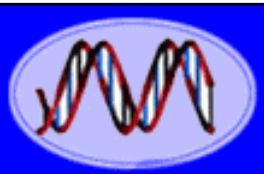
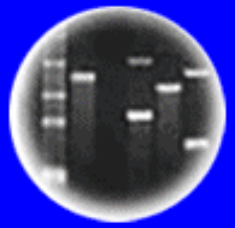


DNA
Genetic Code of Life

Entire Genetic Code
of a Bacteria



DNA Fingerprinting

Cloning: Ethical Issues
and Future Consequences

Plants of Tomorrow

HC70A & SAS70A Spring 2015
Genetic Engineering in Medicine, Agriculture, and Law

Professors Bob Goldberg, Channapatna Prakash & John Harada

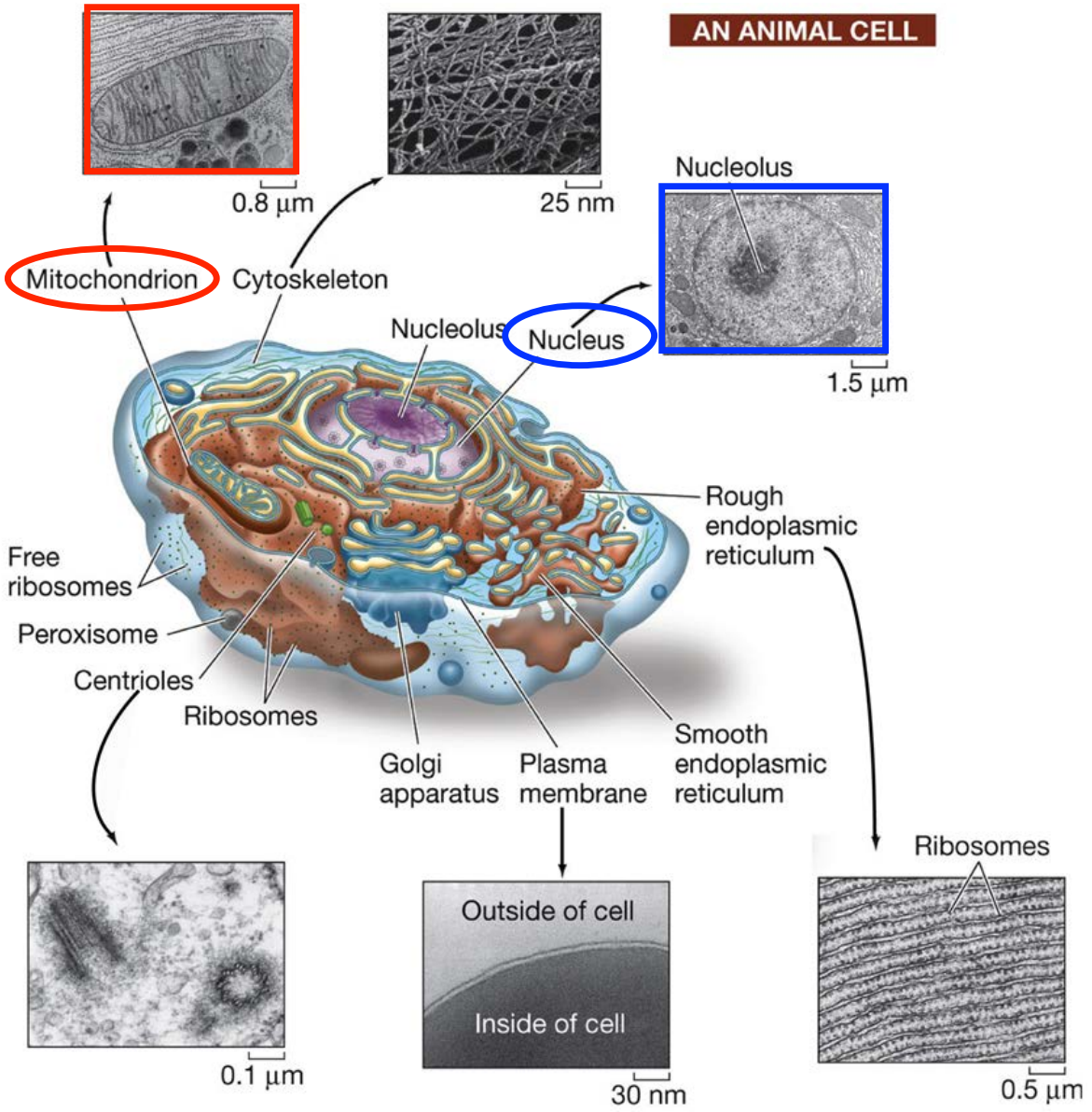
Lecture 7
Your Personal Genome &
Tracing Your Ancestry

UCLA

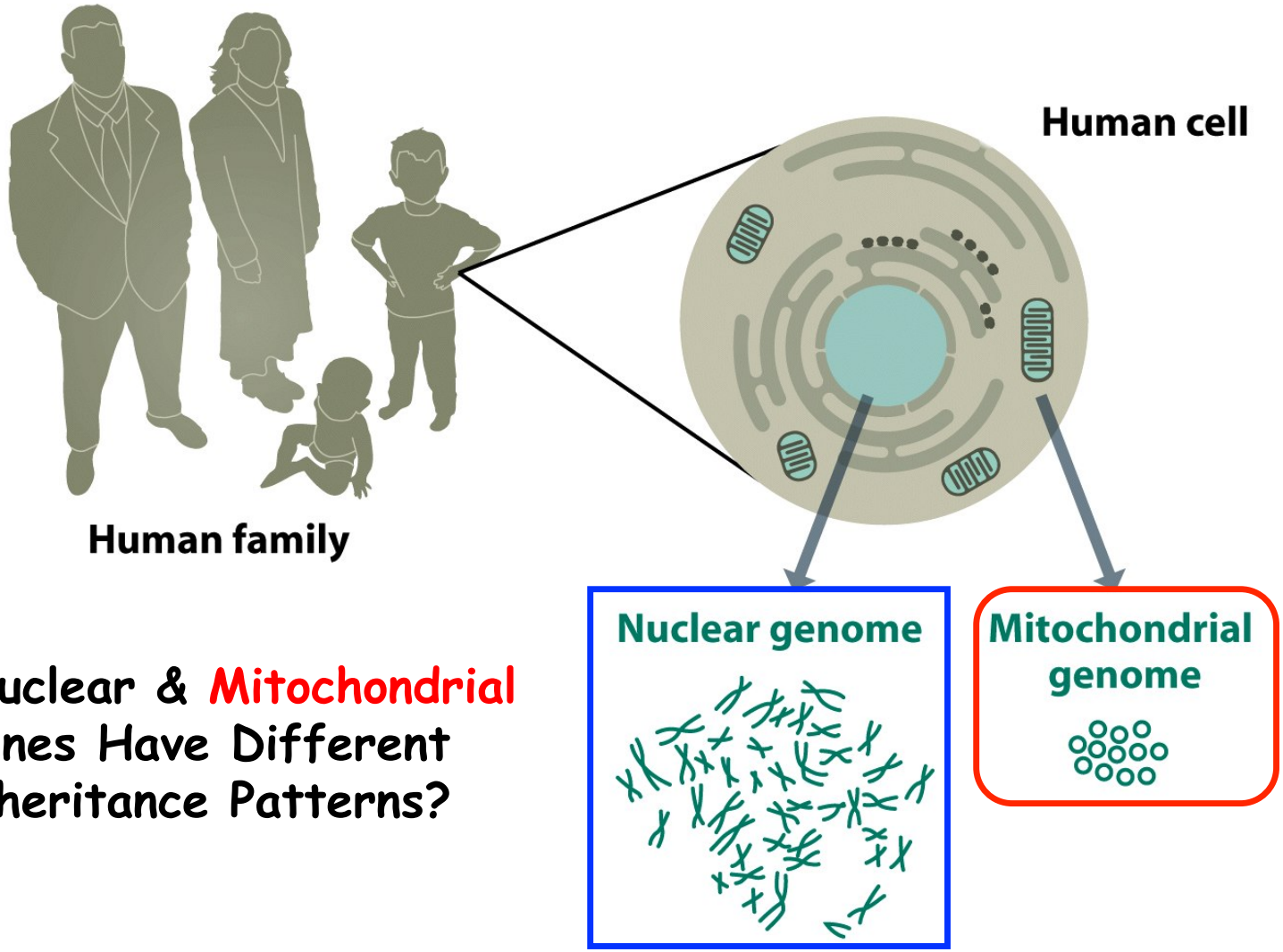
TUSKEGEE UNIVERSITY

UCDAVIS
UNIVERSITY OF CALIFORNIA

Human Cells Have Two Genomes



……One in the Nucleus and One in the Mitochondria



Do Nuclear & Mitochondrial Genes Have Different Inheritance Patterns?

Figure 1-1 Genomes 3 (© Garland Science 2007)

The Nuclear and Mitochondrial Genomes Differ in Size & Shape

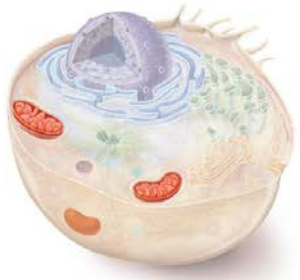
Nuclear	Mitochondrial
3.2 Mb	17 kb
25,000 Genes	30 Genes
24 Linear Pieces	1 Circle – 5 per Mt

Table 9.1: The human nuclear and mitochondrial genomes

	Nuclear genome	Mitochondrial genome
Size	3200 Mb	16.6 kb
No. of different DNA molecules	23 (in XX cells) or 24 (in XY cells); all linear	One circular DNA molecule
Total no. of DNA molecules per cell	46 in diploid cells, but varies according to ploidy	Often several thousands (but variable – see *Box 9.1*)
Associated protein	Several classes of histone and nonhistone protein	Largely free of protein
No. of genes	~ 30 000–35 000	37
Gene density	~ 1/100 kb	1/0.45 kb
Repetitive DNA	Over 50% of genome, see *Figure 9.1*	Very little
Transcription	The great bulk of genes are transcribed individually (*monocistronic transcription units*)	Co-transcription of multiple genes from both the heavy and the light strands (*polycistronic transcription units*)
Introns	Found in most genes	Absent
% of coding DNA	~ 1.5%	~ 93%
Codon usage	See *Figure 1.22*	See *Figure 1.22*
Recombination	At least once for each pair of homologs at meiosis	Not evident
Inheritance	Mendelian for sequences on X and autosomes; paternal for sequences on Y	Exclusively maternal

Mitochondria Power Human Cells and Contain a Circular Genome

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



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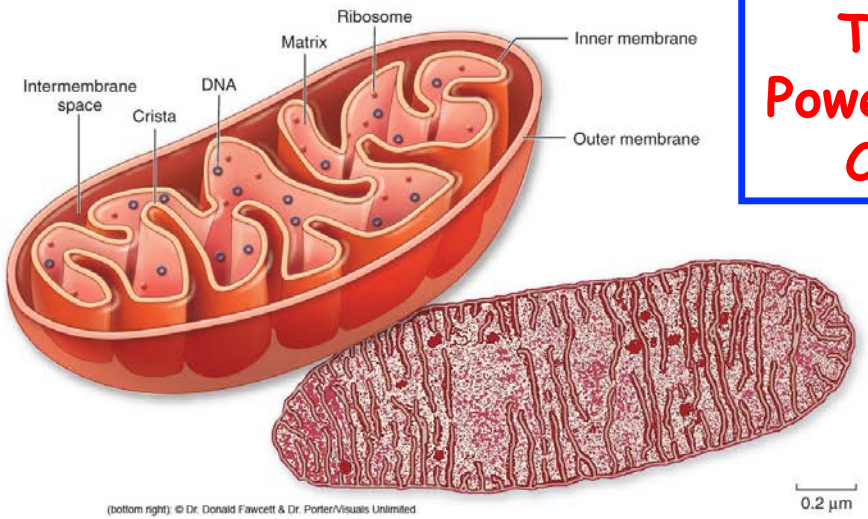


(bottom right): © Dr. Donald Fawcett & Dr. Porter/Visuals Unlimited

Makes ATP Energy That Powers All Cells!

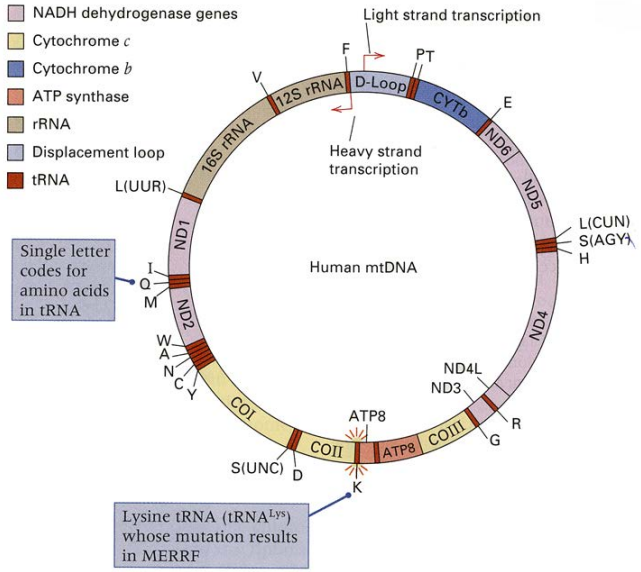


Figure 16.3 Genes in human mitochondrial DNA. The tRNA genes are indicated by the one-letter amino acid symbols; hence $tRNA^{Lys}$ is denoted K. The positions of these and other genes in the mitochondrial DNA are indicated by color according to the key at the upper left. The arrows indicate the promoters 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 Genome

DNA

Divides
Transcription
Translation

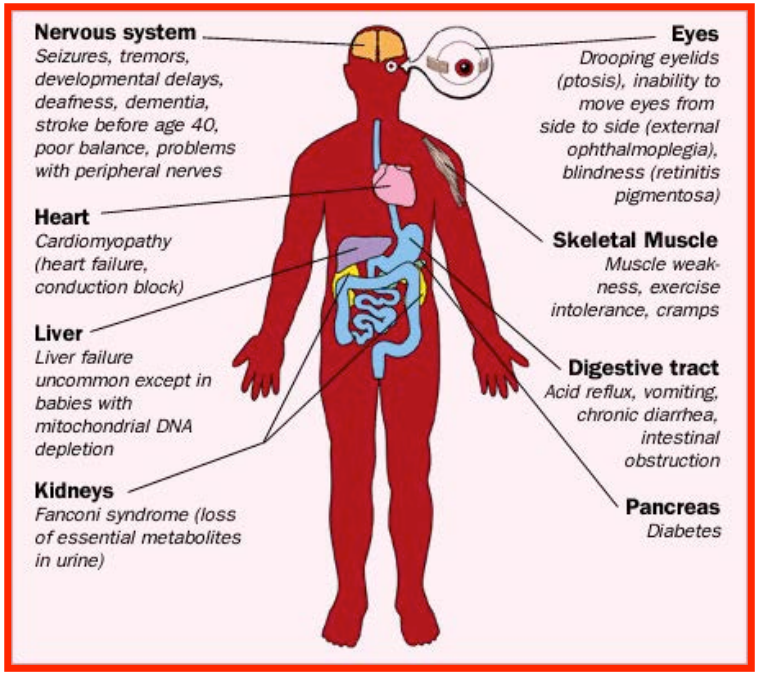
→ **Mitochondrial Proteins**

UNITED MITOCHONDRIAL DISEASE FOUNDATION.
HOPE. ENERGY. LIFE.

Mitochondrial DNA Diseases

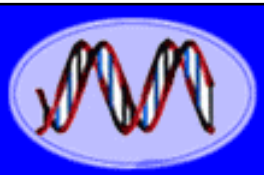
Affect 1/4000 People

- 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.



DNA
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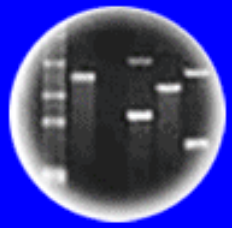
Entire Genetic Code of a Bacteria



DNA Fingerprinting

Cloning: Ethical Issues and Future Consequences

Plants of Tomorrow

MERRF: A Mitochondrial Disease Example

Myoclonic Epilepsy and Ragged-Red Fiber Syndrome

MERRF Is Rare – Affecting 1/400,000 People

MERRF

Long Name: Myoclonic Epilepsy and Ragged-Red Fiber Disease.

Symptoms: Myoclonus, epilepsy, progressive ataxia, muscle weakness and degeneration, deafness, and dementia.

Cause: Mitochondrial DNA point mutations: A8344G, T8356C **Serine tRNA** **[How cause disease?]**

MERRF is a progressive multi-system syndrome usually beginning in childhood, but onset may occur in adulthood. The rate of progression varies widely. Onset and extent of symptoms can differ among affected siblings.

The classic features of MERRF include:

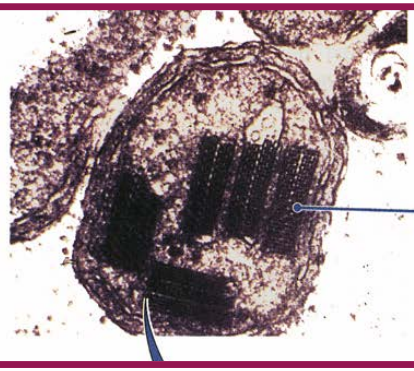
- Myoclonus (brief, sudden, twitching muscle spasms) – the most characteristic symptom
- Epileptic seizures
- Ataxia (impaired coordination)
- Ragged-red fibers (a characteristic microscopic abnormality observed in muscle biopsy of patients with MERRF and other mitochondrial disorders) Additional symptoms may include: hearing loss, lactic acidosis (elevated lactic acid level in the blood), short stature, exercise intolerance, dementia, cardiac defects, eye abnormalities, and speech impairment.

Although a few cases of MERRF are sporadic, most cases are maternally inherited due to a mutation within the mitochondria. The most common MERRF mutation is A8344G, which accounted for over 80% of the cases (GeneReview article). Four other mitochondrial DNA mutations have been reported to cause MERRF. While a mother will transmit her MERRF mutation to all of her offspring, some may never display symptoms.

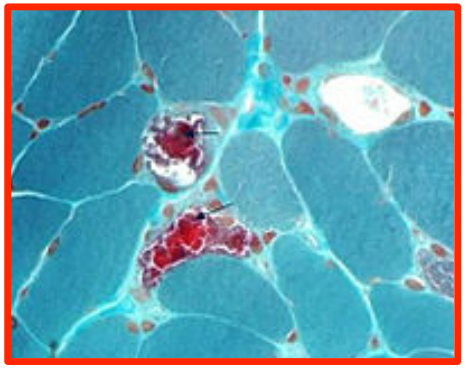
As with all mitochondrial disorders, there is no cure for MERRF. Therapies may include coenzyme Q10, L-carnitine, and various vitamins, often in a "cocktail" combination. Management of seizures usually requires anticonvulsant drugs. Medications for control of other symptoms may also be necessary.

The prognosis for MERRF varies widely depending on age of onset, type and severity of symptoms, organs involved, and other factors.

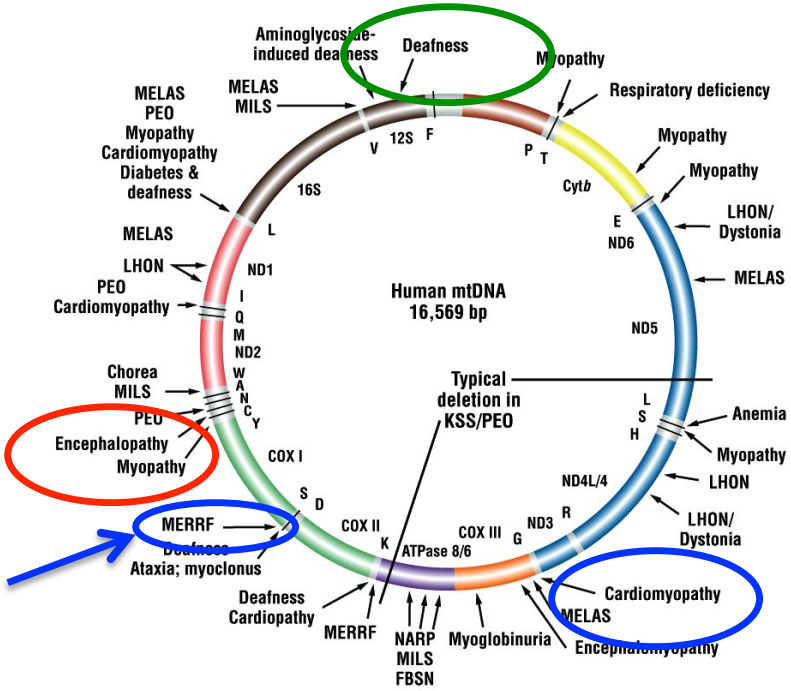
Sources: Dr. Rolf Luft; The development of mitochondrial medicine. [Review] ; *Proceedings of the National Academy of Sciences of the United States of America* ; 1994 ; 91(19) ; 8731-8 & DiMauro



Individuals affected with MERRF have abnormal mitochondria with crystalline inclusions.



The Circular Mitochondrial Genome is Inherited Maternally



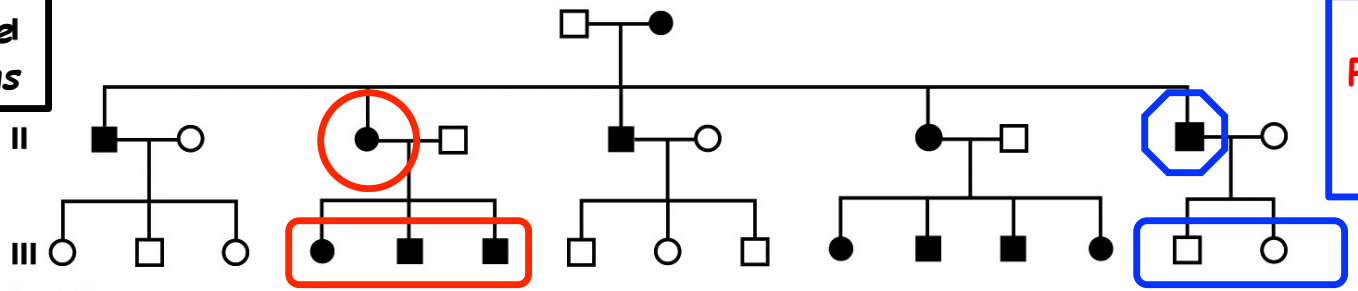
Disease Genes Present on the Mitochondrial Genome

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



Note:
Passed on From Mother to All Children

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

Can Gene Therapy Be Used to "Cure" Mitochondrial Gene Defects?

