear DNA SNPs and Genome Sequences Can Be Used To Trace Human Populations & Origins (Concept Same as For Mt DNA)
GENETIC PROSPECTING
Digging through DNA to find the origins of the first modern humans began 20 years ago through inspection of genetic material in the cell's mitochondria and later in the Y chromosome. Today investigations can scan sections of the whole genome contained in the cell nucleus to compare differences, or polymorphisms, in large numbers of individual nucleotides, the "letters" of the DNA alphabet.
MITOCHONDRIAL DNA
Y CHROMOSOME
WHOLE GENOME
Mitochondrion
Nucleus
Mitochondrial DNA map
Person 1 TCCGAGTCGGTACA
Person 2 TCCGAGTCGGTACA
Person 3 TCTGAGTCGGTACA
Person 4 TCCGAGTCAGTACA
Polymorphisms
Three Different Alleles in Population
Trace Migrations Using SNP Analysis in Distinct Populations
Adam & Eve

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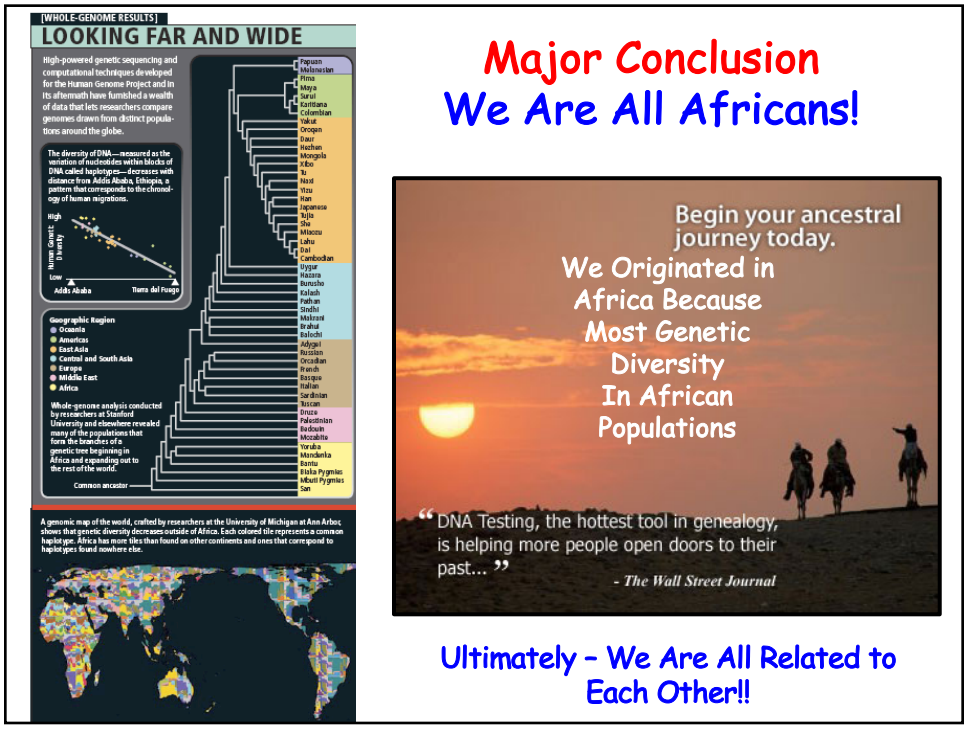
[WHOLE-GENOME RESULTS]
LOOKING FAR AND WIDE
High-powered genetic sequencing and computational techniques developed for the Human Genome Project and in its aftermath have furnished a wealth of data that lets researchers compare genomes drawn from distinct populations around the globe.
The diversity of DNA—measured as the variation of nucleotides within blocks of DNA called haplotypes—decreases with distance from Addis Ababa, Ethiopia, a pattern that corresponds to the chronology of human migrations.
High
Low
Addis Ababa
Tierra del Fuego
Geographic Region
Oceania
Americas
East Asia
Central and South Asia
Europe
Middle East
Africa
Whole-genome analysis conducted by researchers at Stanford University and elsewhere revealed many of the populations that form the branches of a genetic tree beginning in Africa and expanding out to the rest of the world.
Common ancestor
Papuan
Melanesian
Pima
Maya
Surui
Karitiana
Colombian
Yakut
Oroqen
Daur
Hezhen
Mongola
Xibo
Tu
Naxi
Yizu
Han
Japanese
Tujia
She
Miaozu
Lahu
Dai
Cambodian
Uygur
Hazara
Burusho
Kalash
Pathan
Sindhi
Makrani
Brahui
Balochi
Adygei
Russian
Orcadian
French
Basque
Italian
Sardinian
Tuscan
Druze
Palestinian
Bedouin
Mozabite
Yoruba
Mandenka
Bantu
Biaka Pygmies
Mbuti Pygmies
San
A genomic map of the world, crafted by researchers at the University of Michigan at Ann Arbor, shows that genetic diversity decreases outside of Africa. Each colored tile represents a common haplotype. Africa has more tiles than found on other continents and ones that correspond to haplotypes found nowhere else.
Major Conclusion
We Are All Africans!
Begin your ancestral journey today.
We Originated in Africa Because Most Genetic Diversity In African Populations
"DNA Testing, the hottest tool in genealogy, is helping more people open doors to their past..."
- The Wall Street Journal
Ultimately – We Are All Related to Each Other!!