NUCLEAR TRANSPLANTATION

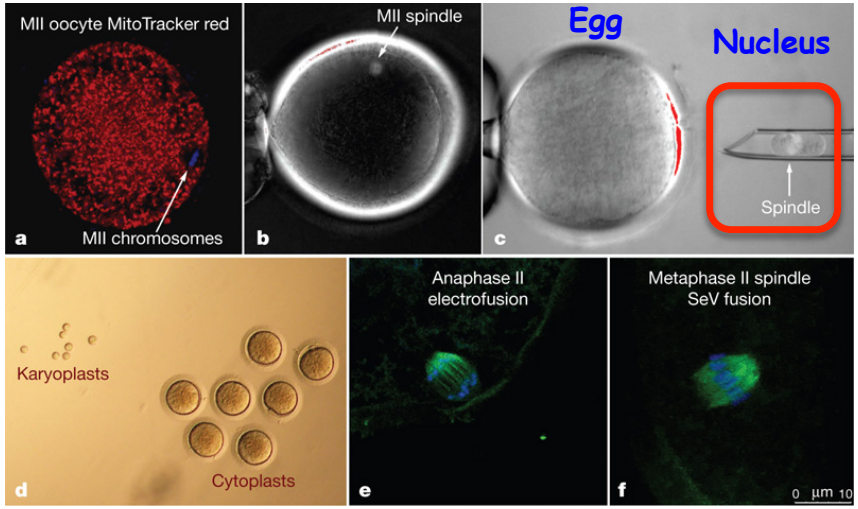
Researchers Prevent Inheritance of Faulty Mitochondria in Monkeys

Vol 461 | 17 September 2009 | doi:10.1038/nature08368 nature

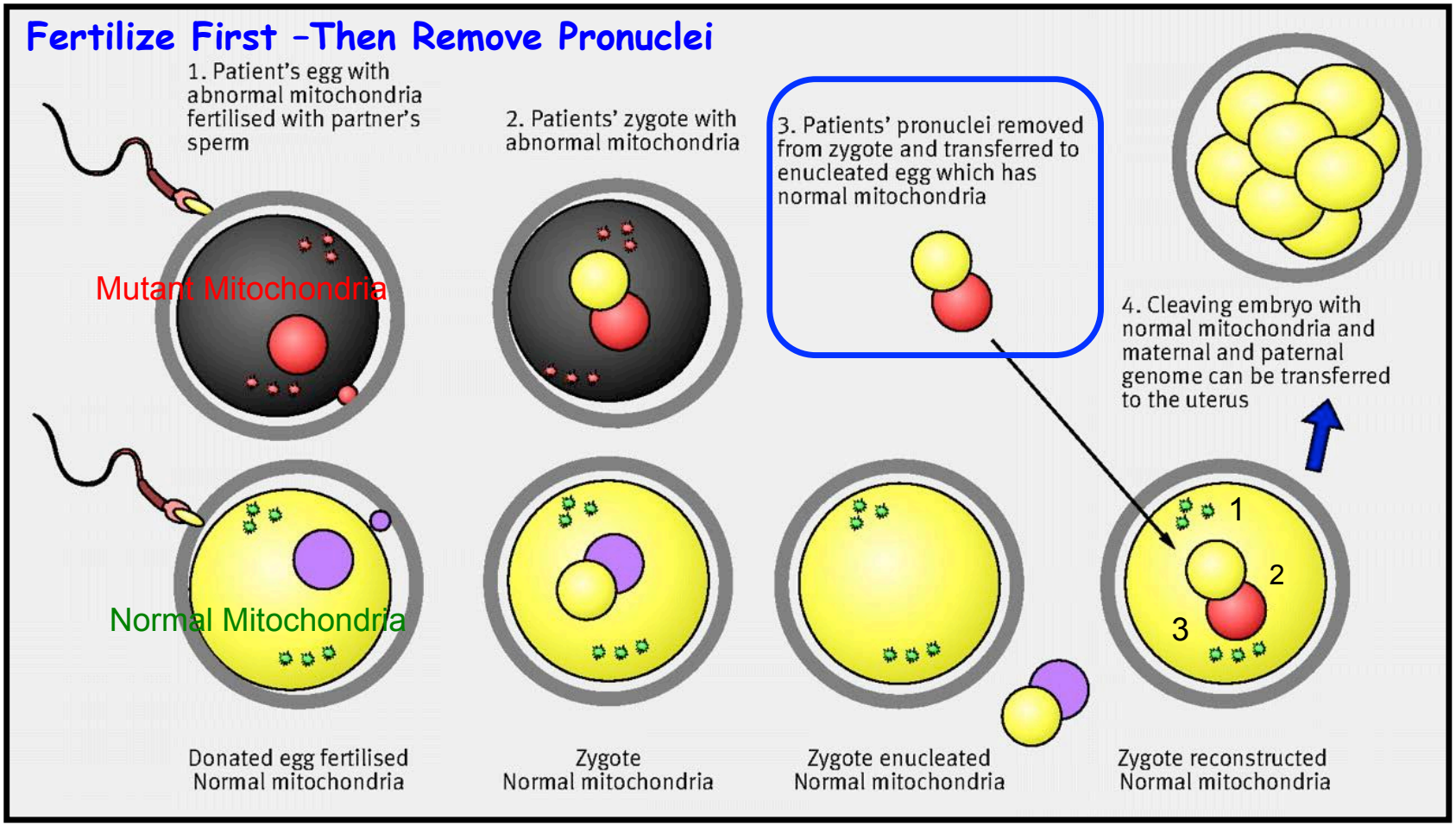
Nature 461, September 17, 2009

ARTICLES

Mitochondrial gene replacement in primate offspring and embryonic stem cells

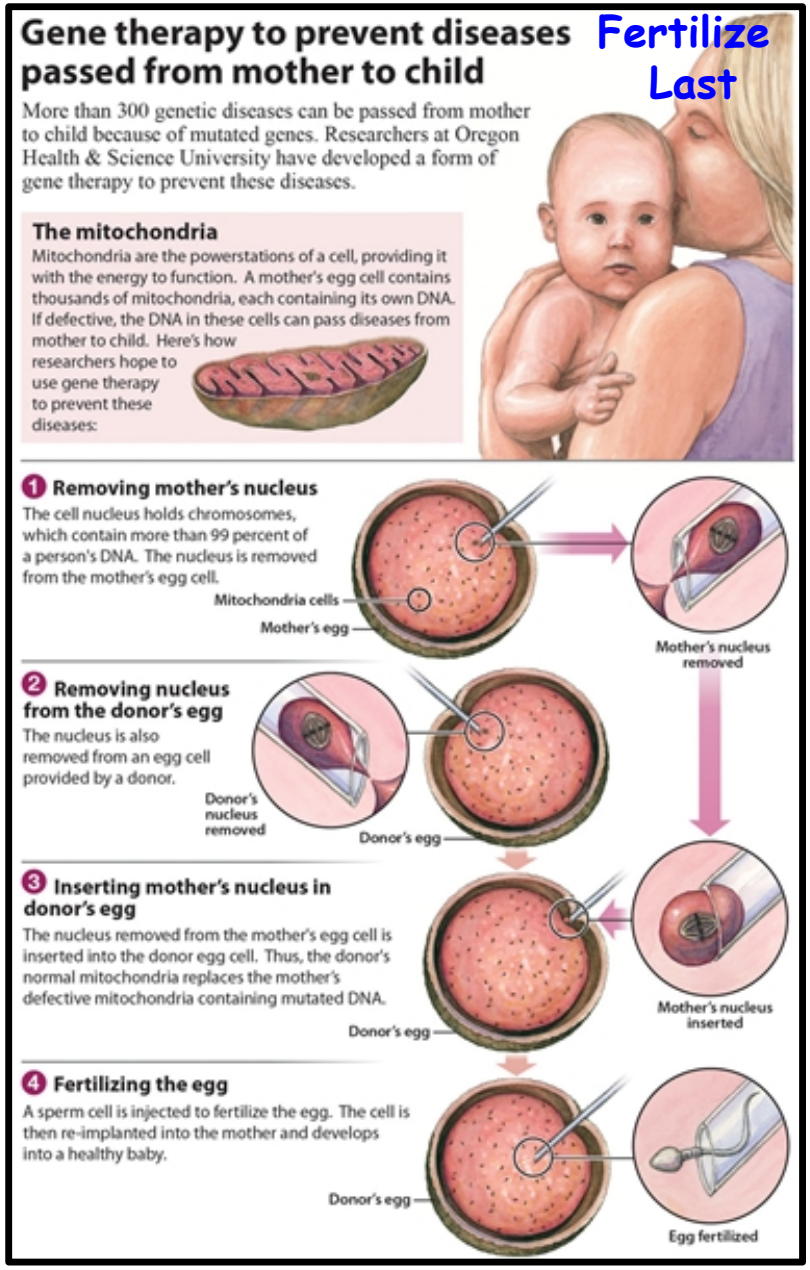


Mitochondrial Pronuclear Replacement Therapy



***Note:* The Zygote Contains THREE Genomes --**
One from Mother, One From Father, and One From Donor Mitochondria

Egg Spindle Replacement Therapy
An Alternative Approach



NATURE | NEWS

DNA-swap technology almost ready for fertility clinic

Mitochondrial transfer could reduce the risk of childhood disease.

David Cyranoski

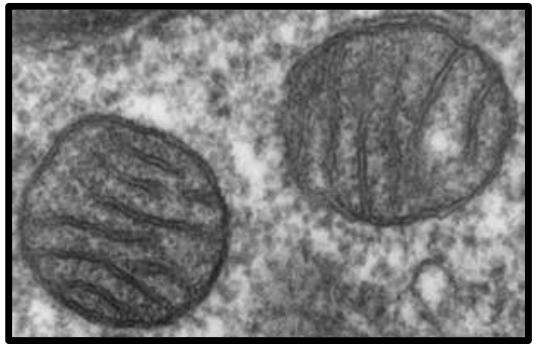
24 October 2012

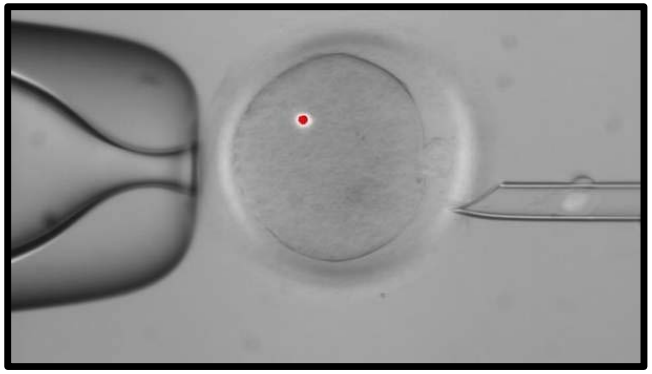
Geneticists Breach Ethical Taboo By Changing Genes Across Generations

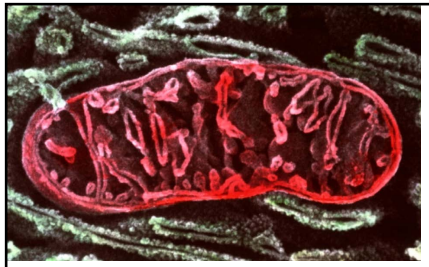
NATURE NEWS BLOG

Bioethics board backs embryo alteration for mitochondrial disease

11 Jun 2012 | 23:01 BST | Posted by Ewen Callaway | Category: Biology & Biotechnology, Health and medicine

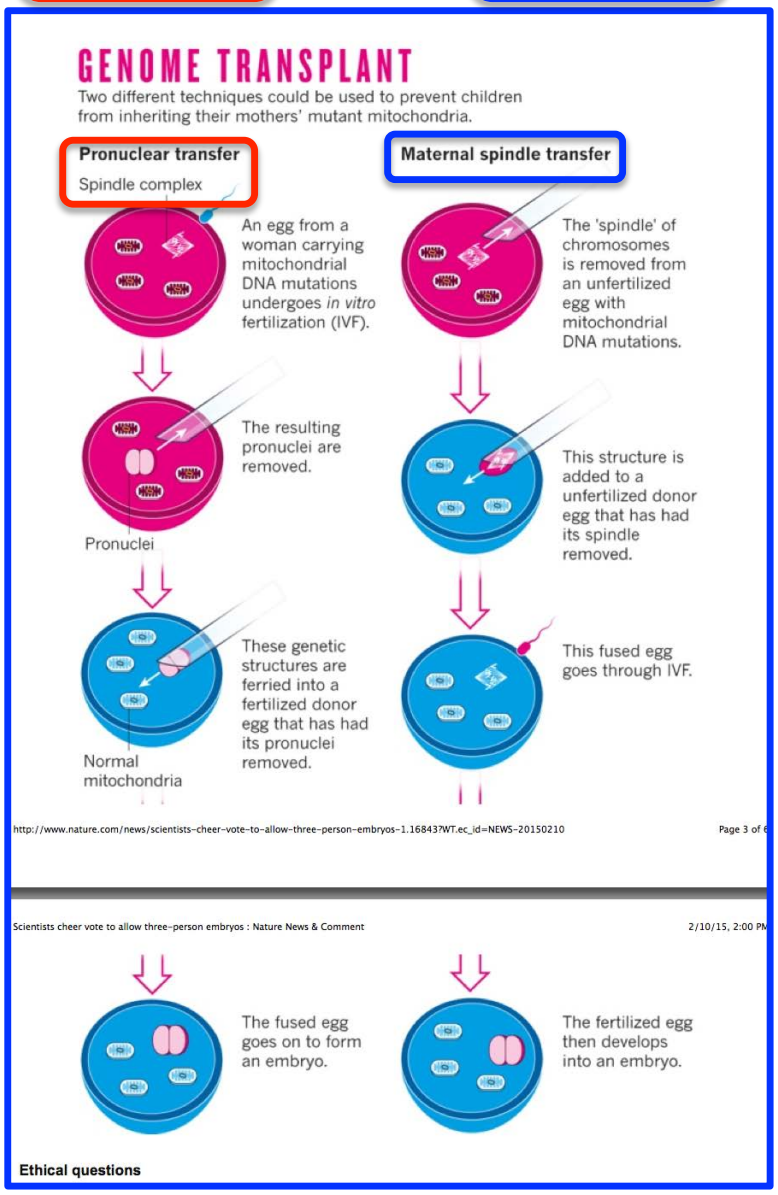






Embryo Destroyed

Egg Destroyed



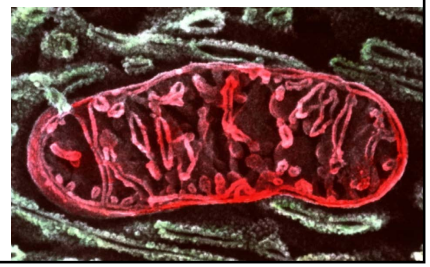
Mitochondrial DNA Diseases

Affect 1/4000 People

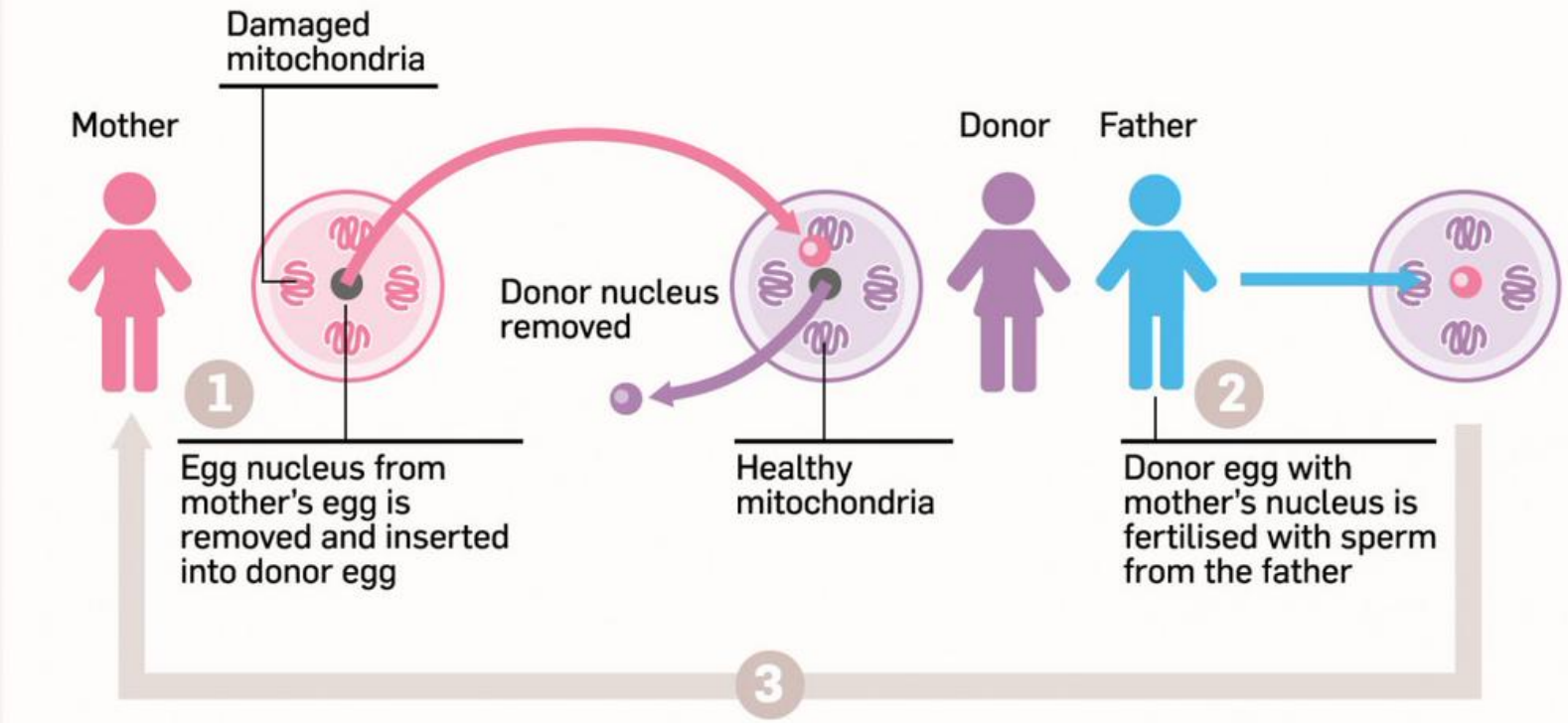
1/5 People

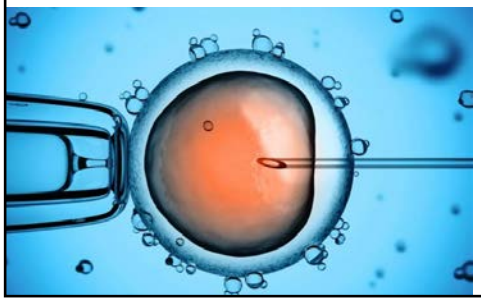
Have Mutations in Some Mitochondrial

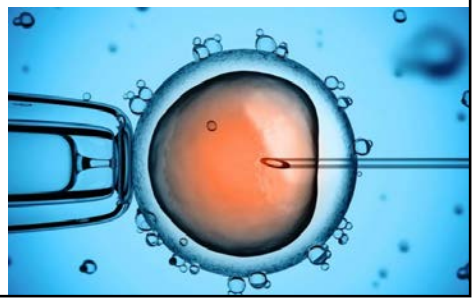
Heteroplasmy



Mitochondrial donation how it works

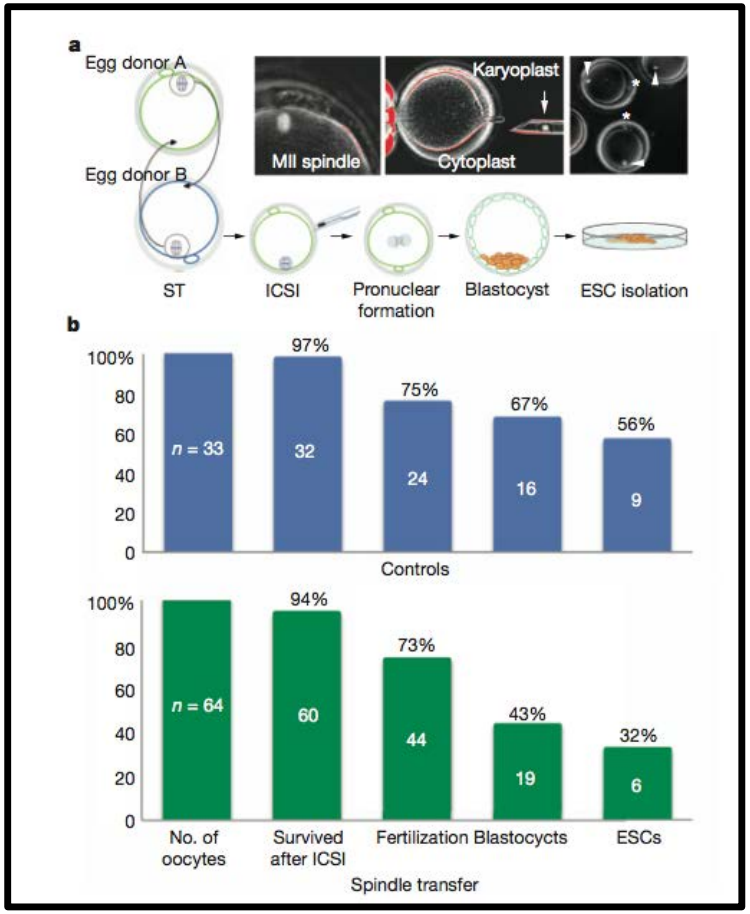






Towards germline gene therapy of inherited mitochondrial diseases

Nature, October, 2012



Using Human Eggs and Embryos

Spindle Transfer Pilot Study Only

Three-Parent Babies: Controversial IVF Procedure To Defeat Genetic Diseases One Step Closer To Being Legalised

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

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

Novel techniques for the prevention of mitochondrial DNA disorders: an ethical review

July, 2013

NUFFIELD COUNCIL ON BIOETHICS

We conclude

Due to the health and social benefits to individuals and families of living free from mitochondrial disorders, and where potential parents express a preference to have genetically-related children, on balance we believe that **if these novel techniques are adequately proven to be acceptably safe and effective as treatments, it would be ethical for families to use them**, if they wish to do so and have been offered an appropriate level of information and support.

Given the above and subject to the appropriate oversight, we believe that **as a research objective it is ethical to gather further information about pronuclear transfer and maternal spindle transfer** in order that they can be considered for treatment use.

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

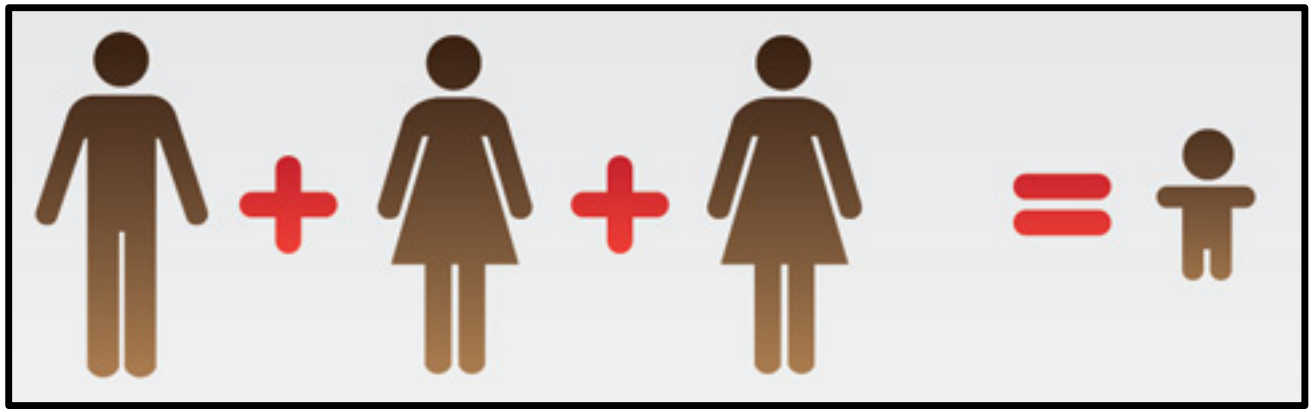
By Carl Engelking | February 3, 2015 1:58 pm

Scientists cheer vote to allow three-person embryos

British decision could be a watershed to approving mitochondrial replacement technique in other countries.

World hails UK vote on three-person embryos

British approval for pioneering fertility technique leads other nations to consider rule changes.



What About The United States?

U.S. Food and Drug Administration
Protecting and Promoting *Your* Health

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Home › Advisory Committees › Advisory Committee Calendar

Advisory Committee Calendar

- 2014 Advisory Committee Tentative Meetings
- 2014 Advisory Committee Calendar
- 2013 Advisory Committee Calendar
- 2012 Advisory Committee Calendar
- 2011 Advisory Committee Calendar
- 2010 Advisory Committee Calendar
- 2009 Advisory Committee Calendar

Resources for You

- 2014 Meeting Materials, Cellular, Tissue and Gene Therapies Advisory Committee
- FR Notice

February 25-26, 2014: Cellular, Tissue, and Gene Therapies Advisory Committee Meeting: Announcement

Center	Date	Time	Location
CBER	February 25, 2014 February 26, 2014	8 a.m. - 5:30 p.m. 8 a.m. - 5 p.m.	Hilton Washington, D.C. North/Gaithersburg, 620 Perry Pkwy., Grand Ballroom, Gaithersburg, MD 20877 (301-977-8900)

Agenda

On February 25, 2014, from 8 a.m. to 5:30 p.m. and on February 26, 2014, from 8 a.m. to approximately 11:15 a.m., the committee will discuss oocyte modification in assisted reproduction for the prevention of transmission of mitochondrial disease or treatment of infertility. On February 26, 2014, from approximately 11:15 a.m. to 11:30 a.m., the committee will hear updates on guidance documents issued from the Office of Cellular, Tissue, and Gene Therapies, Center for Biologics Evaluation and Research (CBER), FDA. On February 26, 2014, from 1 p.m. to approximately 5 p.m., the committee will discuss considerations for the design of early-phase clinical trials of cellular and gene therapy products. CBER published guidance on this topic in July 2013.

Meeting Materials

Materials for this meeting will be available at the Cellular, Tissue, and Gene Therapies Advisory Committee Meeting main page.

Public Participation Information

Interested persons may present data, information, or views, orally or in writing, on issues pending before the committee.

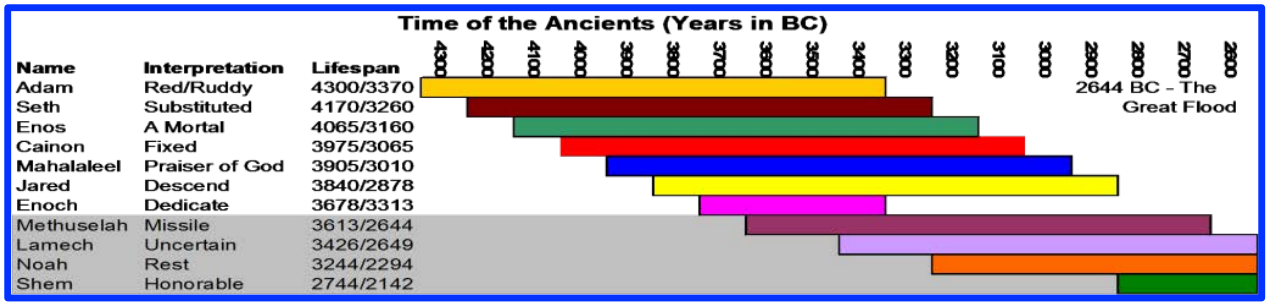
- Written submissions may be made to the contact person on or before February 18, 2014.
- Oral presentations from the public w… heduled between approximately 2:15 p.m. and 3:15 p.m. on February 25, 2014 and between a… 1:45 p.m. and 2:15 p.m. on February 26, 2014. Those individuals interested in making fo… entations should notify the contact person and submit a brief statement of the general nature… r arguments they wish to present, the names and addresses of proposed particip… cation of the approximate time requested to make their presentation on or before Febru… me allotted for each presentation may be limited. If the number of registrants requesting to speak is greater than can be reasonably accommodated during the scheduled open public hearing session, FDA may conduct a lottery to determine the speakers for the scheduled open public hearing session. The contact person will notify interested persons regarding their request to speak by February 11, 2014.
- For those unable to attend in person, the meeting will also be Webcast. The link for the Webcast is available at:
  - February 25, 2014
  - February 26, 2014

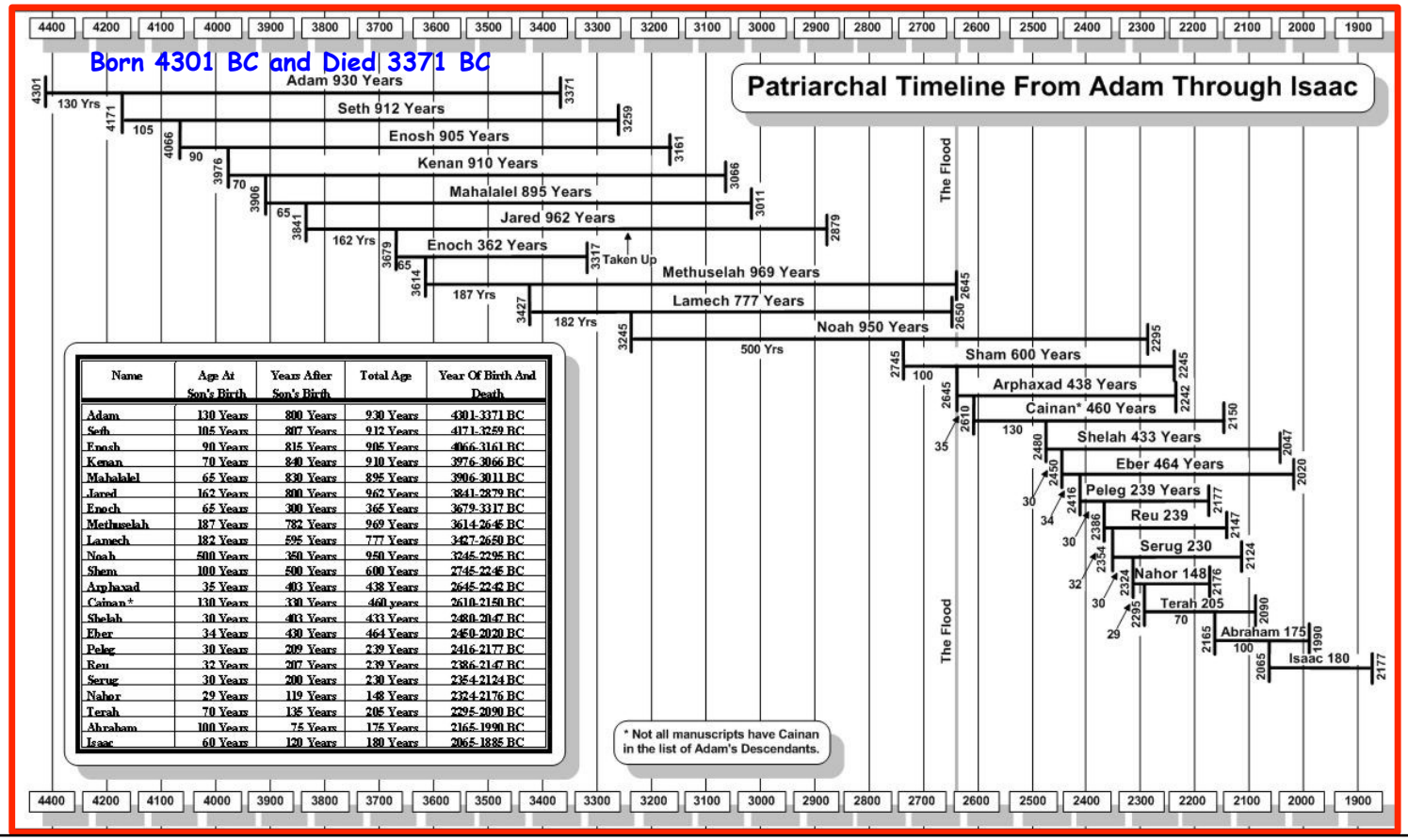
- Focus on All Therapeutics –View MRT as a "drug or biological product"
- National Values - "Moral" Objections to Working on Human Embryos
- Human Embryo Research Controversial and Funding Constrained (no funding for creation of human embryo for research or where human embryo destroyed – Dickey-Wicker Amendment)
- Embryo Research)
- Tangled in Political and Religious Debate Over Abortion
- Minimal Public Consultation

- Focus Specifically on Human Fertility & Reproductive Matters
- Legal in Great Britain to Conduct Research on Human Embryos up to Day 14
- Views MRT as an Extension of Existing and Familiar Technologies (e.g., IVF)
- National Values - No "Moral" Objections to Working on Human Embryos
- Extensive Public Consultation

Science 348,178-180, April 10, 2015

When Did Adam & Eve Live? According to the Book of Genesis ~ 6,000 Years Ago!!





Name	Age At Son's Birth	Years After Son's Birth	Total Age	Year Of Birth And Death
Adam	130 Years	800 Years	930 Years	4301-3371 BC
Seth	105 Years	807 Years	912 Years	4171-3259 BC
Enosh	90 Years	815 Years	905 Years	4066-3161 BC
Kenan	70 Years	840 Years	910 Years	3976-3066 BC
Mahalalel	65 Years	830 Years	895 Years	3906-3011 BC
Jared	162 Years	800 Years	962 Years	3841-2879 BC
Enoch	65 Years	300 Years	365 Years	3679-3317 BC
Methuselah	187 Years	782 Years	969 Years	3614-2645 BC
Lamech	182 Years	595 Years	777 Years	3427-2650 BC
Noah	500 Years	350 Years	950 Years	3245-2295 BC
Shem	100 Years	500 Years	600 Years	2745-2245 BC
Arphaxad	35 Years	403 Years	438 Years	2645-2242 BC
Cainan *	130 Years	330 Years	460 years	2610-2150 BC
Shelah	30 Years	403 Years	433 Years	2480-2047 BC
Eber	34 Years	430 Years	464 Years	2450-2020 BC
Peleg	30 Years	209 Years	239 Years	2416-2177 BC
Reu	32 Years	207 Years	239 Years	2386-2147 BC
Serug	30 Years	200 Years	230 Years	2354-2124 BC
Nahor	29 Years	119 Years	148 Years	2324-2176 BC
Terah	70 Years	135 Years	205 Years	2295-2090 BC
Abraham	100 Years	75 Years	175 Years	2165-1990 BC
Isaac	60 Years	120 Years	180 Years	2065-1885 BC

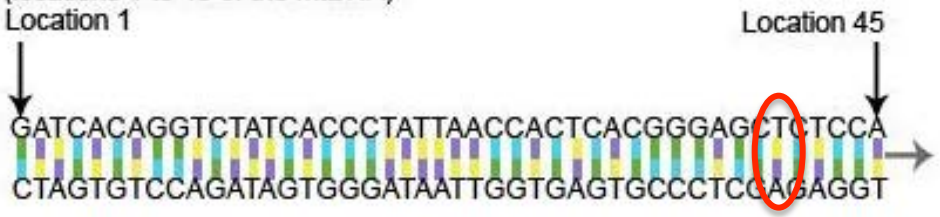
Mitochondrial DNA SNPs in Human Populations

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.

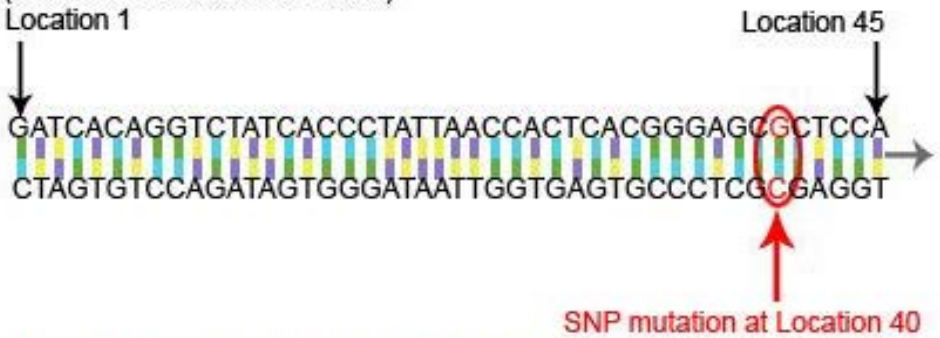
DNA consists of two chains of nucleotides, designated A, C, T, and G. "A" is always linked to "T", and "C" is always linked to "G" on the opposite chain. In this diagram, we will take a closer look at a short segment of mtDNA, namely locations 1 to 45. The unique combination of nucleotides in the chain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

DNA Sequence
(locations 1 to 45 of the mtDNA)



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)



TA to GC SNP
@ NT 45
Becomes a MARKER!

This mutation is documented as follows:

- Location: 40
- Nucleotide Change: T>g (also indicated as T40G)

RFLPs and SNPs Can Be Used to Identify Individuals and Ancestors Using Mitochondrial DNA

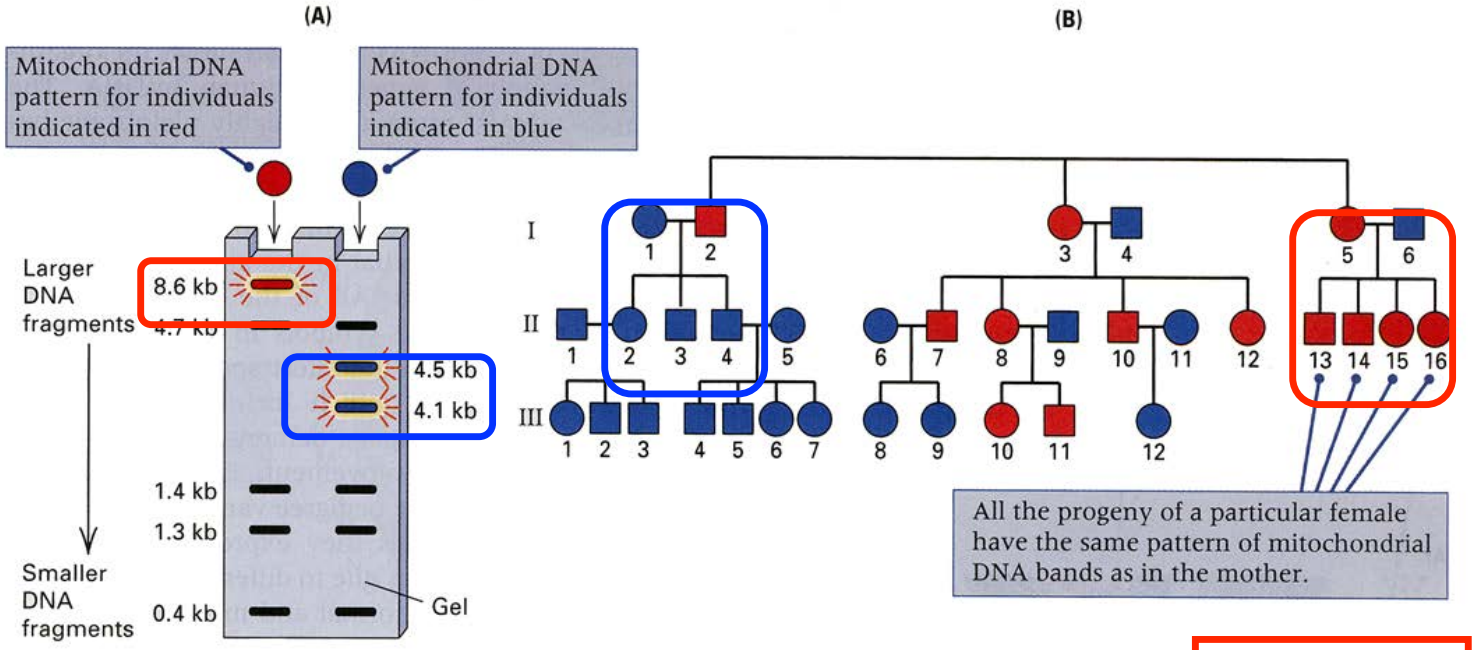
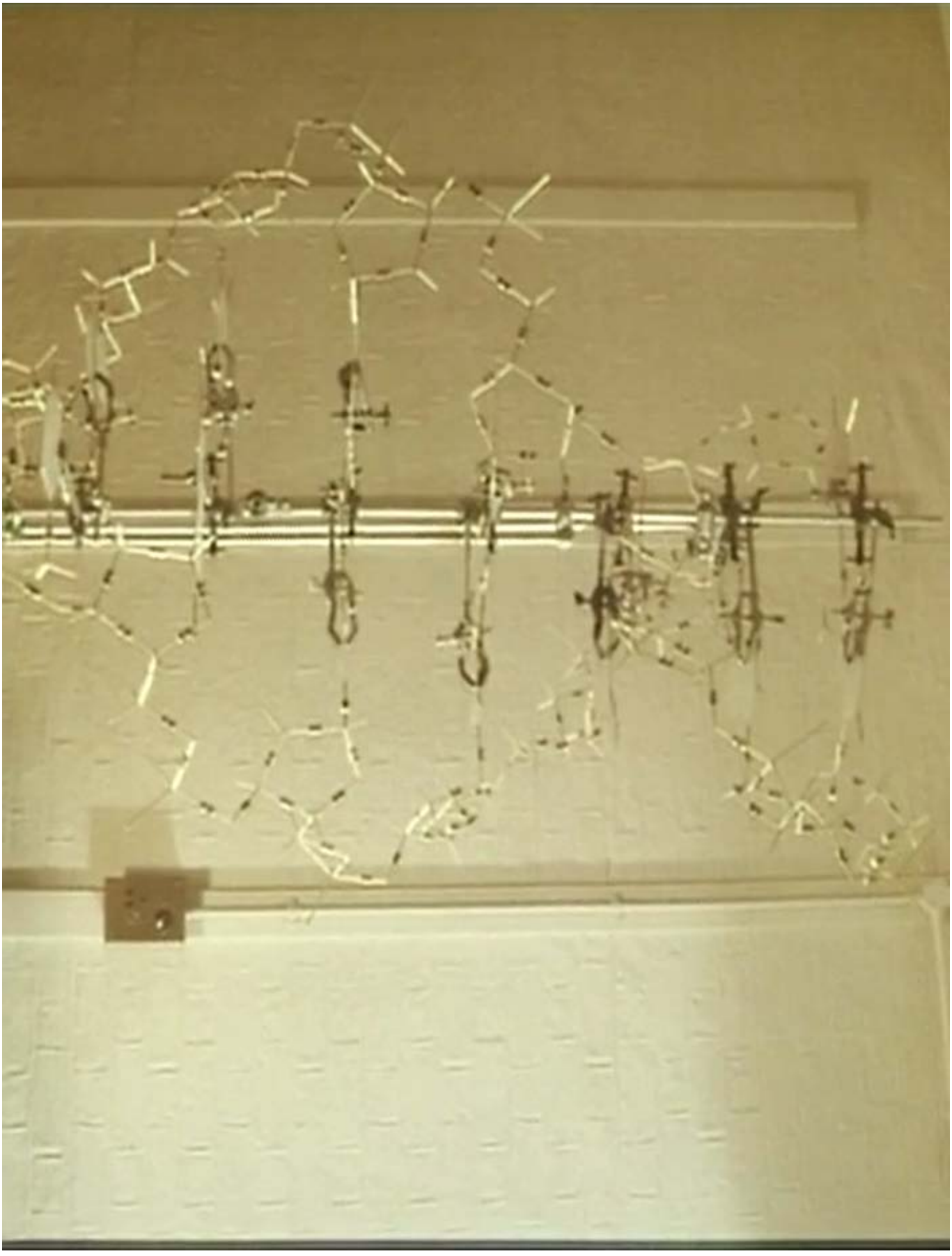


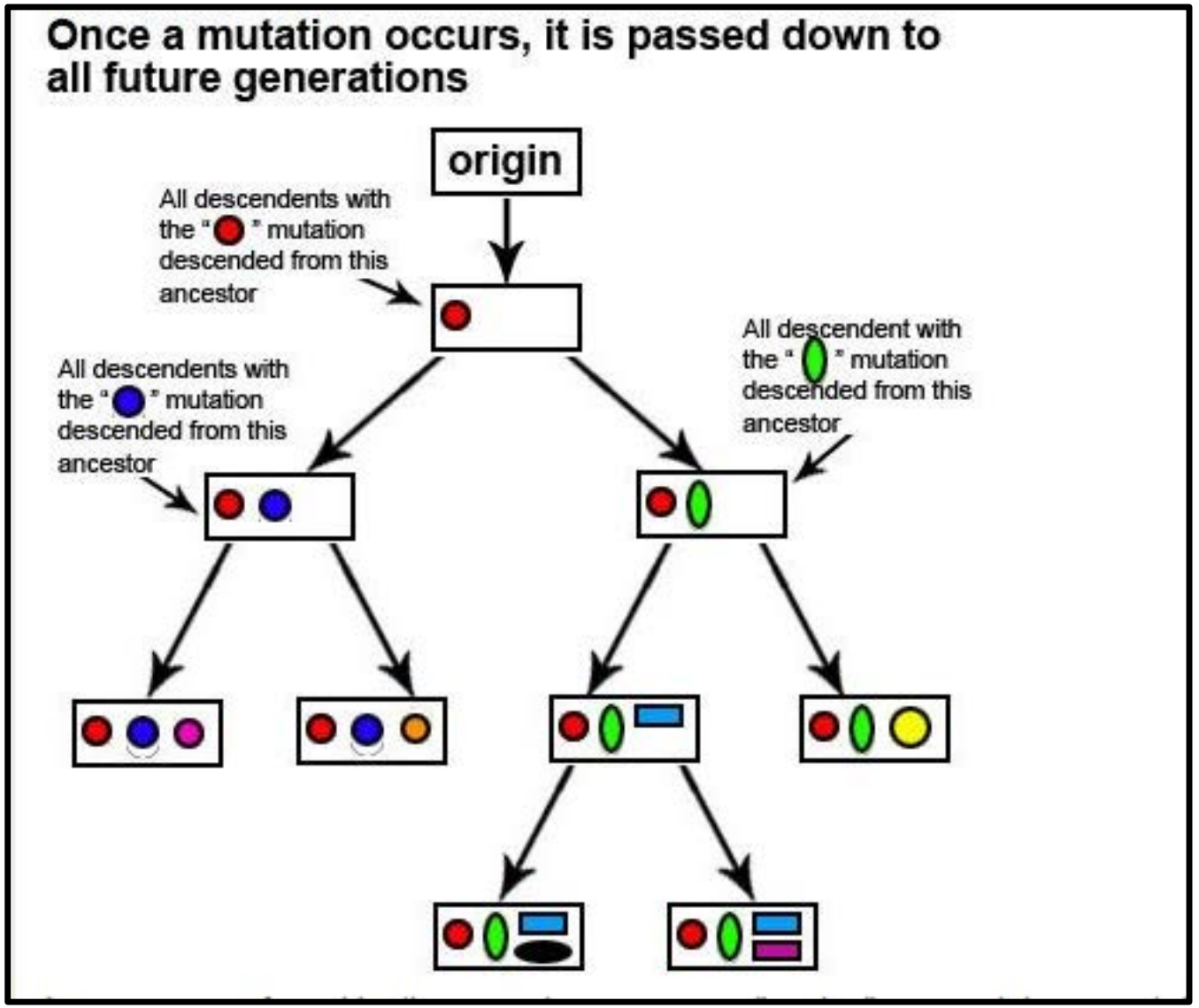
Figure 16.1 Maternal inheritance of human mitochondrial DNA. (A) Pattern of DNA fragments obtained when mitochondrial DNA is digested with the restriction enzyme *Hae*II. The DNA type at the left includes a fragment of 8.6 kb (red). The DNA type at the right contains a cleavage site for *Hae*II within the 8.6-kb fragment, which results in smaller fragments of 4.5 kb and 4.1 kb (blue). (B) Pedigree showing maternal inheritance of the DNA pattern with the 8.6-kb fragment (red symbols). The mitochondrial DNA type is transmitted only through the mother. [After D. C. Wallace. 1989. *Trends in Genetics* 5: 9.]

100% of Children Have 8.6 kb DNA Fragment From Mother

Note How Mitochondrial RFLP Markers Are Inherited !!



How Trace Ancestry Using Mitochondrial DNA SNPs?



How Trace Ancestry Using Mitochondrial DNA SNPs

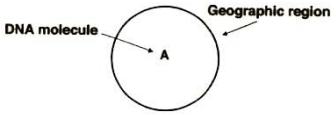
Oldest Populations Contain the Most Diversity

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.

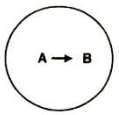
Here's the logic behind the hypothesis.



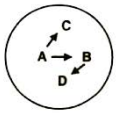
Start with A.

Time

Detected By Using Specific Markers (RFLPs or SNPS)



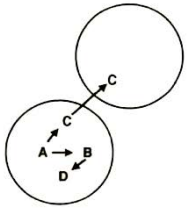
Mutation generates B from A;
now have individuals with both A and B DNAs in population.



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

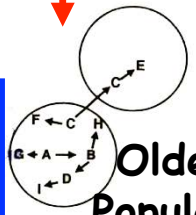
Newest Population

Subset of "Old" Variants + New Variants



C migrates to form separate population.

Lots of "Old" Variants



Oldest Population

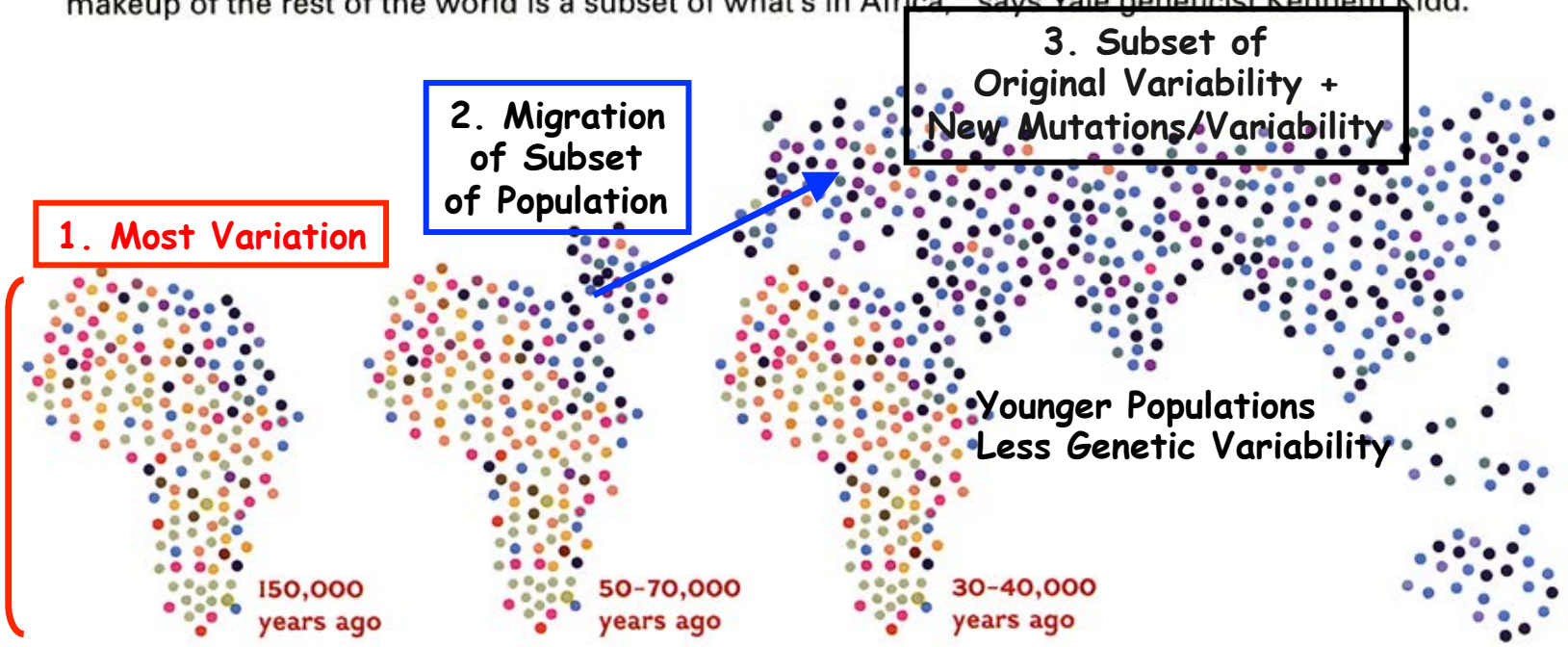
Additional mutations diversify DNAs in populations:
original population more diverse (A, B, C, D, F, G, H, I) than newer population (C, E).

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

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

Diverse From the Start

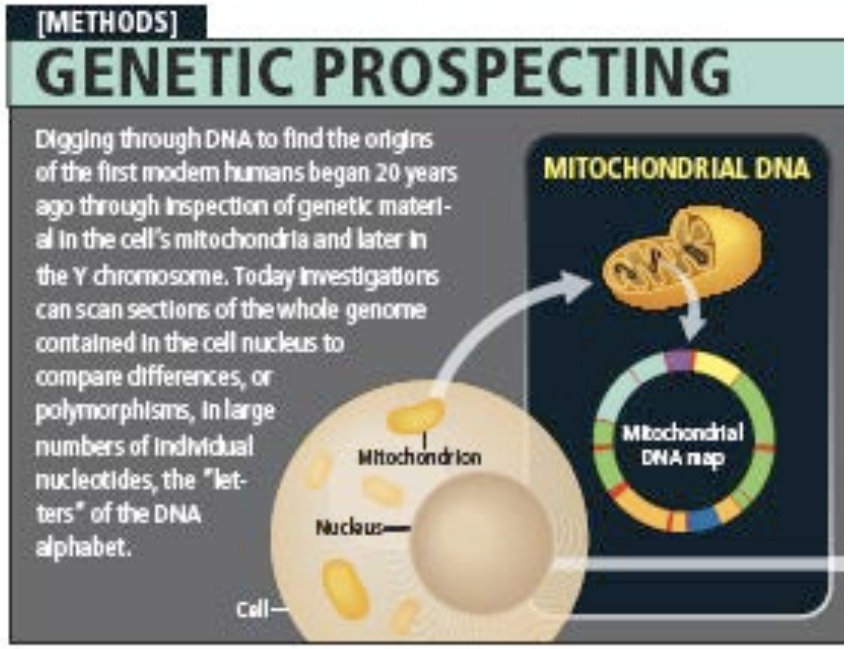
The diversity of genetic markers is greatest in Africa (multicolored dots in map), indicating it was the earliest home of modern humans. Only a handful of people, carrying a few of the markers, walked out of Africa (center) and, over tens of thousands of years, seeded other lands (right). "The genetic makeup of the rest of the world is a subset of what's in Africa," says Yale geneticist Kenneth Kidd.