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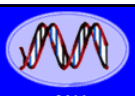
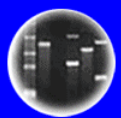


DNA
Genetic Code of Life

Entire Genetic Code of a Bacteria



DNA Fingerprinting

Cloning: Ethical Issues and Future Consequences

Plants of Tomorrow

Finally…Human Genome Diversity & The Concept of "Race"

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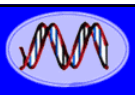
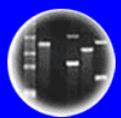


DNA
Genetic Code of Life

Entire Genetic Code of a Bacteria

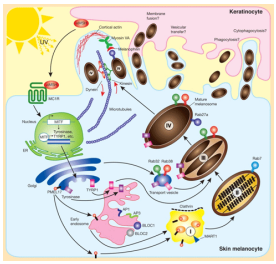


DNA Fingerprinting

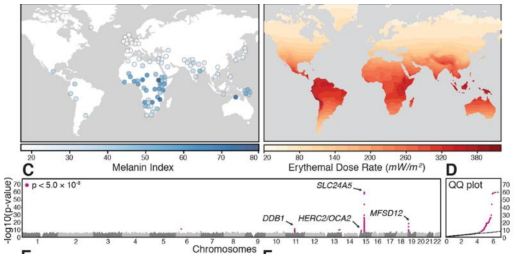
Cloning: Ethical Issues and Future Consequences

Plants of Tomorrow

The Biology of Skin Color



The Genetics of Skin Color (Four Major Loci!)



Loci associated with skin pigmentation identified in African populations Science, December, 2017

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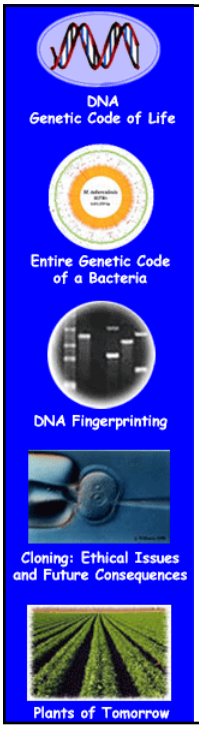
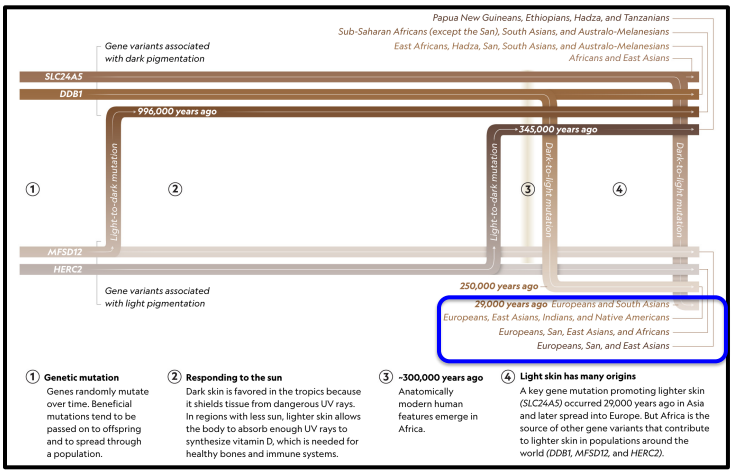


Skin Color Mutations Occurred Many Times in Human Evolution & Correlated With Geographical Migrations (i.e., Adaptions to Sunlight)



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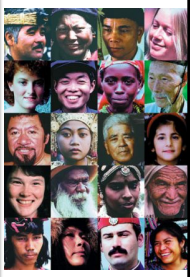
There is More Genetic (Allelic) Diversity Within Populations Than Between Populations!! So Much for the Concept of Racial "Purity"!!!!