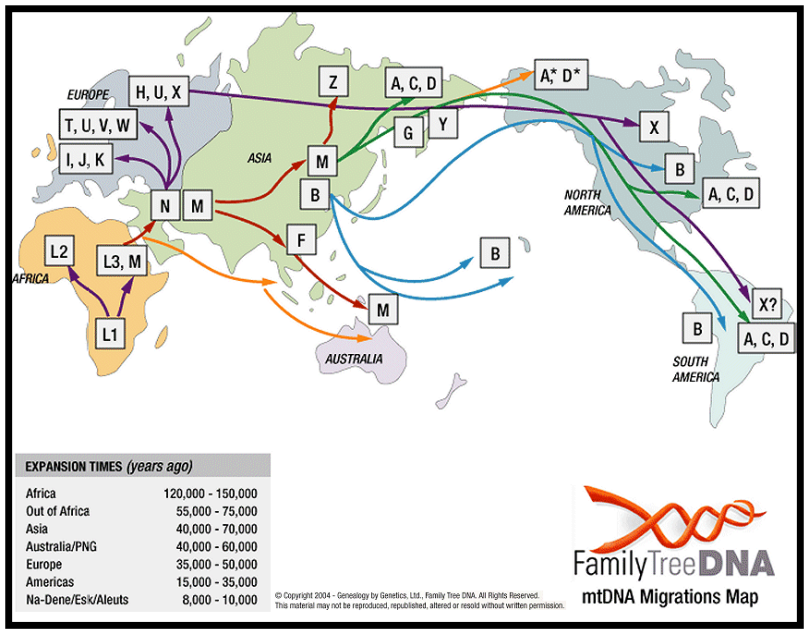


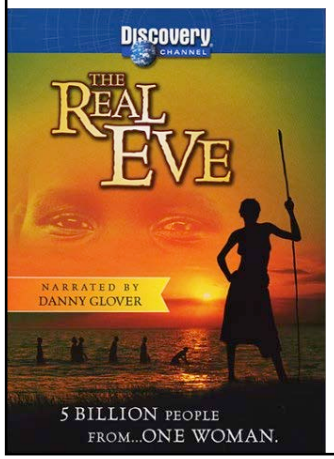
Genetic Variation Proportional to Population Age

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

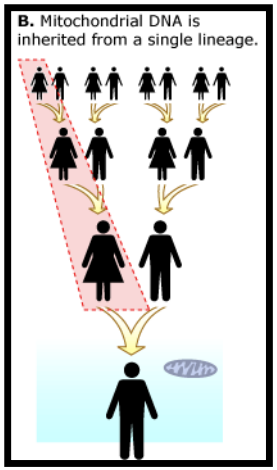
Tracing Human Populations Using Mitochondrial DNA Polymorphisms (SNPs) - Back to Eve!



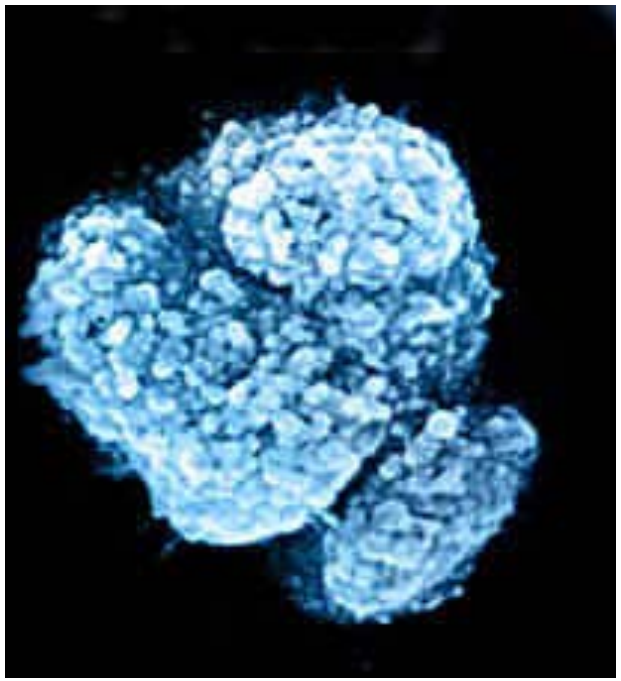


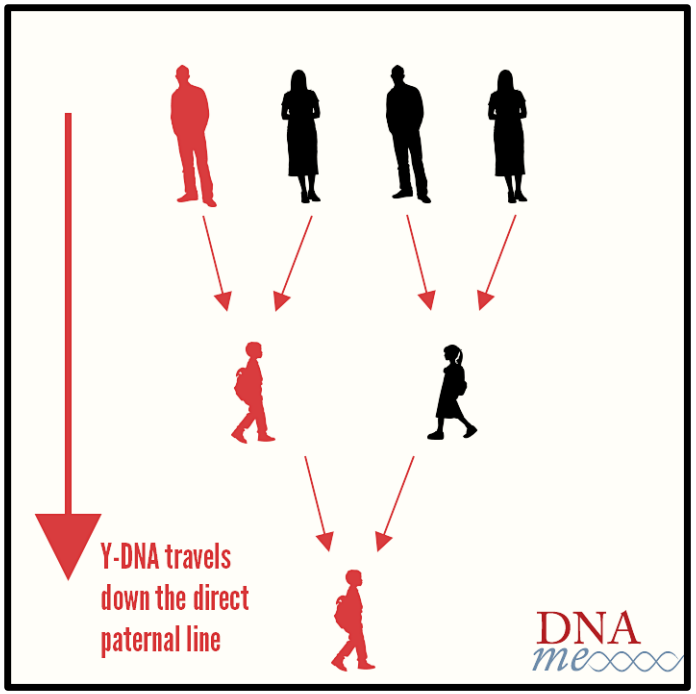


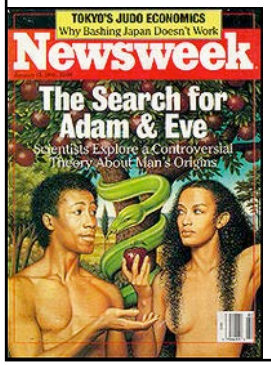
Eve Lived ~200,000 Years Ago!!



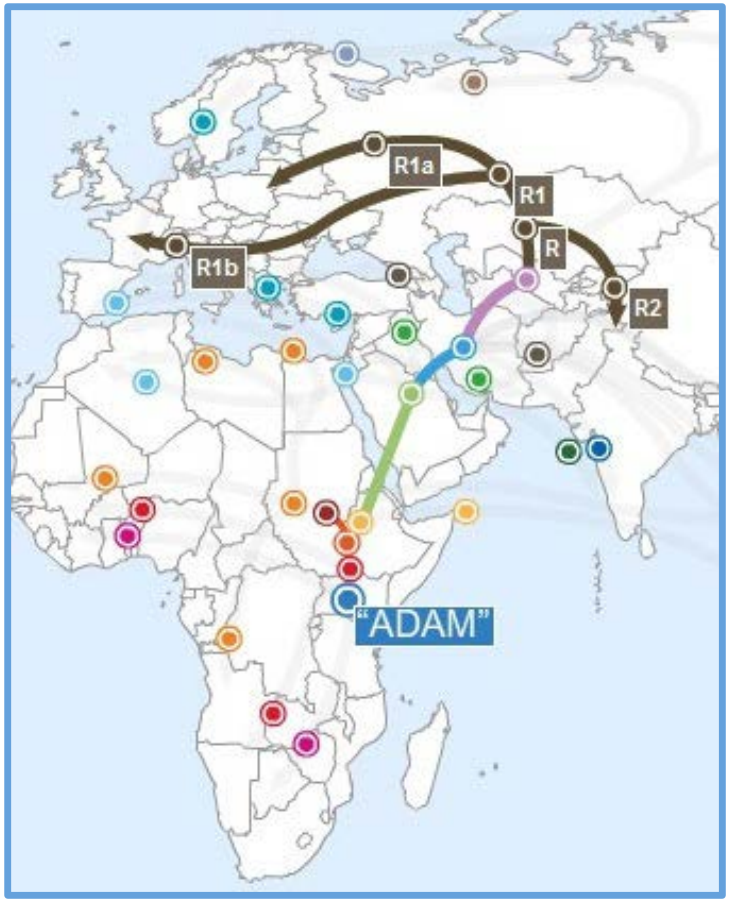
When Did Adam Live?
Tracing Human Populations Using Y DNA Polymorphisms







Adam Also Lived
~200,000
Years Ago!



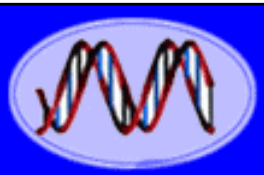
Ancient ancestry: **The Artisans**
Haplogroup: **R1b1a2a1a1a4**

You belong to haplogroup R1b, The Artisans, who first arrived in Europe from west Asia about 35,000- 40,000 years ago at the dawning of the Aurignacian culture. This cultural was remarkable for its subtle yet significant technological progress, like the shift from random flint collection to the...
Learn more

CDYa	CDYb	DYS19a	DYS385a	DYS385b	DYS388	DYS389I	DYS389II	DYS390	DYS391
37	40	14	11	14	12	13	29	23	11

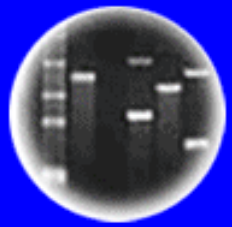
DYS392	DYS393	DYS395S1a	DYS395S1b	DYS406S1	DYS413a	DYS413b	DYS425	DYS426	DYS436
13	13	15	16	10	23	23	12	12	12

DYS437	DYS438	DYS439	DYS442	DYS444	DYS446	DYS447	DYS448	DYS449	DYS450
15	12	11	17	13	13	25	19	28	8



DNA
Genetic Code of Life

Entire Genetic Code
of a Bacteria

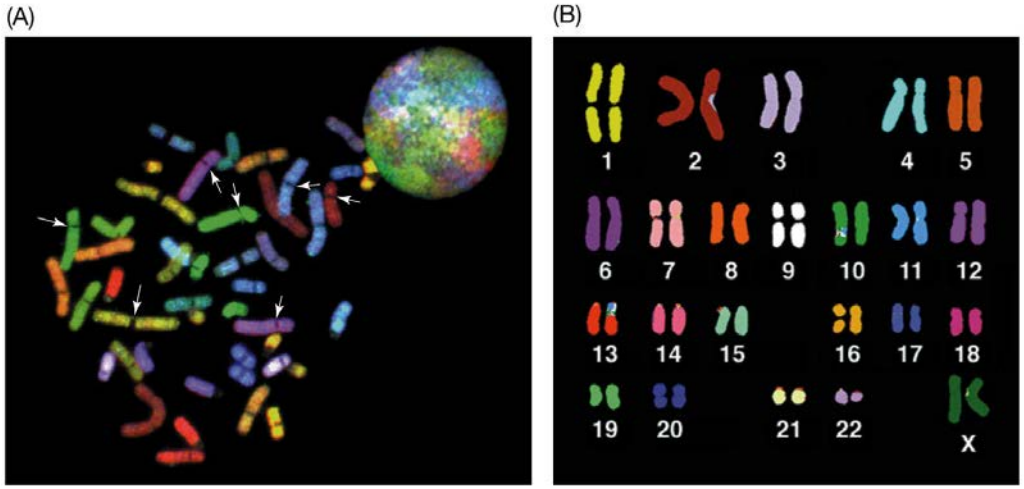


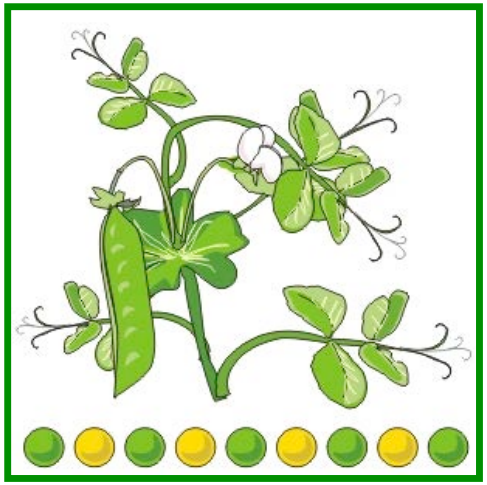
DNA Fingerprinting

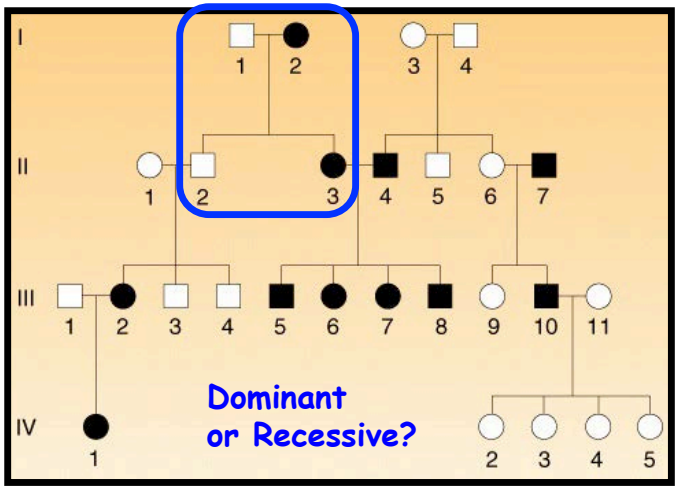
Cloning: Ethical Issues
and Future Consequences

Plants of Tomorrow

The Nuclear Genome

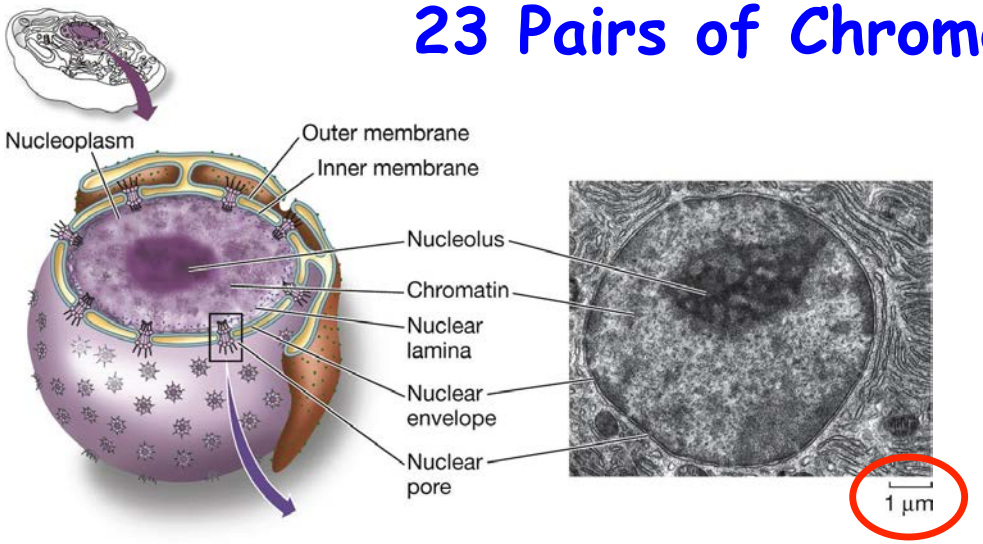






Note: Gene is Inherited in a Mendelian Pattern

The Nucleus Is A Complex Organelle With 23 Pairs of Chromosomes (Humans)



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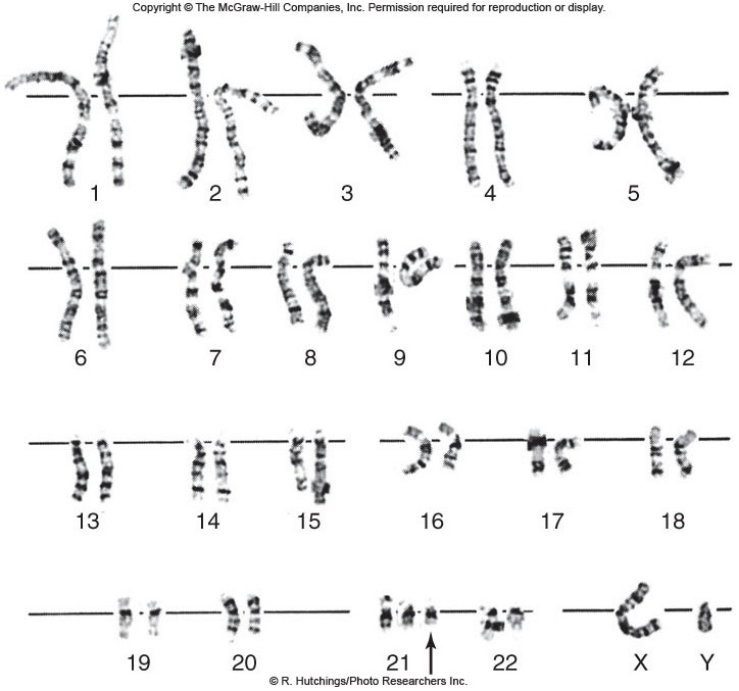

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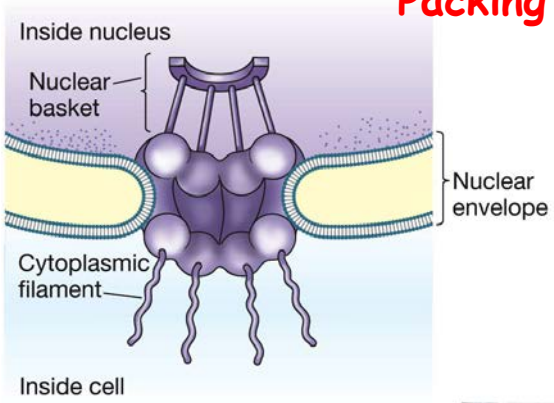
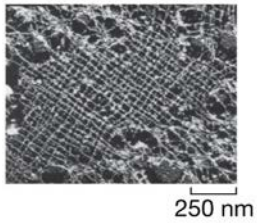
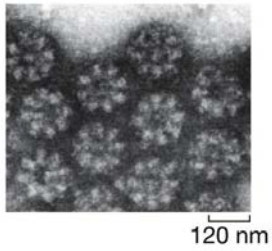
Packing Problem?





RNA & Protein Transport



LIFE 8e, Figure 4.8 (Part 2)

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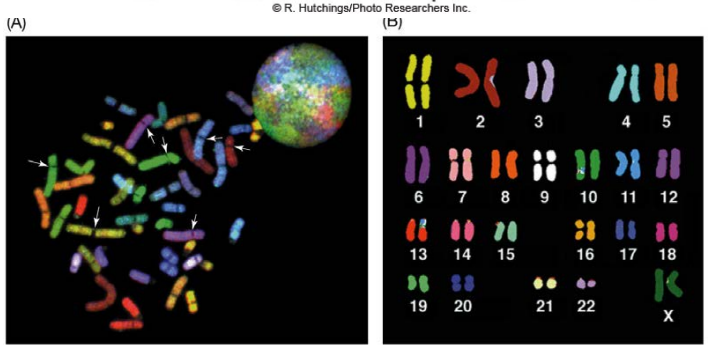
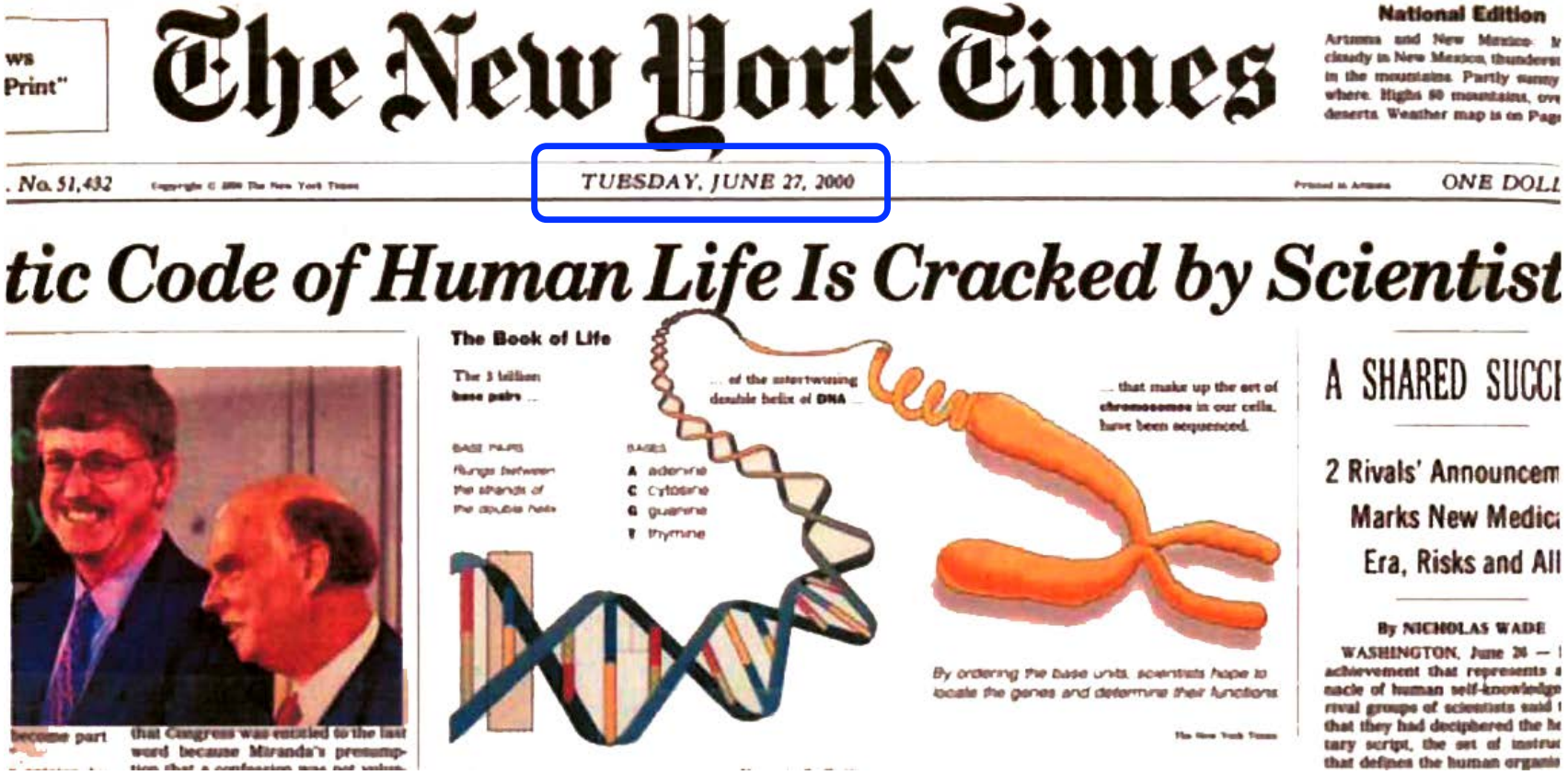


The Human Genome End to End is 1.1 Meters in Length!!!!!!

Note: Chromosome Sizes & Bands = Markers

The Human Genome Was Sequenced Fifteen Years Ago!

The Human Genome Project



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Print"

The New York Times

National Edition

. No. 51,432 TUESDAY, JUNE 27, 2000 ONE DOLL

tic Code of Human Life Is Cracked by Scientist

The Book of Life

... that make up the set of chromosomes in our cells, have been sequenced.

By ordering the base units, scientists hope to locate the genes and determine their functions.

A SHARED SUCCI

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

By NICHOLAS WADE

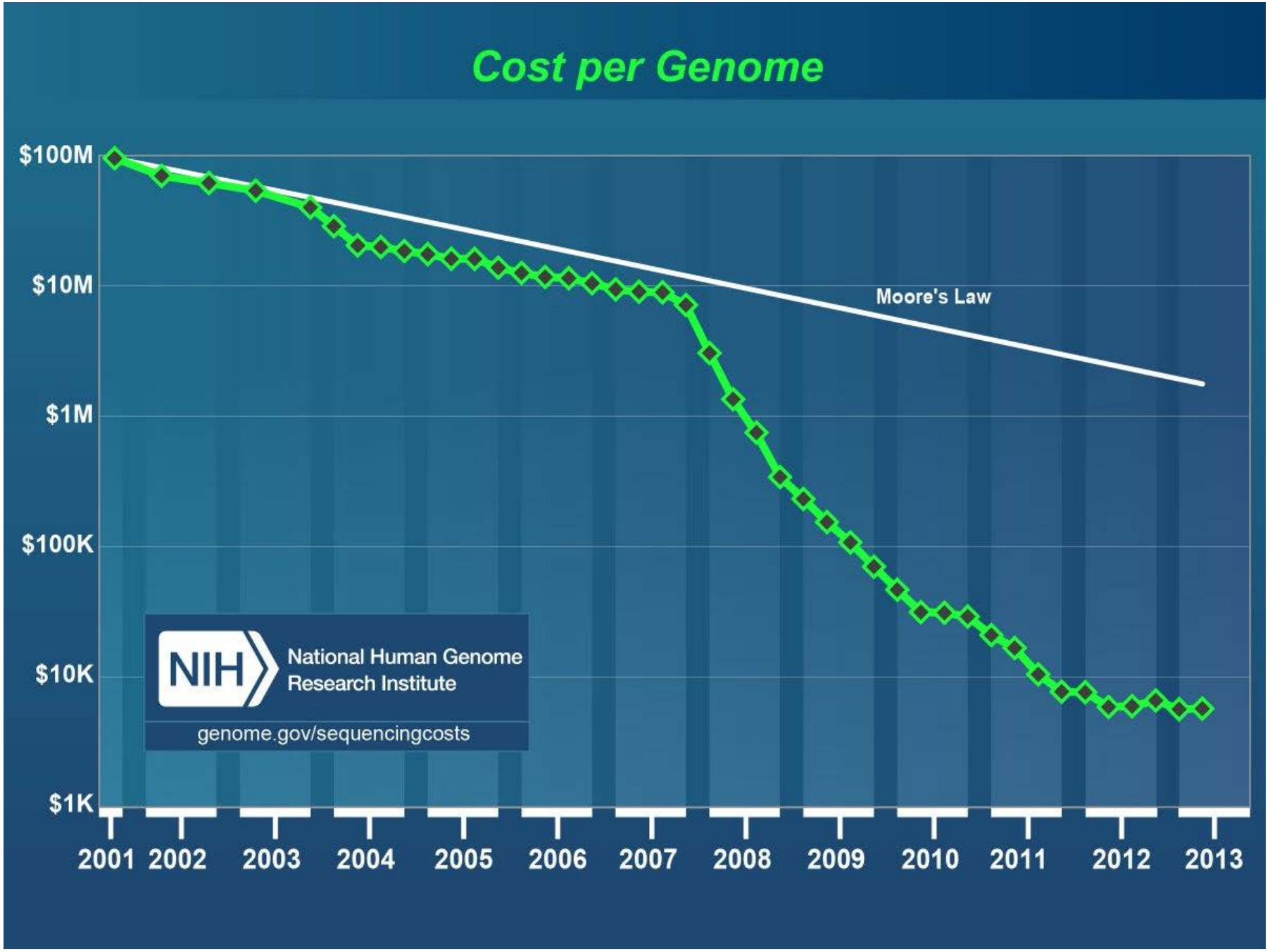
WASHINGTON, June 26 —

become part

that Congress was entitled to the last word because Miranda's presump-

Public & Private Effort Using Different Strategies - A Race!

3 Billion Dollars & Took 15 Years


Cost per Genome
$100M
$10M
$1M
$100K
$10K
$1K
Moore's Law
NIH
National Human Genome Research Institute
genome.gov/sequencingcosts
2001
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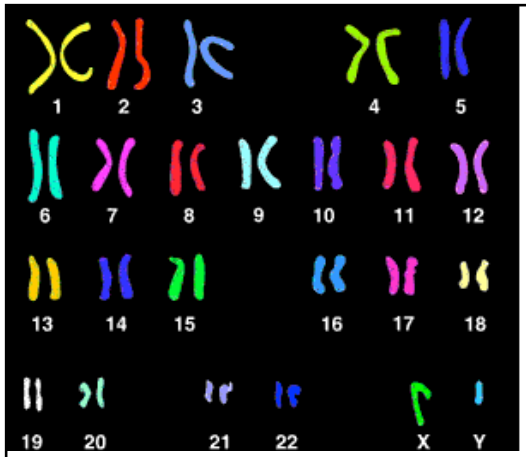
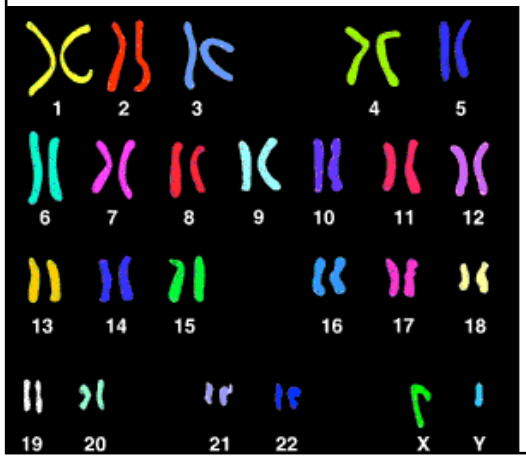


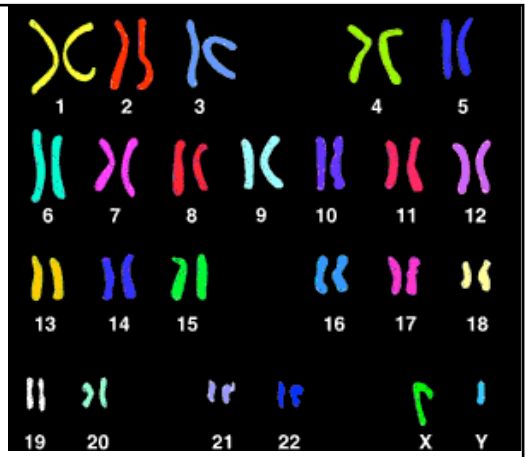
The Human Genome

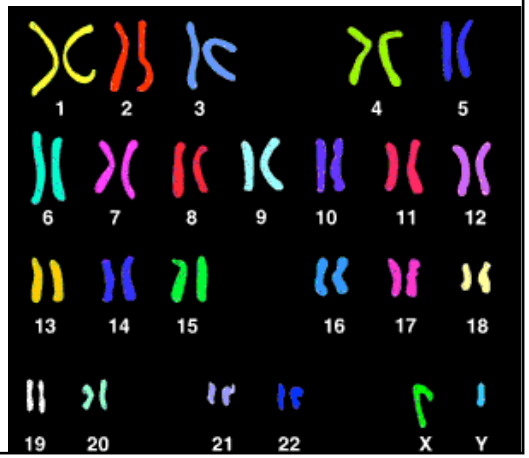
Large

Small

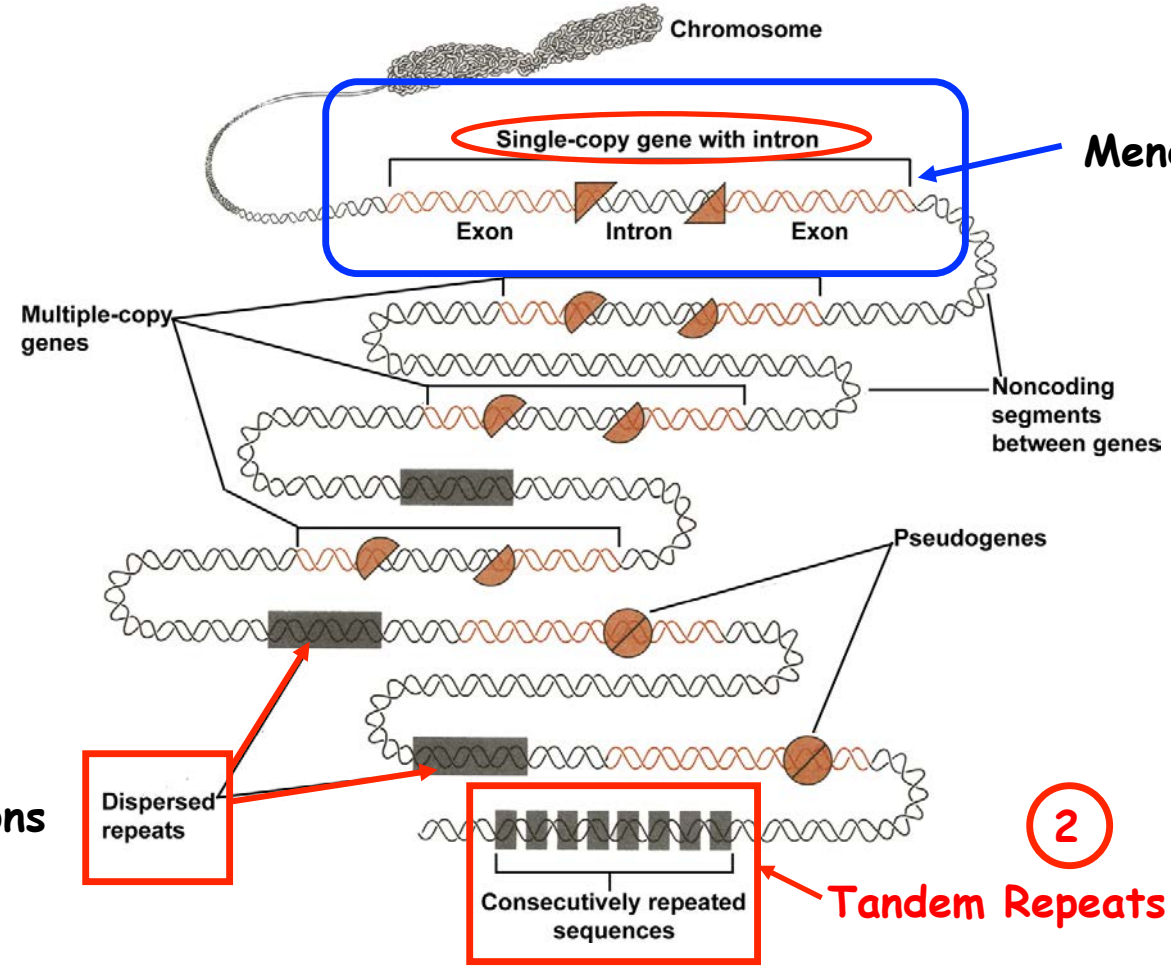
Chromosome	Including gaps	Sequenced	Gaps
1	247,249,719	224,999,719	22,250,000
2	242,951,149	237,712,649	5,238,500
3	199,501,827	194,704,827	4,797,000
4	191,273,063	187,297,063	3,976,000
5	180,857,866	177,702,766	3,155,100
6	170,899,992	167,273,992	3,626,000
7	158,821,424	154,952,424	3,869,000
8	146,274,826	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**







The Human Genome Landscape



1

Mendelian Gene

Transposons

2

Tandem Repeats (VNTR)

Tandem Repeats or VNTRs are Useful for DNA Fingerprinting Studies!

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

Only A Small Fraction of the Human Genome Encodes Proteins

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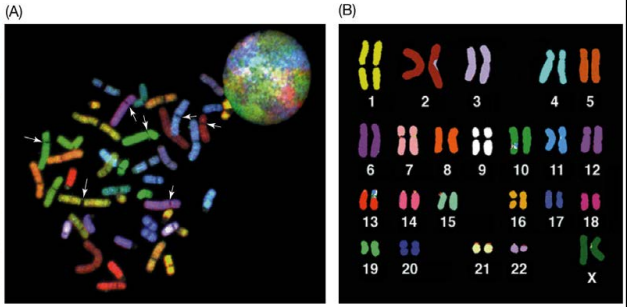
TABLE 18.1 Classes of DNA Sequences Found in the Human Genome

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



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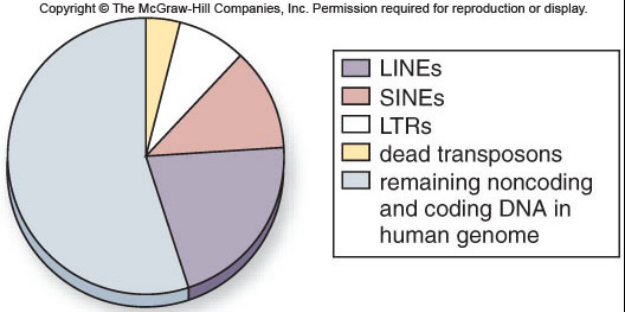
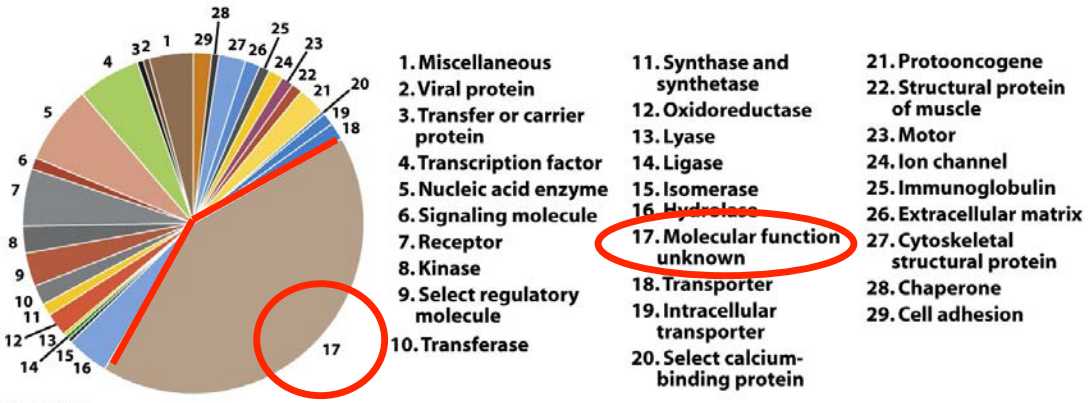


Table 20.6 Average characteristics of genes in the human genome

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

Table 20-6

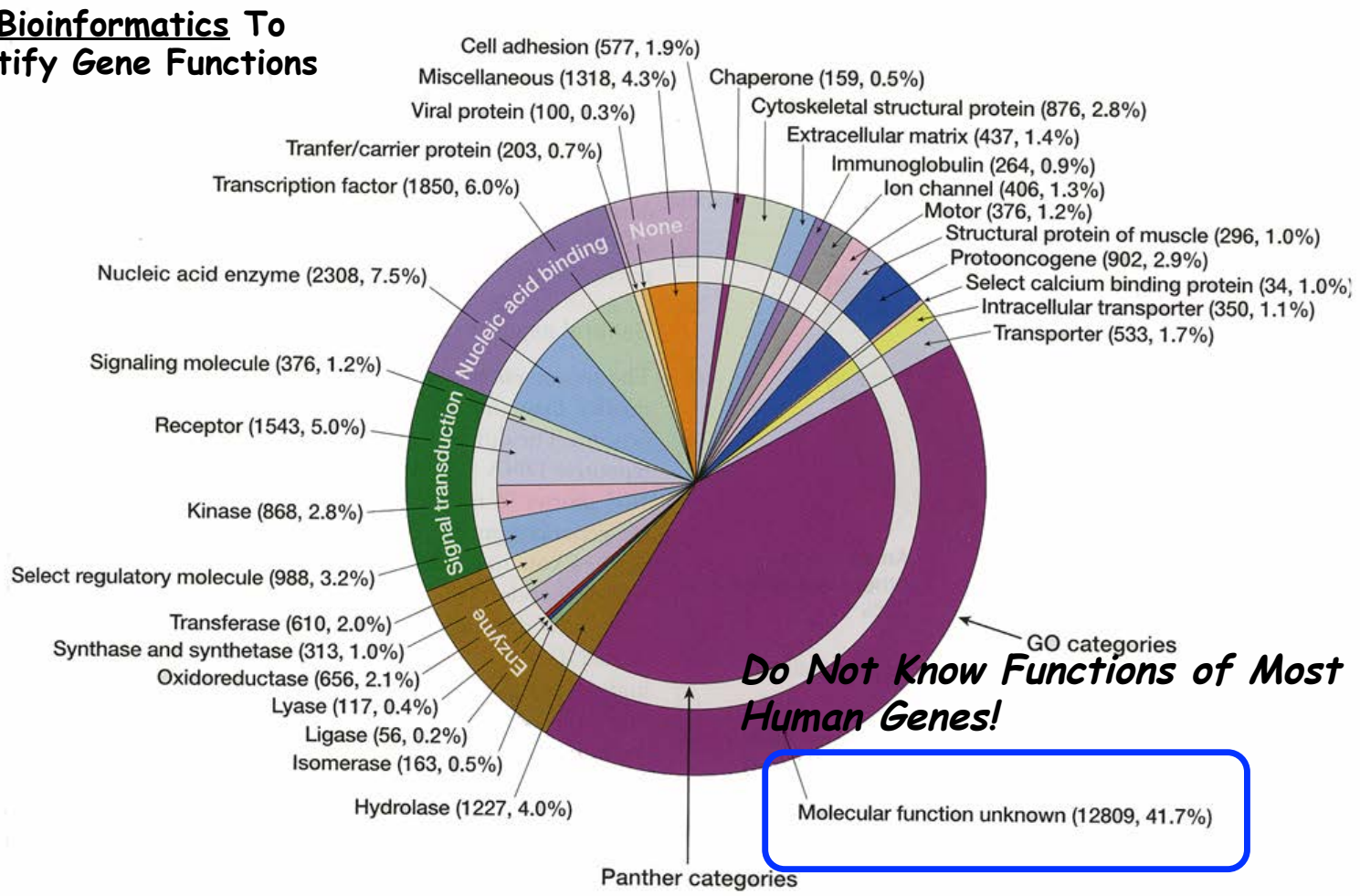
The Human Genome Has DNA Sequences Present Once As Well as Repeated Many Times



Human Genes are Large but Contain Mostly Introns

The Human Genome Contains ~25,000 Different Genes

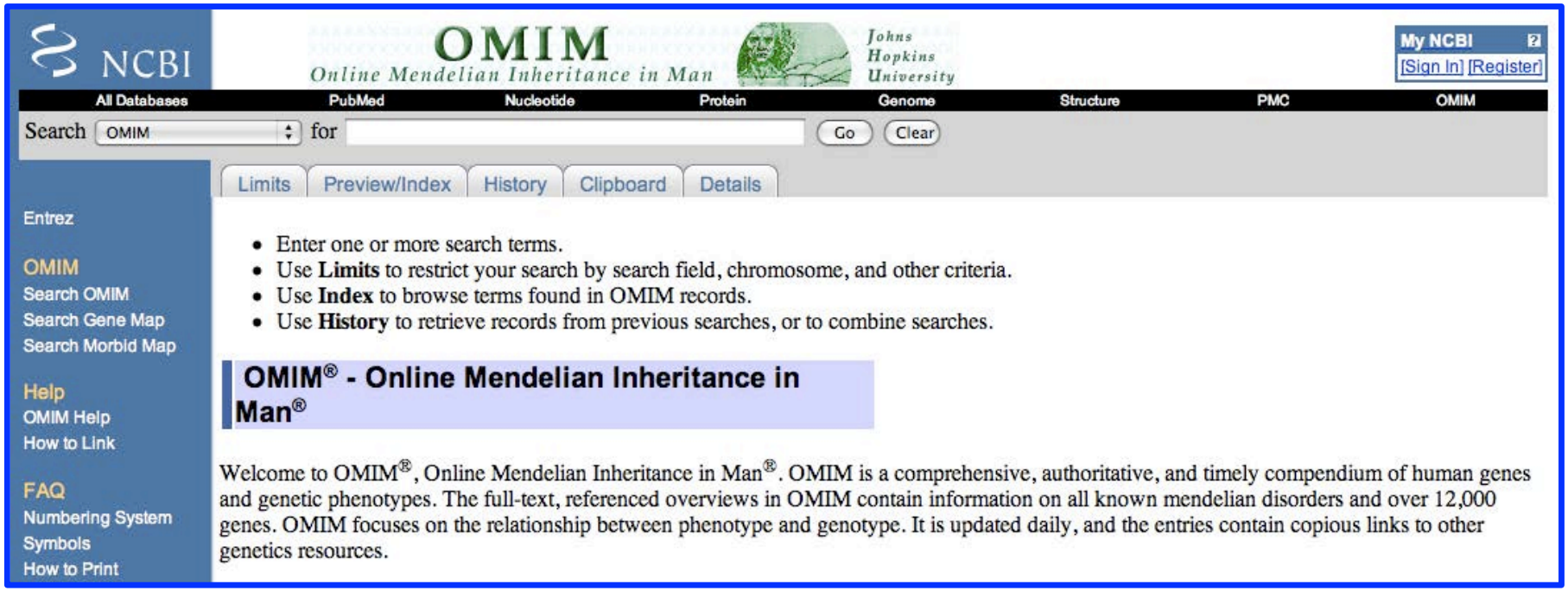
Use Bioinformatics To Identify Gene Functions



Do Not Know Functions of Most Human Genes!

How Many Encoded Proteins? Alternative Splicing?

How Many Human Disease Genes Have Been Identified?

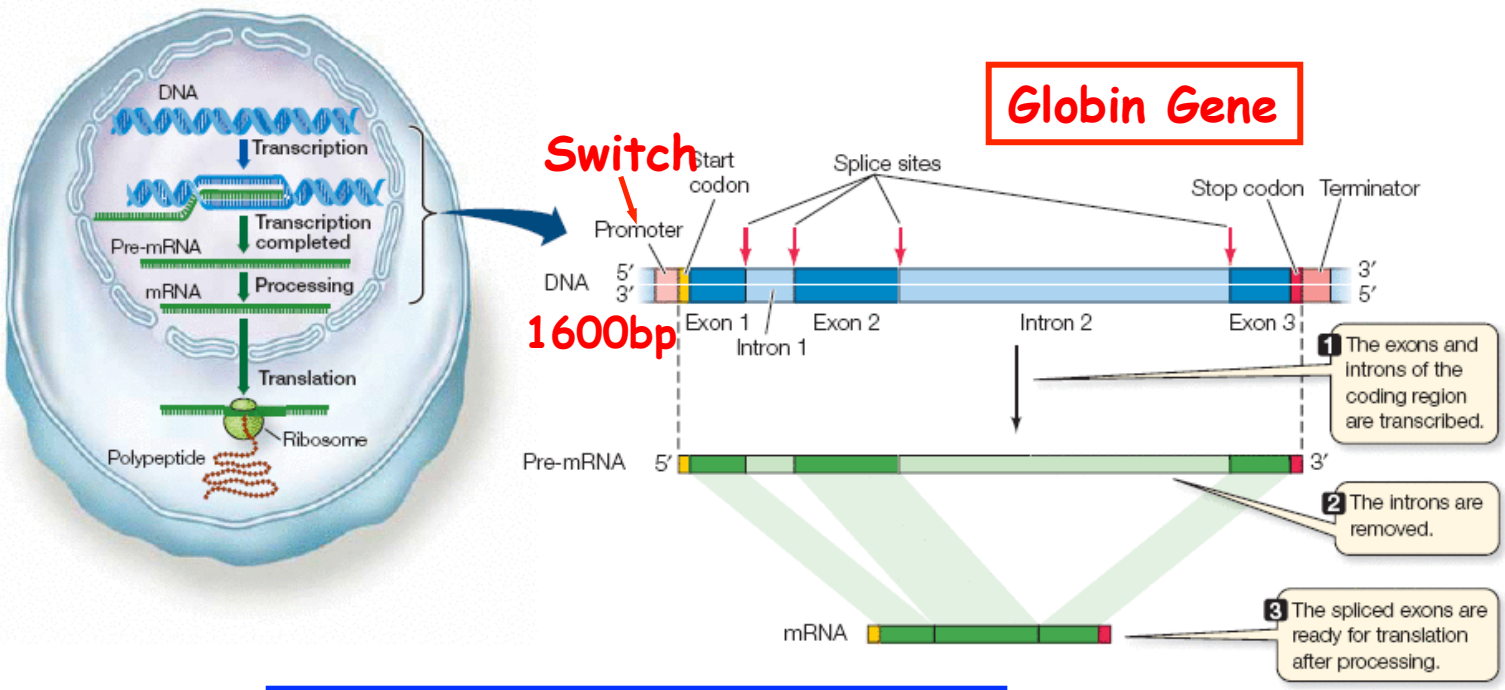


There are ~25,000 Genes in The Human Genome

1. ~4034 Genes Correlate With a Disease Phenotype
2. The Molecular Basis of These Genetic Diseases Are Known (e.g., Sickle Cell Anemia, Hemophilia A)
3. ~1717 Disease Genes – Molecular Basis Unknown

OMIM 2/13/14

RNA Splicing- Removing Non-Coding Sequences From Primary Transcripts & Generating Functional mRNAs



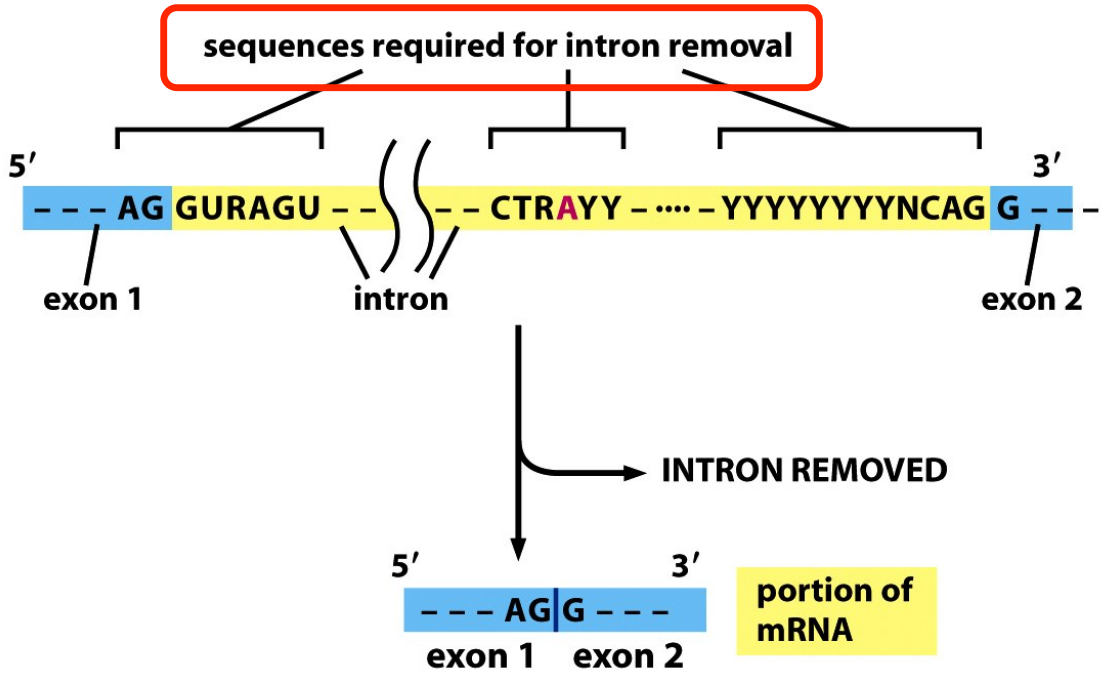
Mutations→ Blood Disorders
Where can these occur?