Proportion of genetic diversity accounted for within and between populations and races

Gene	Total $H_{species}$	Proportion Within Populations	Within Races between Populations	Between Races
Hp	.994	.893	.051	.056
Ag	.994	.834	—	—
Lp	.639	.939	—	—
Xm	.869	.997	—	—
Ap	.989	.927	.062	.011
6PGD	.327	.875	.058	.067
PGM	.758	.942	.033	.025
Ak	.184	.848	.021	.131
Kidd	.977	.741	.211	.048
Duffy	.938	.636	.105	.259
Lewis	.994	.966	.032	.002
Kell	.189	.901	.073	.026
Lutheran	.153	.694	.214	.092
P	1.000	.949	.029	.022
MNS	1.746	.911	.041	.048
Rh	1.900	.674	.073	.253
ABO	1.241	.907	.063	.030
Mean		.854	.083	.063

Source: R. C. Lewontin, *Genetic Basis of Evolutionary Change* (Columbia University Press, 1974).

More Genetic Diversity Within Any Population Than Between Populations



1. 85% of Human Genetic Variations Occurs Within Populations & Between Individuals in that Populations!
2. Remaining 15% of Human Genetic Variation Split Between Different Populations of Same "Race" (8%) & Between Different "Races" (6%)
3. Only 6% of Human Genetic Variation are to Differences Between Races!!! Mostly Geographic. Note: THERE ARE GROUP DIFFERENCES! Most likely as a result of geographical isolation and adaptive significance in that population (e.g., skin color, UVB intensity, and Vitamin D production) – But they are Small!

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Major Conclusion

Within Population Differences Account For 95% of Human Genetic Variation

Genetic Structure of Human Populations

Noah A. Rosenberg,[1]* Jonathan K. Pritchard,[2] James L. Weber,[3] Howard M. Cann,[4] Kenneth K. Kidd,[5] Lev A. Zhivotovsky,[6] Marcus W. Feldman[7]

We studied human population structure using genotypes at 377 autosomal microsatellite loci in 1056 individuals from 52 populations. Within-population differences among individuals account for 93 to 95% of genetic variation; differences among major groups constitute only 3 to 5%. Nevertheless, without using prior information about the origins of individuals, we identified six main genetic clusters, five of which correspond to major geographic regions, and subclusters that often correspond to individual populations. General agreement of genetic and predefined populations suggests that self-reported ancestry can facilitate assessments of epidemiological risks but does not obviate the need to use genetic information in genetic association studies.

Table 1. Analysis of molecular variance (AMOVA). Eurasia, which encompasses Europe, the Middle East, and Central/South Asia, is treated as one region in the five-region AMOVA but is subdivided in the seven-region design. The World-B97 sample mimics a previous study (6).

Sample	Number of regions	Number of populations	Variance components and 95% confidence intervals (%)		
			Within populations	Among populations within regions	Among regions
World	1	52	94.6 (94.3, 94.8)	5.4 (5.2, 5.7)	
World	5	52	93.2 (92.9, 93.5)	2.3 (2.4, 2.6)	4.3 (4.0, 4.7)
World	7	52	94.1 (93.8, 94.3)	2.4 (2.3, 2.5)	3.6 (3.3, 3.9)
World-B97	5	14	89.8 (89.3, 90.2)	5.0 (4.8, 5.3)	5.2 (4.7, 5.7)
Africa	1	6	96.9 (96.7, 97.1)	3.1 (2.9, 3.3)	
Eurasia	1	21	98.5 (98.4, 98.6)	1.5 (1.4, 1.6)	
Eurasia	3	21	98.3 (98.2, 98.4)	1.2 (1.1, 1.3)	0.5 (0.4, 0.6)
Europe	1	8	99.3 (99.1, 99.4)	0.7 (0.6, 0.9)	
Middle East	1	4	98.7 (98.6, 98.8)	1.3 (1.2, 1.4)	
Central/South Asia	1	9	98.6 (98.5, 98.8)	1.4 (1.2, 1.5)	
East Asia	1	18	98.7 (98.6, 98.9)	1.3 (1.1, 1.4)	
Oceania	1	2	93.6 (92.8, 94.3)	6.4 (5.7, 7.2)	
America	1	5	88.4 (87.7, 89.0)	11.6 (11.0, 12.3)	

But - There Are Differences! But…They Fall Into Geographical Groups -- Groups Divided Originally by Geographic Barriers (Ocean, Desert, Mountains). The 5% Difference Allows Us to Mark and Trace Ancestry!