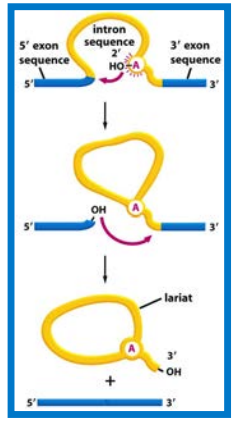
Mutations Can Occur in Coding Region, Switch, & RNA Splice Sites

→ Mutant Phenotype

Implications For Engineering Eukaryotic Gene in Bacterial Cell For Expression?

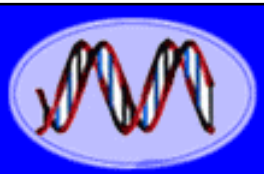
Yo! It's In The Sequences!





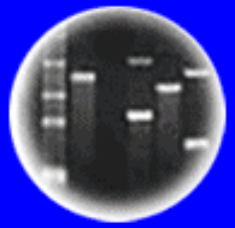
Specific Sequences Required For RNA Splicing!

What Happens If These Sequences Are Mutated in a Gene?



DNA
Genetic Code of Life

Entire Genetic Code
of a Bacteria



DNA Fingerprinting

Cloning: Ethical Issues
and Future Consequences

Plants of Tomorrow

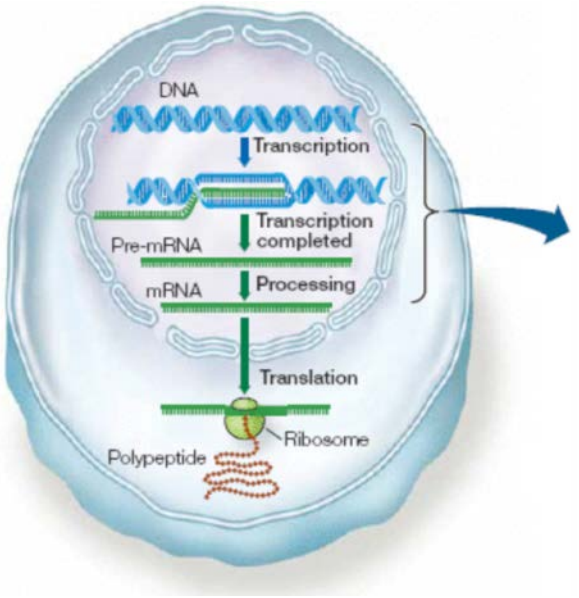
Implications For "Yo - Its in The DNA!!"

Modular Organization of Sequences

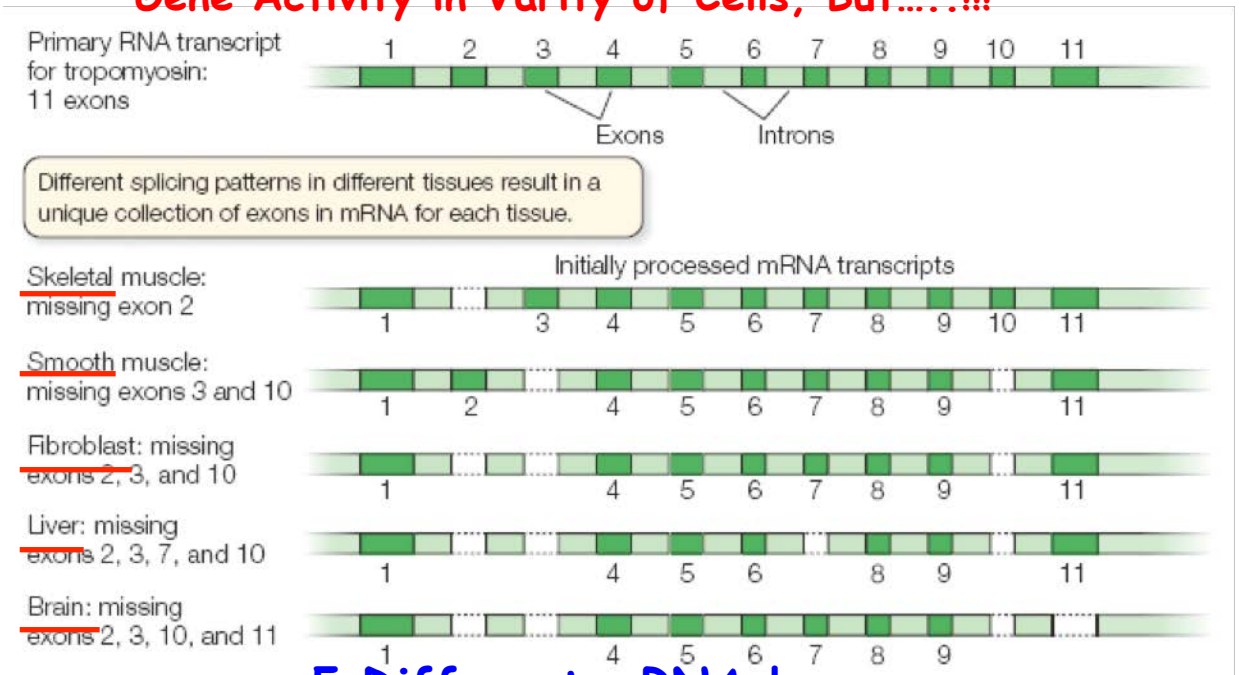
1. DNA Replication
   - Ori
2. Transcription
   - Switch/Regulator
   - Terminator
3. Processing of RNA (Eukaryotes)
   - Splicing Sites
4. Translation
   - Start
   - Stop
   - Genetic Code/Codons
5. Coding Sequence
   - Genetic Code

Modules → Anything You Want To Do Using Genetic Engineering!

Alternative Splicing- One Gene → Several mRNAs & Proteins



Gene Activity in Varity of Cells, But…..!!!



5 Different mRNAs!

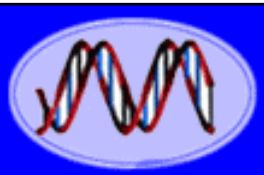
Different mRNA = Different Proteins = Different Functions!

Implication- Human Genome Has Only 25,000 Genes But Can Give Rise to Many More Proteins which Are Responsible For Producing the Phenotype

95% of Human Mutiexonic Genes Are Alternatively Spliced

Reason Why Human Genome Can Contain Same Number of Genes as Fly and Plant Genomes!!

Implications for Genetic Engineering? Use Specific cDNA!



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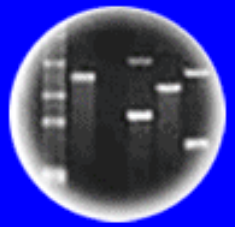

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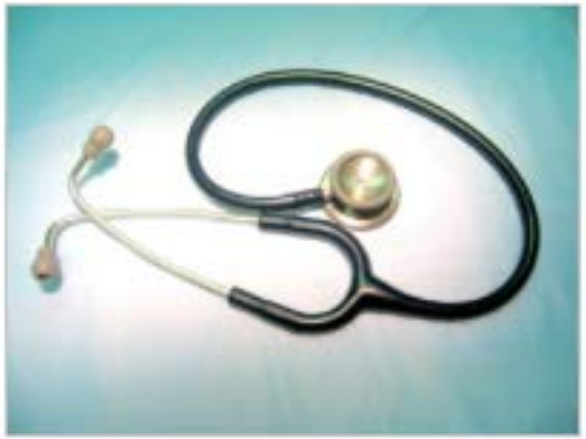
Mutations in Splicing Sequences Can Cause Human Diseases

Alternative Splicing and Disease

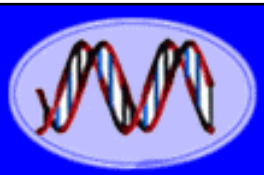


More than two thirds of the human protein-coding genes undergo alternative splicing, thus changes and misregulation of this mechanism can have severe effects and cause diseases.

About 15% of mutations connected with disease affect splicing.

Mutations completely impeding the splicing event cause severe disease patterns due to the lack of the correct gene product.

Mutations disturbing regulatory pathways lead to the appearance of misspliced gene products causing milder but more varied courses of disease.



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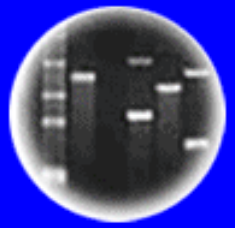

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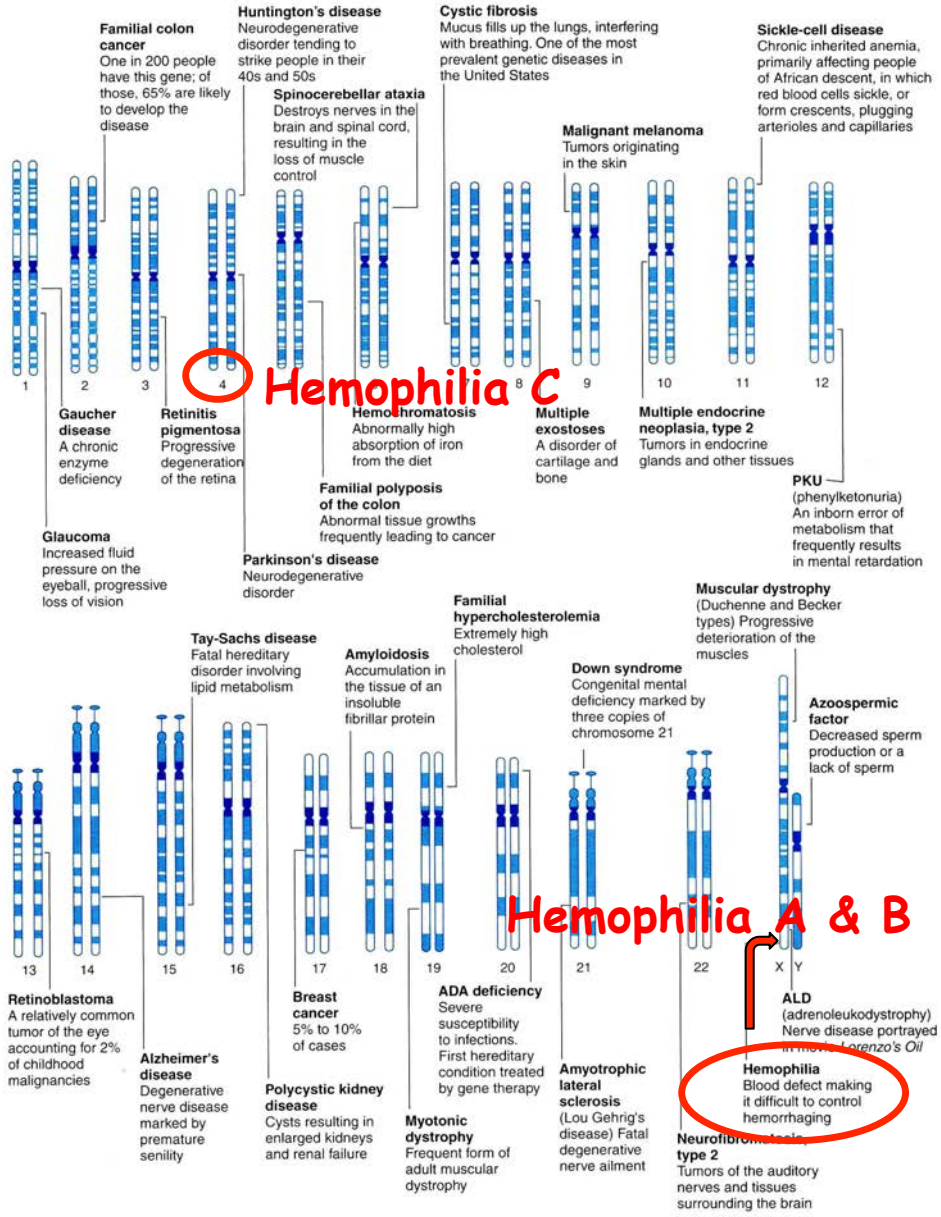
Human Disease Genes Are Present on All Chromosomes

Can Be Caused By Mutations in ANY of the "Legos!"



Structure, function and diversity of the healthy human microbiome

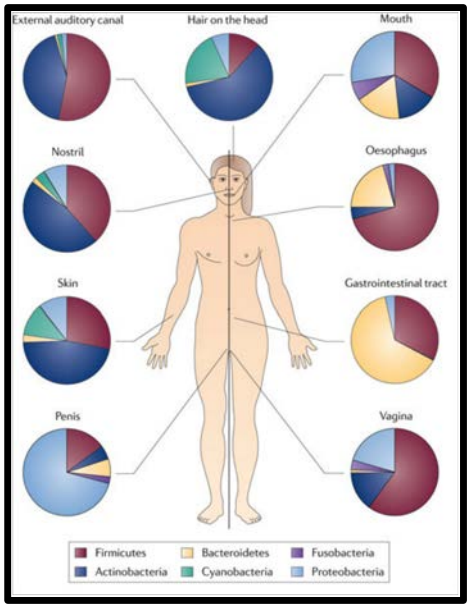
Microbe census maps out human body's bacteria, viruses, other bugs

It gives scientists a reference point of what the microbial community looks like in healthy people, and they plan to use it to study how changes in a person's microbiome can lead to illness.

By Rosie Mestel, Los Angeles Times

5:20 PM PDT, June 13, 2012

The Human Microbiome Project



Now that they have a picture of what a healthy microbiome looks like, scientists say they can use it as a reference point to compare with the microscopic life inside those who are sick, and probe whether changes in their microbial communities could be contributing to their illnesses.

Already, studies have linked microbial conditions to forms of inflammatory bowel disease such as ulcerative colitis and Crohn's disease. But there are suggestions that our flora may be involved in many more disorders, such as diabetes, psoriasis, asthma, heart disease, rheumatoid arthritis, obesity and colorectal cancer.

In time, researchers hope to develop therapies to put a perturbed or just plain broken microbiome back to rights. They might feed a person corrective bacteria, for example, or the type of food that would encourage the right microbes to grow.

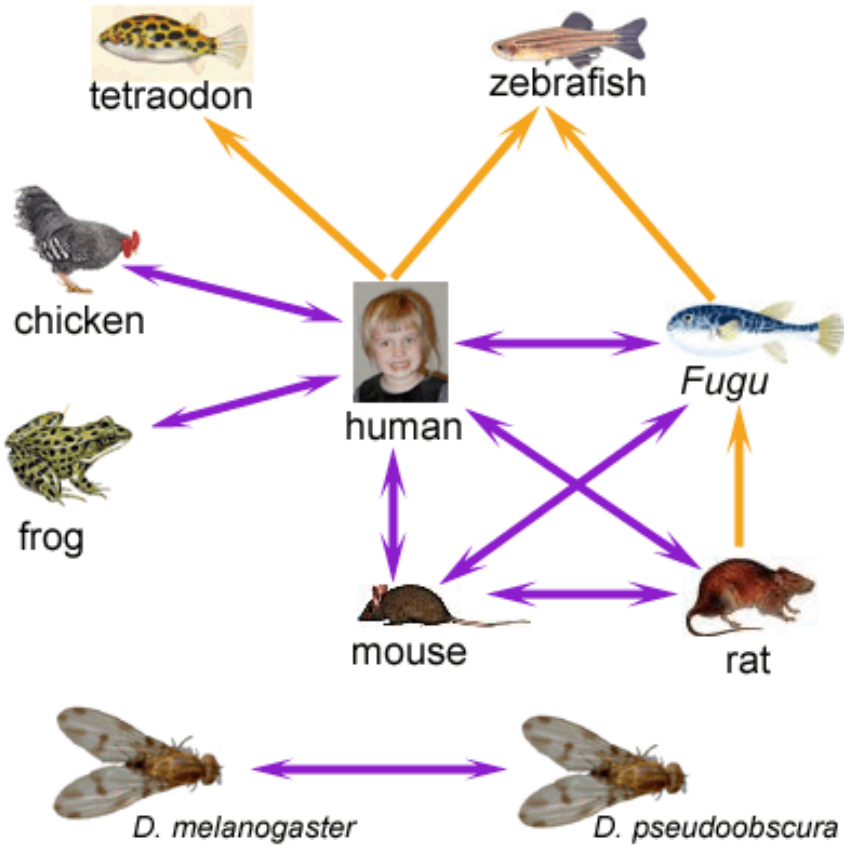
In one small but dramatic example of what might one day be routine, Finnish researchers reported in March that patients with recurring *Clostridium difficile* infections recovered after fresh fecal material from healthy donors was transplanted into their guts.

Despite the current preoccupation with probiotics as cure-alls, scientists say they have a long way to go before they truly know how to design such therapies.

The emerging appreciation for bacteria raises important questions about whether overuse of antibiotics is contributing to disease, said Dr. David A. Relman, a microbiologist and infectious-disease clinician at the Stanford University School of Medicine, who wrote a commentary that accompanies the Nature papers. For instance, *C. difficile* infections can occur when antibiotic treatments kill off normal gut flora and permit the dangerous bacteria to flourish.

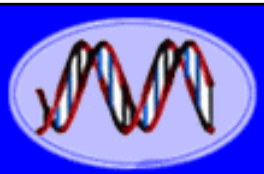
The Genomes of Many Organisms Have Been Sequenced Providing New Knowledge About Our Origins and Cellular Functions

The Future is Unlimited!



183 Eukaryotic &
3,950 Prokaryotic
Genomes Have Been
Sequenced as of 2013
&
17,500 Genome Projects
Ongoing!
http://www.genomesonline.org/cgi-bin/GOLD/bin/gold.cgi

Providing Thousands of New Genes and Proteins To Be Engineered For Practical Applications (e.g., cellulases in termite gut bacteria for biofuel production)



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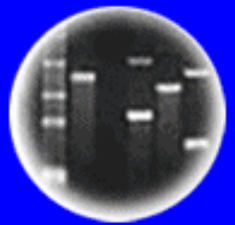

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A New Comparative Genomics Field Has Emerged Allowing the Comparison of Entire Genomes!

Comparison of Mammalian Genomes Attempts To Determine "What Makes a Man, a Man and a Mouse a Mouse"

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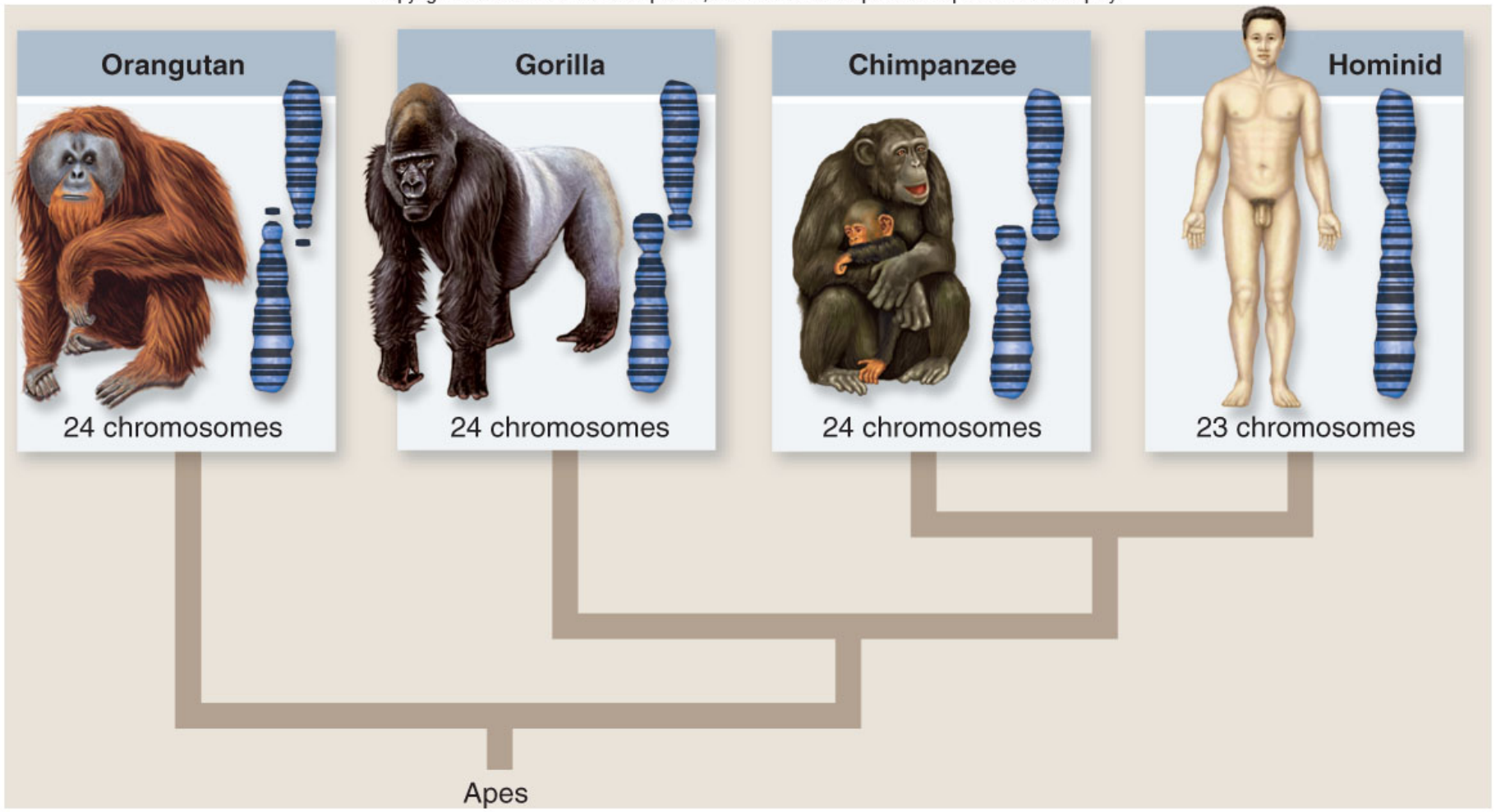
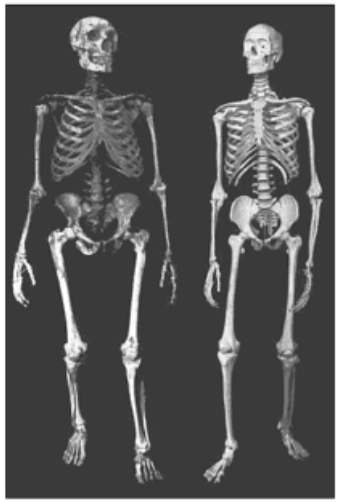
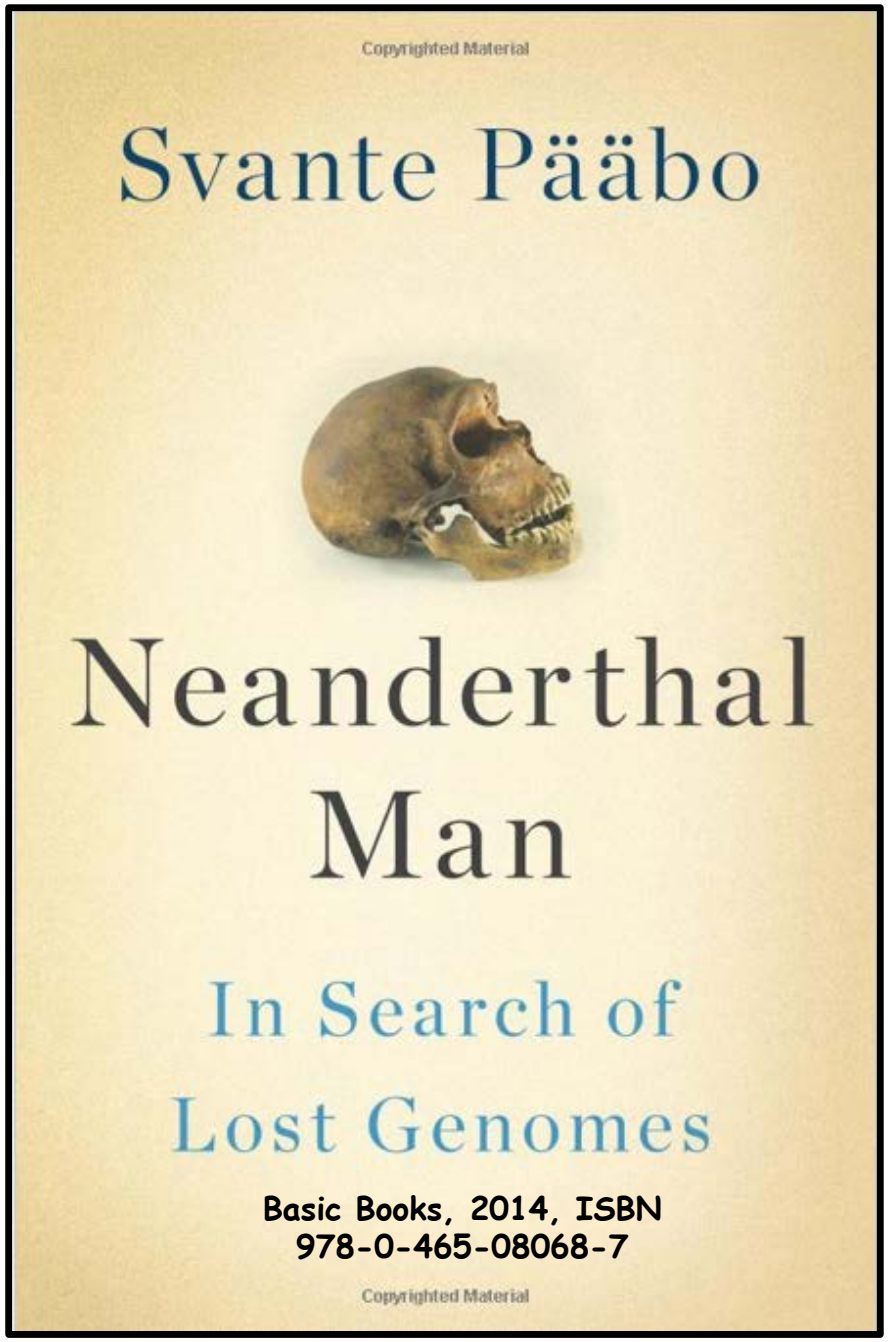
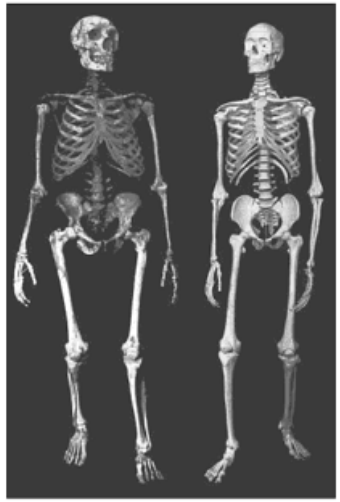


There is <1% Difference Between Human & Chimpanzee DNAs!





Using DNA to Unravel Our Human Heritage



RESEARCH ARTICLE

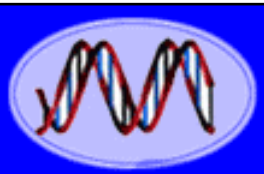
Science, May 7, 2010 (328, 710-722)

A Draft Sequence of the Neandertal Genome

From a 45,000 Year-Old Bone

Reconstruction by Kennis & Kennis / Photograph by Joe McNally

For the first time, a Neanderthal female peers from the past in a reconstruction informed by both fossil anatomy and ancient DNA. At least some of her kind carried a gene for red hair and pale skin.



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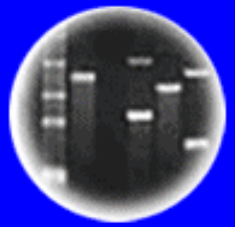

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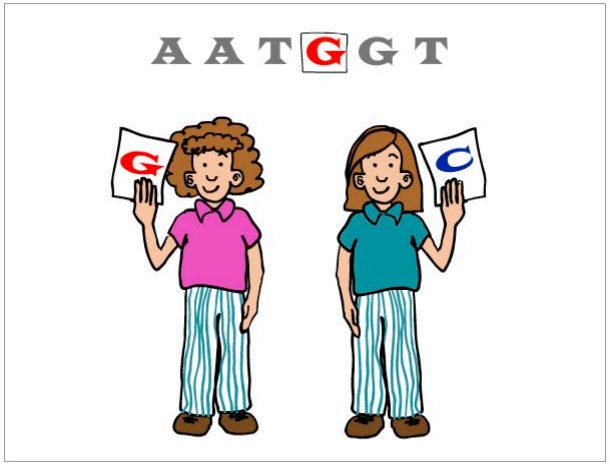
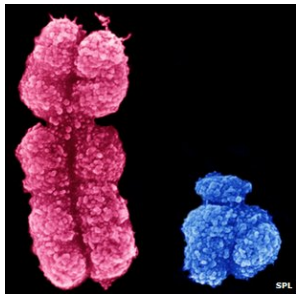
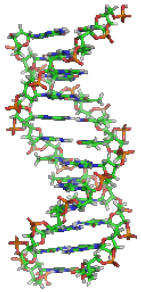
DNA Sequences Can Be Used To Specify Eye Color…..



…As Well As Gender





Yo……..It's In the DNA!

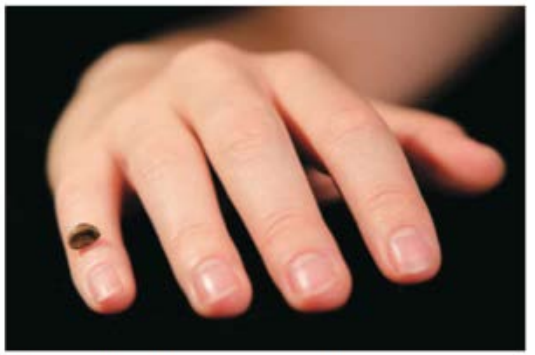
Science, October 12, 2012 (338,222-226)

ANCIENT DNA

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

COMPLETE DNA Sequence From 40,000 Year Old Fossil DNA With Accuracy of Sequencing Our Own Genome!!

Had 23 Chromosomes Like "Us" and Split From Human Line Between 150k and 700k Years Ago



Slice of life. This replica of a tiny finger bone from Denisova Cave (*right*) yielded an entire genome.

New DNA Analysis Shows Ancient Humans Interbred with Denisovans

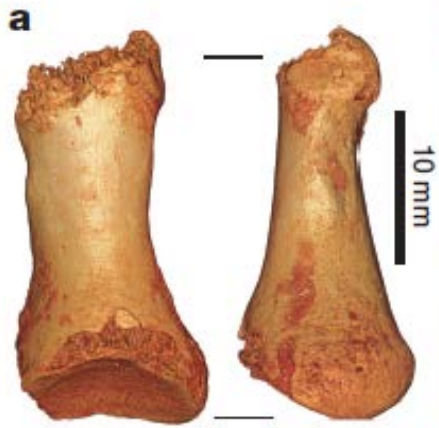
A new high-coverage DNA sequencing method reconstructs the full genome of Denisovans--relatives to both Neandertals and humans--from genetic fragments in a single finger bone

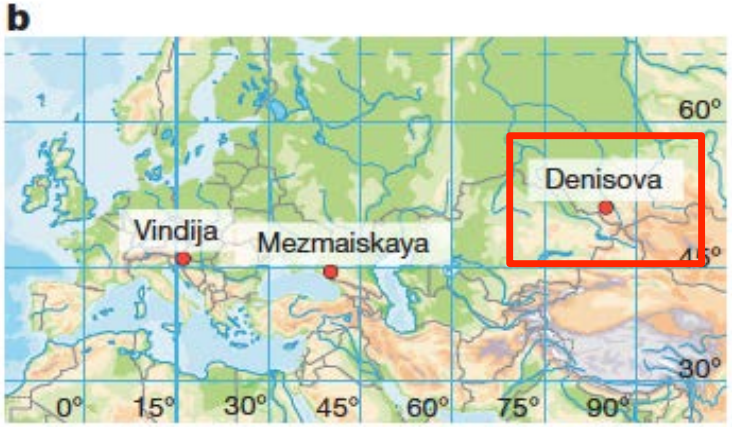
Nature, January 2, 2014 (505, 43-49)

The complete genome sequence of a Neanderthal from the Altai Mountains

130,000 Year-Old Neanderthal

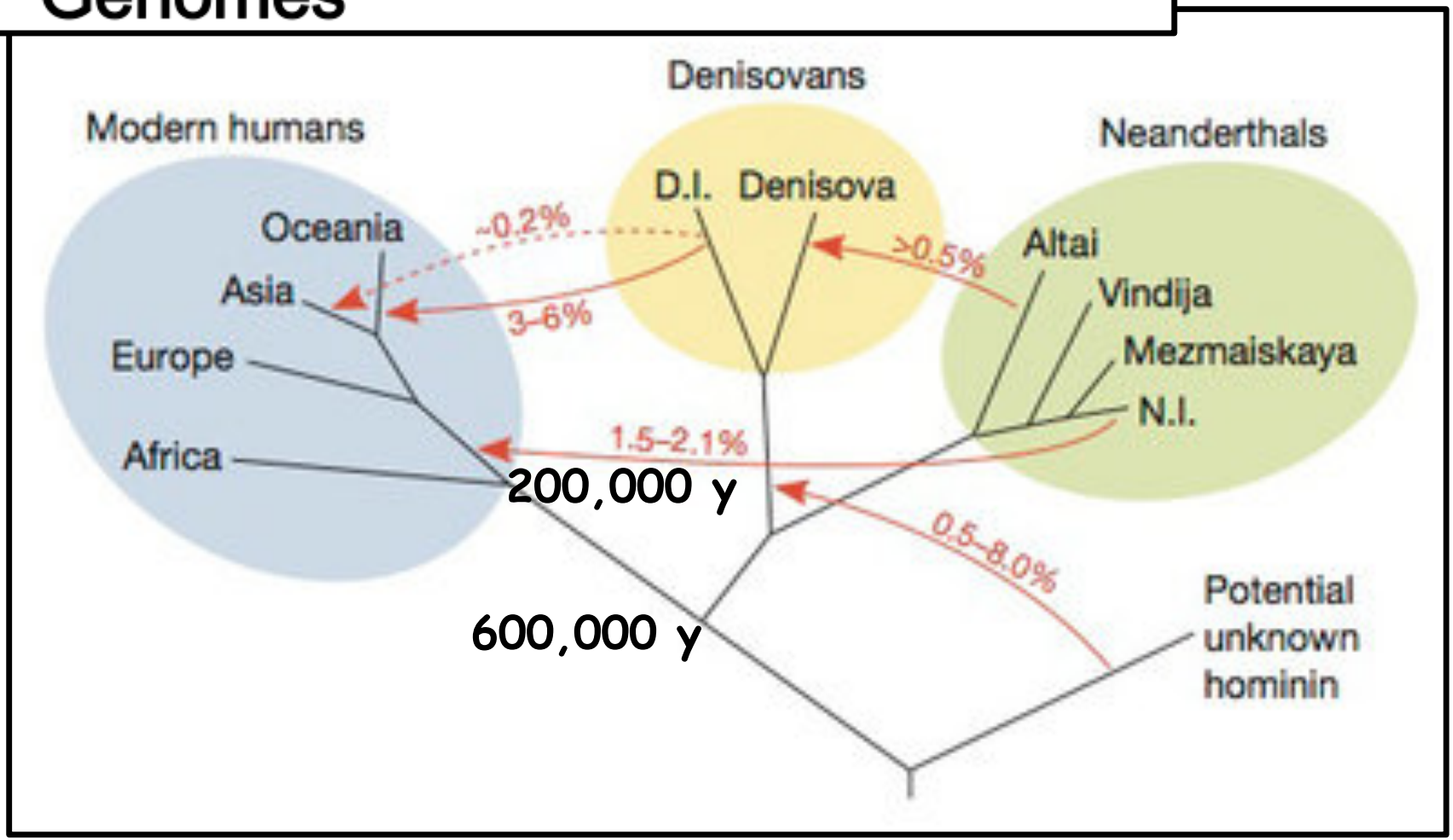
Toe Fossil Provides Complete Neanderthal Genome





Resurrecting Surviving Neandertal Lineages from Modern Human Genomes

story!



The genomic landscape of Neanderthal ancestry in present-day humans

Nature, January 29, 2014

Neandertals and Moderns Made Imperfect Mates

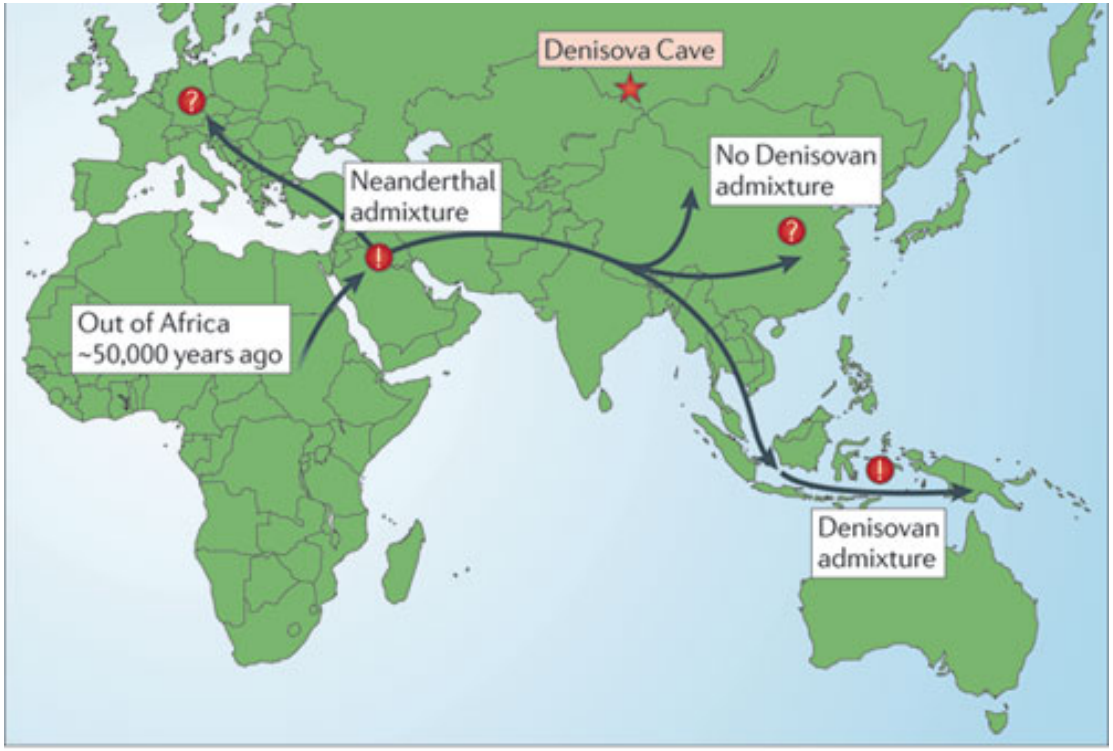
2-4% of Human Genome Consists of Neanderthal Sequences!

Conditions Associated With Neandertal Alleles
Lupus
Primary biliary cirrhosis
Crohn's disease (2 alleles)
Type 2 diabetes
Variation in keratin in skin and hair (several alleles)
Variation in interleukin-18 levels
Variation in optic disc size
Variation in smoking behavior

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 Diffferent Human Ancestor Lineages!!



We Have Neanderthal & Genes in Our Chromosomes

Nature Reviews | Genetics
September, 2011

It's All in the DNA!

The genomic landscape of Neanderthal ancestry in present-day humans

Nature, January 29, 2014

Neanderthals Were Highly Inbred!

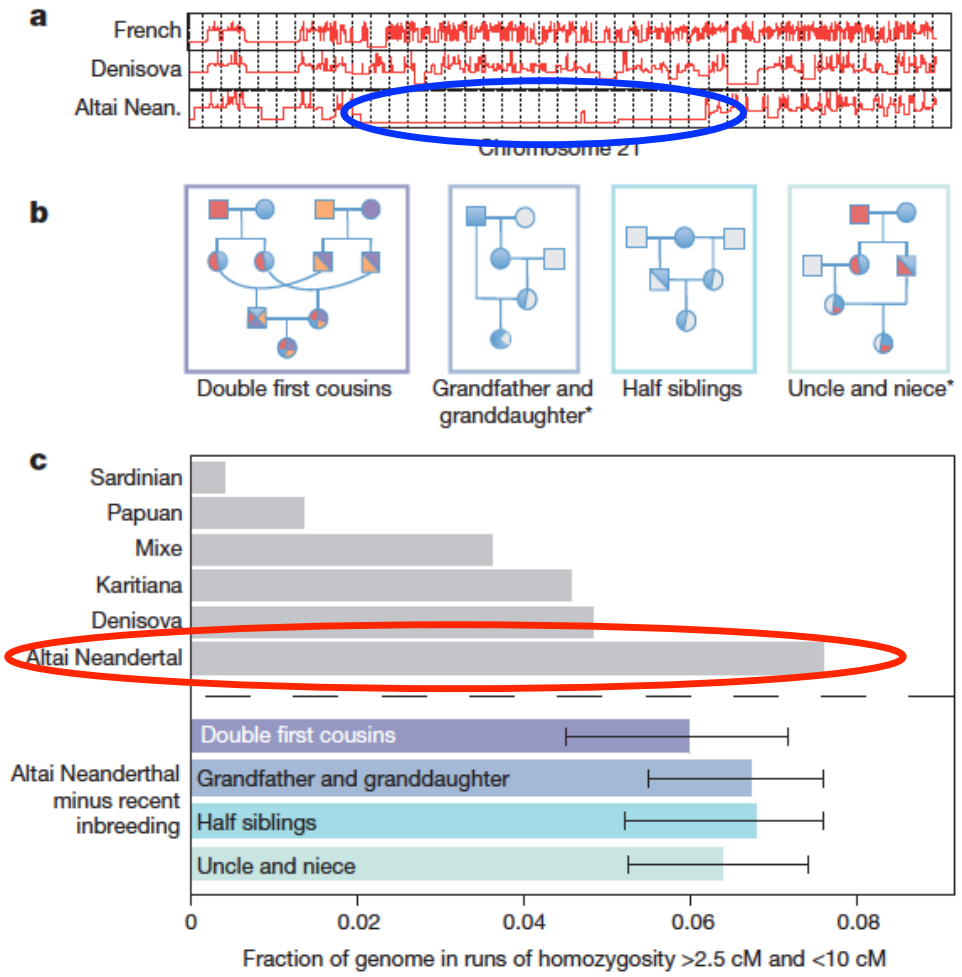
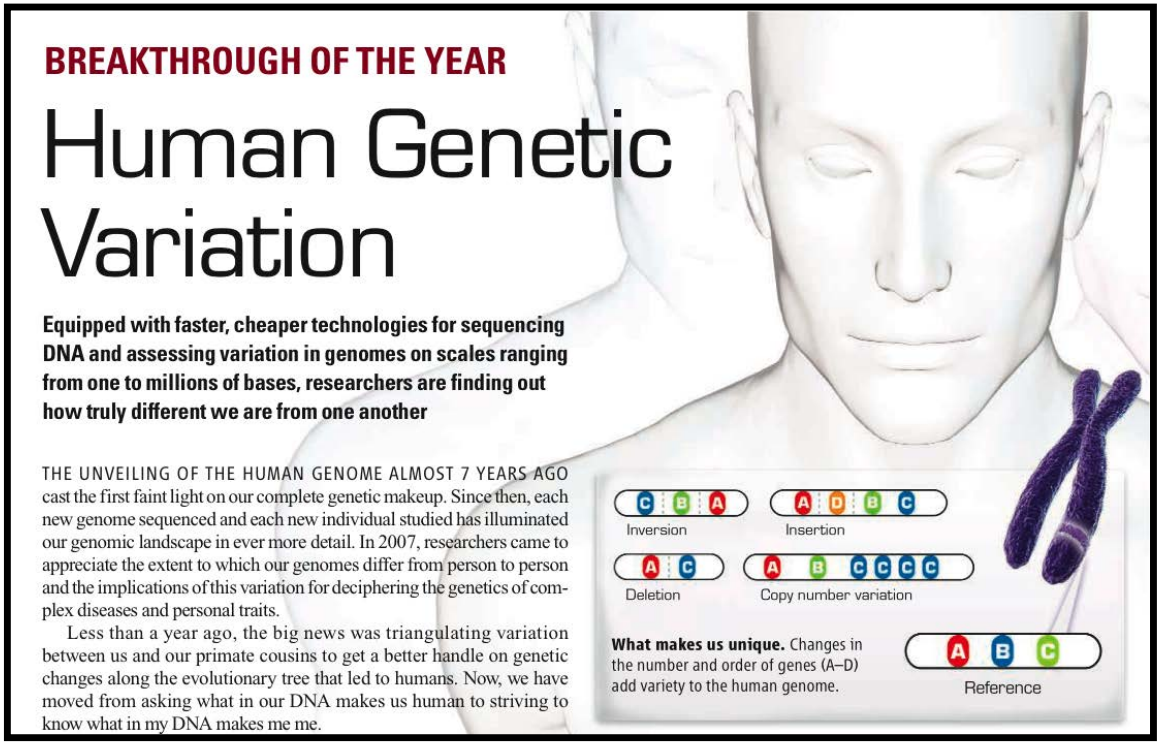


Figure 3 | Indications of inbreeding in the Altai Neanderthal individual.

Identifying DNA Variations (SNPs) Between Individuals Has Many Uses

1. Marking and Identifying Disease Genes
2. Paternity, Individual Identification, Forensics
3. Human Population History and Origins



BREAKTHROUGH OF THE YEAR

Human Genetic Variation

Equipped with faster, cheaper technologies for sequencing DNA and assessing variation in genomes on scales ranging from one to millions of bases, researchers are finding out how truly different we are from one another

THE UNVEILING OF THE HUMAN GENOME ALMOST 7 YEARS AGO cast the first faint light on our complete genetic makeup. Since then, each new genome sequenced and each new individual studied has illuminated our genomic landscape in ever more detail. In 2007, researchers came to appreciate the extent to which our genomes differ from person to person and the implications of this variation for deciphering the genetics of complex diseases and personal traits.

Less than a year ago, the big news was triangulating variation between us and our primate cousins to get a better handle on genetic changes along the evolutionary tree that led to humans. Now, we have moved from asking what in our DNA makes us human to striving to know what in my DNA makes me me.

What makes us unique. Changes in the number and order of genes (A–D) add variety to the human genome.

The Ultimate Measure of Individuality Personal Genome Sequence & Comparing Individual Human Genomes

Genomes for ALL

Next-generation technologies that make reading DNA fast, cheap and widely accessible are coming in less than a decade. Their potential to revolutionize research and bring about the era of truly personalized medicine means the time to start preparing is now

Find DNA Variability in <u>All</u> Genes & Associate with Specific Traits!

Large-scale whole-genome sequencing of the Icelandic population

Ultimately-You <u>Are</u> What Is In Your Genome

The 1,000 Genomes Project Will Provide Novel Insight in Human Genomes, Ancestry, & Disease Genes & Is Now the 100,000 Genome Project!!!

Only Possible Using New Sequencing Methods

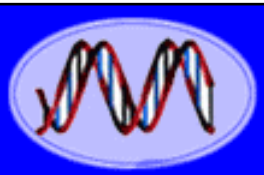
1,000 Genomes

Gene-sequencing projects keep getting bigger.
Tuesday, January 22, 2008
By Emily Singer

In a testament to the steady plummet in sequencing costs, today the National Human Genome Research Institute (NHGRI) announced a massive international collaboration to sequence the genomes of 1,000 people from around the world.

The 100,000 Genomes Project

You can read all about the 100,000 Genomes Project in the different sections below or download all of this information in our full narrative here: Narrative – Genomics England and the 100,000 Genomes Project.



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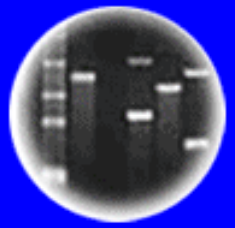

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ARTICLE Nature, October 28, 2010 doi:10.1038/nature09534

A map of human genome variation from population-scale sequencing

The 1000 Genomes Project Consortium*

The 1000 Genomes Project aims to provide a deep characterization of human genome sequence variation as a foundation for investigating the relationship between genotype and phenotype. Here we present results of the pilot phase of the project, designed to develop and compare different strategies for genome-wide sequencing with high-throughput platforms. We undertook three projects: low-coverage whole-genome sequencing of 179 individuals from four populations; high-coverage sequencing of two mother-father-child trios; and exon-targeted sequencing of 697 individuals from seven populations. We describe the location, allele frequency and local haplotype structure of approximately 15 million single nucleotide polymorphisms, 1 million short insertions and deletions, and 20,000 structural variants, most of which were previously undescribed. We show that, because we have catalogued the vast majority of common variation, over 95% of the currently accessible variants found in any individual are present in this data set. On average, each person is found to carry approximately 250 to 300 loss-of-function variants in annotated genes and 50 to 100 variants previously implicated in inherited disorders. We demonstrate how these results can be used to inform association and functional studies. From the two trios, we directly estimate the rate of *de novo* germline base substitution mutations to be approximately 10^{-8} per base pair per generation. We explore the data with regard to signatures of natural selection, and identify a marked reduction of genetic variation in the neighbourhood of genes, due to selection at linked sites. These methods and public data will support the next phase of human genetic research.

- Sequenced Genomes of ~900 individuals
- From Seven Different Global Populations
- Identified 15,000,000 SNPs
- 50-100 Variants in Disease Genes Per Person
- 10^{-8} Mutations Per bp Per Generation (~30 per Genome)
- 3,000,000 Unique SNPs Per Person
- 750,000 Unique Indels Per Person

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

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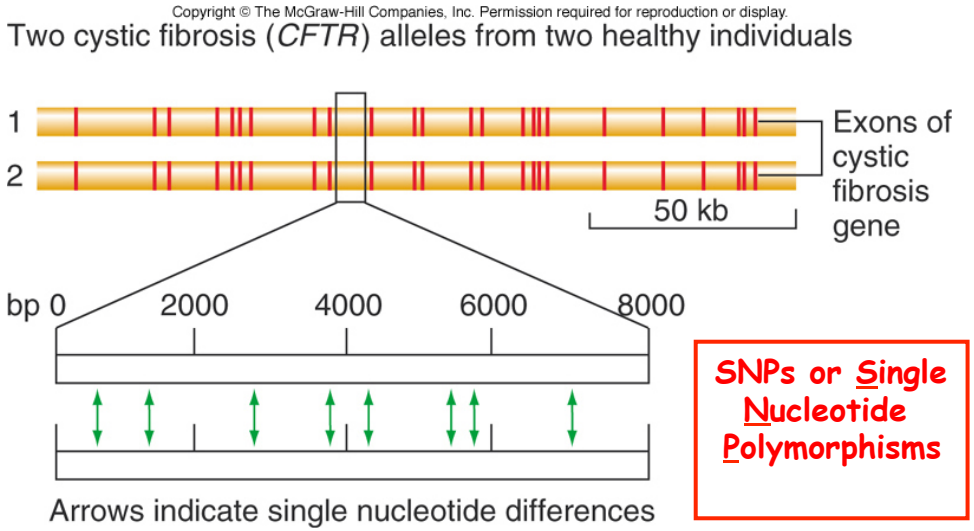

SNPs or Single Nucleotide Polymorphisms

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

This is What Makes Us Unique Individuals!