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Major Conclusions

85% Within Population Genetic Variability

8% Between Populations of Same "Race"

7% Between "Race" Genetic Variability

Variation That Occurs in Ancestral Population

1. If 85% of Human Genetic Variation Occurs Between Different People Within Any Given Population (localized)
2. If only 7% of Human Genetic Variation Occurs Between "Races" (novel alleles specific to "races")
3. Then Losing all "Races" Except One Retains 93% of all Human Genetic Variation!

[85% + (15%-7%)]= 93%

4. ∴ Humans Are Highly Heterozygous or Hybrids- & If Above Not True- Most of Us Would Not Be Here- Need Genetic Variation to Survive!

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Humans Are Highly Heterozygous or Hybrids- & If Above Not True- Most of Us Would Not Be Here- Need Genetic Variation to Survive!

GENOMICS · 06 SEPTEMBER 2019 Nature Communications

'Extreme inbreeding' revealed by massive human-genome survey

Inbreeding Depression

Analysis suggests that roughly one in 3,600 people studied were born to closely related parents.

The researchers found that the genomes of one in 3,652 people born in the United Kingdom between 1938 and 1967 show extreme inbreeding, with the two sets of chromosomes sharing more than 10% of their DNA. This indicates unions between full siblings, a parent and a child, a grandparent and a grandchild, or other relatives with similar degrees of relatedness.

People whose genomes showed extreme inbreeding tended to be shorter, less muscular and have weaker cognitive abilities than average.

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So What is a "Race"?

1. Primarily a sociological concept- but could be a localized or "inbred population" that has a higher frequency of alleles at a *very small number of loci*. Affects several physical features.
2. High frequency alleles in one "race" are present at lower frequencies in other "races". All humans have same genes- differ in form mostly within populations!
3. Heterozygosity (variation) high in human populations- all populations. None homozygous at all loci!
4. No such thing as a "pure" race - would have little variation
5. *Genes affecting physical features not representative of genes across genome — "selected" traits with adaptive significance (e.g., vitamin D synthesis, sexual selection, pathogen susceptibility, etc.)*

Geographical Ancestry is relevant-many "racial" groups now have multiple ancestries because of admixture and migration

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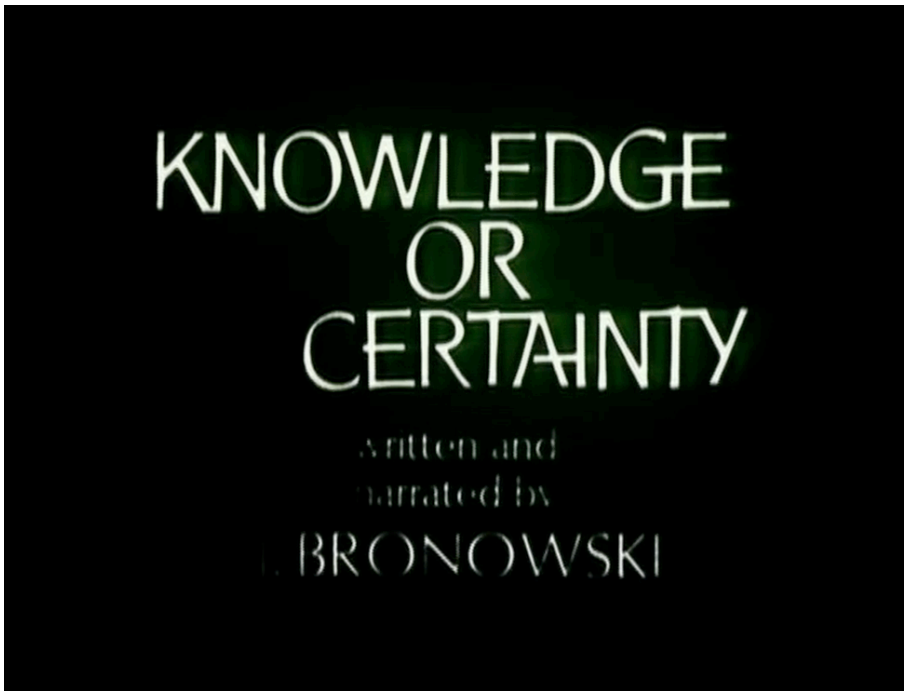
KNOWLEDGE
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