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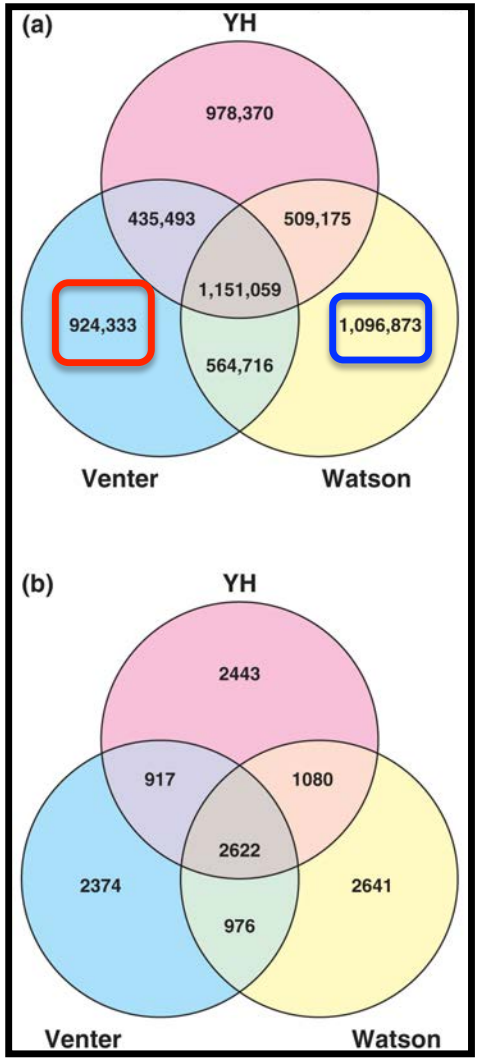
There is ~1bp Change per 700bp in Human Genomes or ~3.4 Million bp Differences Between Individuals ~0.1% of Genome

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



YH= Anonymous Chinese Man

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(a)

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

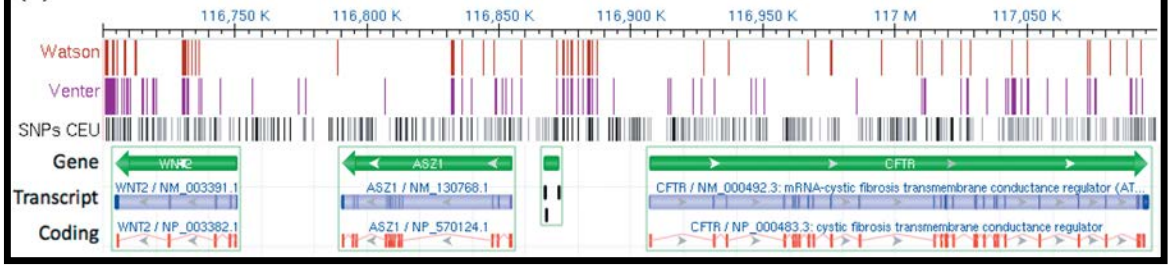
(b)

Genotype	Notation
Homozygous T	TT
Heterozygous T	TC
Homozygous C	CC

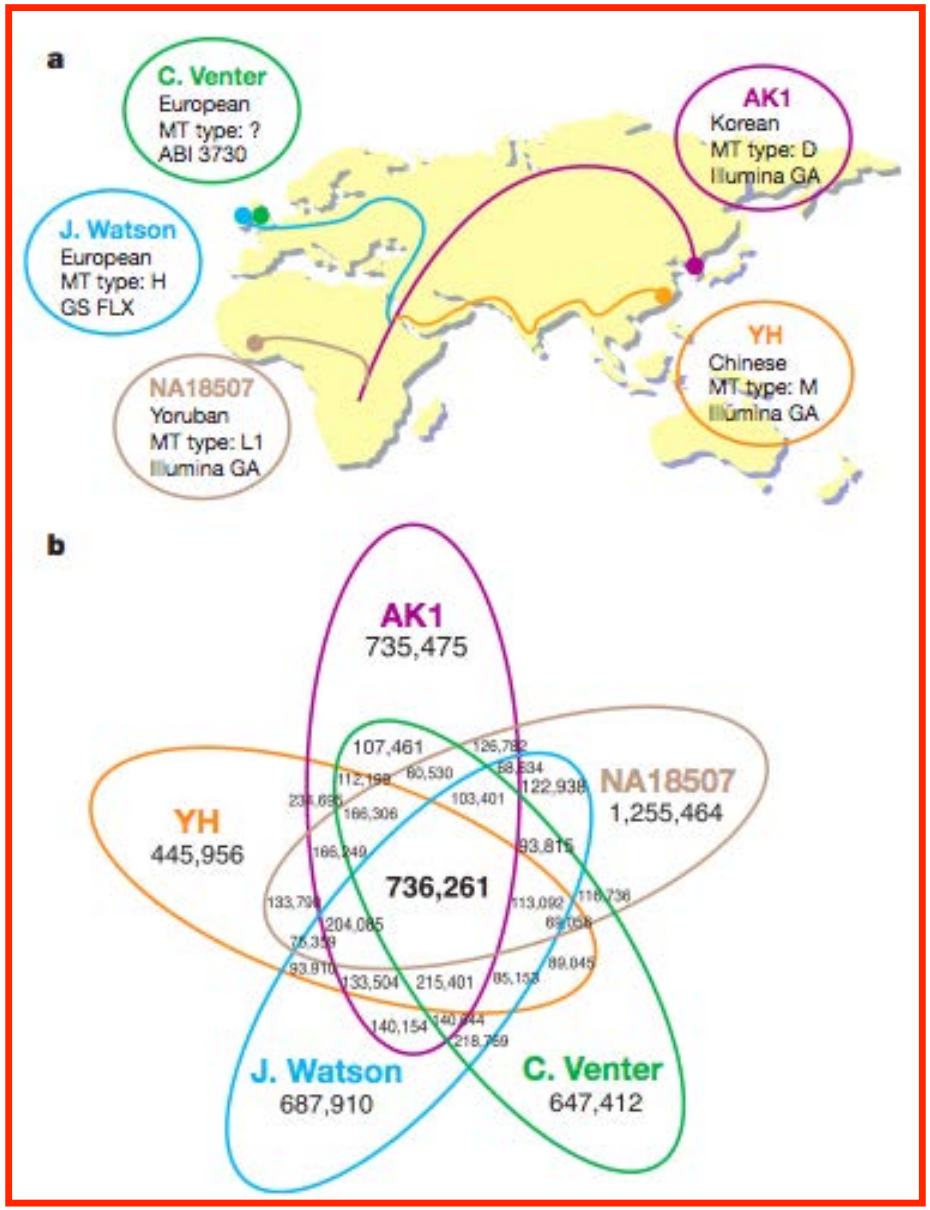
(c)

Human 1 TTGACGTATAAATGATCTTTATATTTTCAGAAGTC
Human 2 TTGACGTATAAATGATCTTTATATCTTCAGAAGTC
Chimp TTGACATATAAATGATCTTTATATCTTCAGAAGTC

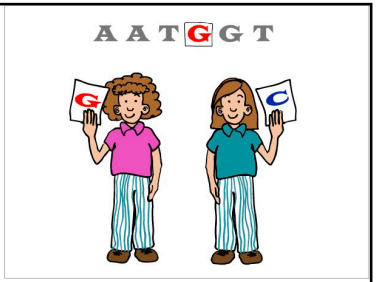
(d)



In Fact, Everyone Has a Large Number of Unique SNPs!



SNPs Can Be Associated/Linked With Specific Physical Traits



OCA2

From SNPedia

OCA2, the oculocutaneous albinism gene (also known as the human P protein gene, or, DN10), is a gene associated with albinism and certain pigmentation effects in general such as eye color, skin color, and hair color.

A large (>3,000 individuals) study of Caucasians indicates that the following **OCA2** variants, all located in the first intron of the gene, are preferentially linked to blue eye color inheritance; together, they form haplotypes that (in some cases at least) predict eye color with greater than 50:50 odds. [PMID 17236130; OMIM 203200.0013 (http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=203200&a=203200_AllelicVariant0013)]

- rs7495174
- rs6497268
- rs11855019

The haplotypes are defined in order as listed above for these 3 SNPs, so, for example, the TGT haplotype refers to rs745174(T)-rs6497268(G)-rs11855019(T). The correspondence between diplotypes (the two haplotypes in one individual) and the % of individuals with blue/gray, green/hazel/ and brown eye color , respectively, was reported as follows for the most common diplotypes[PMID 17236130]:

- TGT/TGT: 62.5, 28.0, 9.5
- TGT/***TTC***: 47.1, 20.3, 32.6
- TGT/***CGT***: 28.6, 14.3, 57.1
- TGT/***TGC***: 27.9, 22.1, 50.0
- ***TGC***/***TTC***: 25.0, 8.3, 66.7
- ***TTT***/***TGC***: 20.7, 31.0, 48.3
- TGT/***TTT***: 17.6, 38.5, 44.0
- TGT/***CTC***: 7.9, 23.3, 68.8

The haplotypes shown in ***bold italics*** represent the ones reported by the authors of this study to be most associated with brown eye color. Furthermore, the haplotypes shown above are as published, and the associated SNPs - which have since changed # as well - are not in the orientation shown in dbSNP.

More recently, a study of a large Danish family led to associations with 2 SNPs in a different region of **OCA2** as linked to blue or brown eye color:

- rs12913832
- rs1129038

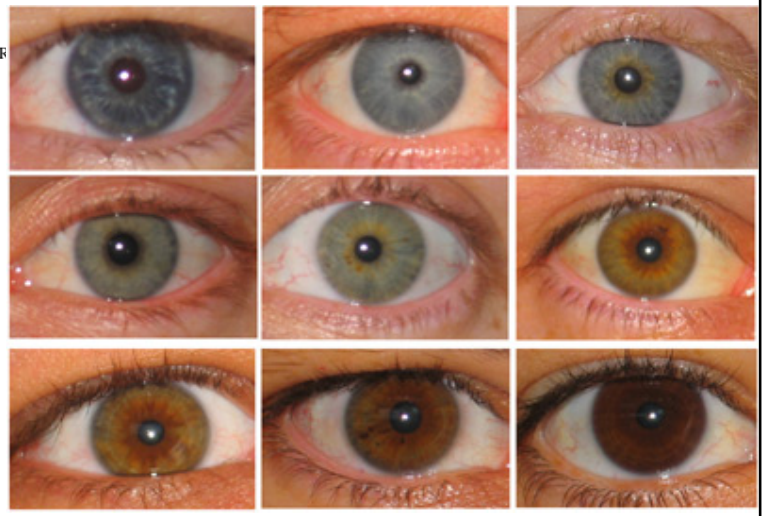
Earlier studies found different regions of the **OCA2** gene to also be predictive of eye color;

- **OCA2** SNP rs1800401 helps predict brown eye color. [PMID 12163334, PMID 15889046; OMIM 203200.0011 (http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=203200&a=203200_AllelicVariant0011)]
- **OCA2** SNP rs1800407 may be associated with green/hazel eye color in some populations, but not others. [PMID 12163334, PMID 15889046; OMIM 203200.0012 (http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=203200&a=203200_AllelicVariant0012)]

is a	gene
is	mentioned by
wikipedia	OCA2 (http://en.wikipedia.org/wiki/OCA2)
google	OCA2 (http://www.google.com/search?hl=en&q=OCA2)
gopubmed	OCA2 (http://www.gopubmed.org/search?q=OCA2)
23andMe	OCA2 (https://www.23andme.com/you/explorer/gene/?gene_name=OCA2)
GeneRIF	4948 (http://www.ncbi.nlm.nih.gov/sites/entrez?Db=gene&Cmd=ShowDetailView&TermToSearch=4948&ordinalpos=1&itool=EntrezSystem2.PEntrez.Gene.Gene_ResultsPanel.Gene_R
dbSNP	4948 (http://www.ncbi.nlm.nih.gov/SNP/snp_ref.cgi?locusId=4948&chooseRs=all)
PubMed	4948 (http://www.ncbi.nlm.nih.gov/sites/entrez?db=gene&cmd=Link&LinkName=gene_pubmed&from_uid=4948)
HugeNav	4948 (http://hugenavigator.net/HuGENavigator/huGEPedia.do?firstQuery=OCA2}&geneID=4948&typeSubmit=GO&check=y&typeOption=gene&which=2&pubOrderType=pubD)

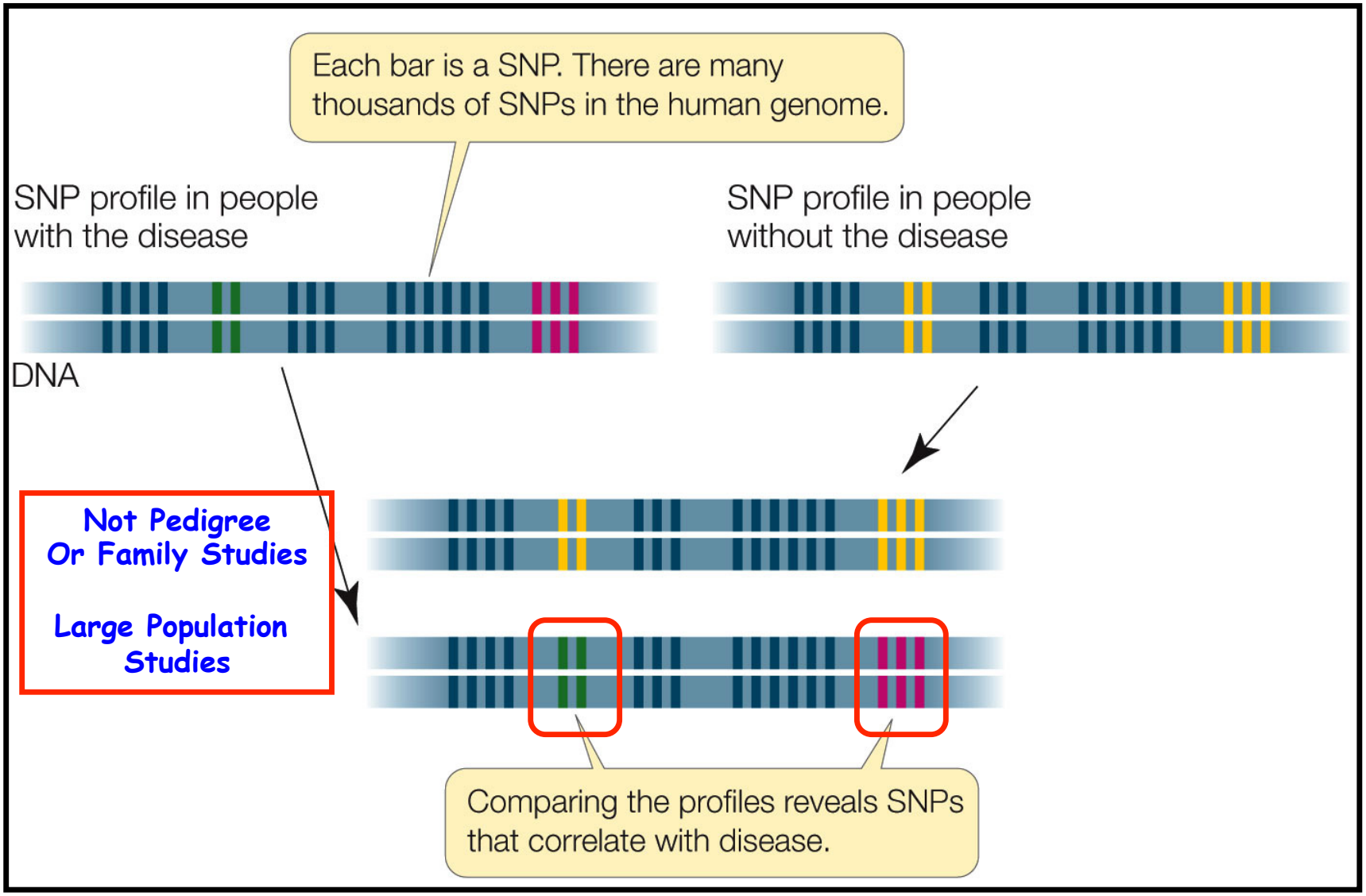
	Chromosome position
Rs1129038	26,030,454
Rs11631797	26,175,874
Rs12593929	26,032,853
Rs1800401	25,933,648
Rs1800407	25,903,913
Rs2238289	26,126,810
Rs2240203	26,167,797
Rs28934272	25,903,842
Rs3935591	26,047,607
Rs3940272	26,142,318
Rs4778241	26,012,308
Rs7170852	26,101,581
Rs7183877	26,039,328
Rs7495174	26,017,833
Rs8028689	26,162,483
Rs916977	26,186,959

SNPs in Human P Protein (OCA2) Gene Lead To Different Eye Colors (Physical & Molecular Markers)

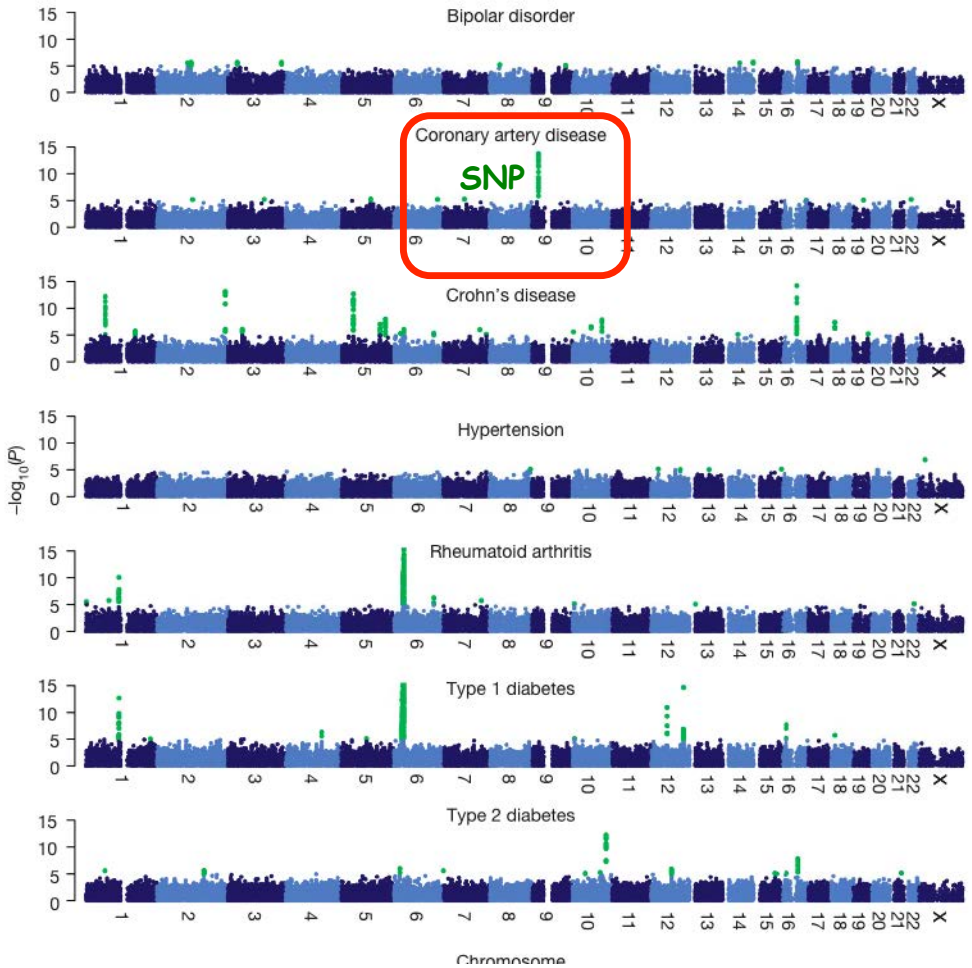


Human Eye Color

Using SNPs and Population Association Studies to Find Disease Markers and Genes



Correlating SNPs With Specific Diseases Using SNP Chips & Association Studies



Note: Probability

SNPs May Be Near Or In Relevant Genes

Using Large Populations SNPs Can Be Used As Markers For Specific Genes/Traits

SNPedia (http://www.snpedia.com/)

- New model for prostate cancer based on 5 SNPs
- rs1815739 sprinters vs endurance athletes
- rs4420638 and rs429358 can raise the risk of Alzheimer's disease by more than 10x
- rs6152 can prevent baldness
- rs9939609 triggers obesity
- rs662799 prevents weight gain from high fat diets
- rs7495174 green eye color
- rs7903146 in 3% of the population greatly increases the risk of type-2 diabetes
- rs12255372 linked to type-2 diabetes and breast cancer
- rs2395029 asymptomatic HIV viral load set point
- rs324650 influences intelligence and alcohol dependence
- rs1799971 makes alcohol cravings stronger
- rs17822931 determines earwax

Caution

How Will You Use the Information?
How Good Are The Correlations?
What To Do With The Information?
Privacy Issues?
Group Differences? Discrimination?

- rs53576 in the oxytocin receptor influences social behavior and personality
- rs1815739 muscle performance
- rs7412 and rs429358 can raise the risk of Alzheimer's disease by more than 10x
- rs6152 can influence baldness
- rs333 resistance to HIV
- rs1800497 in a dopamine receptor may influence the sense of pleasure
- rs1805007 determines red hair and sensitivity to anesthetics
- rs9939609 triggers obesity and type-2 diabetes
- rs662799 prevents weight gain from high fat diets
- rs7495174 green eye color and rs12913832 for blue eye color
- rs7903146 in 3% of the population greatly increases the risk of type-2 diabetes
- rs12255372 linked to type-2 diabetes and breast cancer
- rs1799971 makes alcohol cravings stronger
- rs17822931 determines earwax
- rs4680 varied cognitive effects
- rs1333049 coronary heart disease
- rs1801133 folate metabolism and several cancers
- rs1051730 and rs3750344 nicotine dependence
- rs4988235 lactose intolerance

Examples of SNPs in SNPedia Database

Examples of Whole Genomes in SNPedia Database

(http://www.snpedia.com/)

These are the 105 public genomes. They are from real people who've chosen to share their data to help all of us learn more about our genomes. but be sure to check the report header to understand how up to date each is.

	Platform	Raw data available	Summary
Aaron Vollrath	23andMe v2		Male on 23andMe
Almelina	23andMe v2	true	Female with cancer 2x
Bgreshake	23andMe v3		German Male 23andMe v3
Blainebettinger	23andMe v2 FTDNA Family Finder		23andMe v. FTDNA Family Finder data
Corpas aunt	23andMe v3		Visualized family snps; whole family 23andMe genotypes
Corpas dad	23andMe v3		Visualized family snps; whole family 23andMe genotypes
Corpas mom	23andMe v3		Visualized family snps; whole family 23andMe genotypes
Corpas sister	23andMe v3		Visualized family snps; whole family 23andMe genotypes
Daniel MacArthur	23andMe v3 23andMe v2 Lumigenix		1st Lumigenix, GNZ, 23andMe v2+3, blogger
David Ewing Duncan	Complete Genomics 23andMe v2 DeCODEme Navigenics		Full genome from Complete Genomics, but also microarrays from 23a
DeCODEme	DeCODEme		Sample deCODEme male
Denisova	Full Sequencing		a 41k year old member of the genus Homo
Dichro	23andMe v2 23andMe v1	true	23andMe male (v1 + v2)

DNA Can Be Used To Test For Hundreds of Disease Genes and Human Traits and Generate Personalized Gene Profiles

What Are the Problems & Laws That Govern Direct To Consumer DNA Tests?

And Before Birth!!!

23andMe

Complete Genomics | Powering large-scale human genome studies

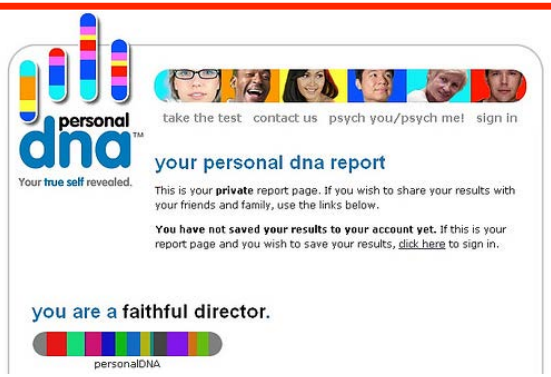
Corporate | Technology | Services | Data Release | Future Applications | Resources | Contact Us

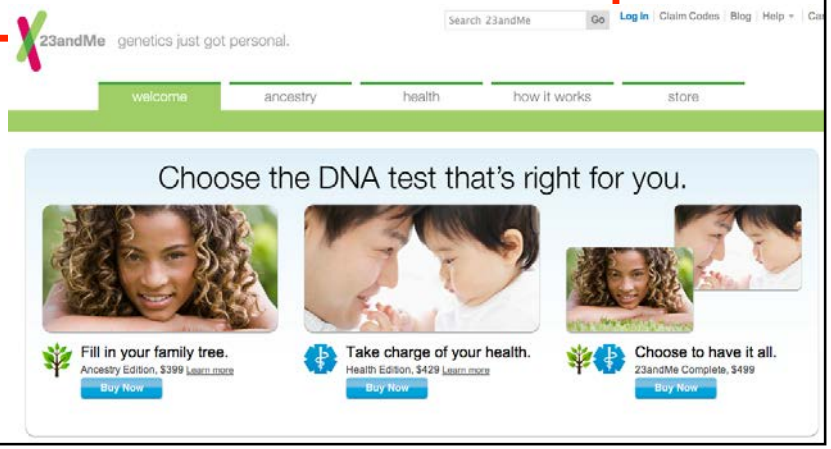
DNA Lady

Ancestry Family Forensic Medical

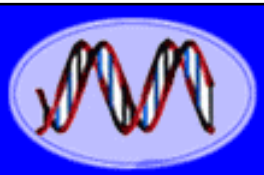
The Problems With Human Genome Testing Companies Are?

a. Reliability of Results?
b. Validity of Association Studies
c. Privacy?
d. What To Do With Information Obtained?
e. FDA Regulatory Oversight?
f. Deceptive Practices
g. All of Above?



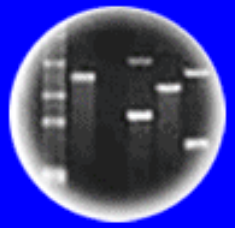


Knome



DNA
Genetic Code of Life

Entire Genetic Code of a Bacteria



DNA Fingerprinting

Cloning: Ethical Issues and Future Consequences

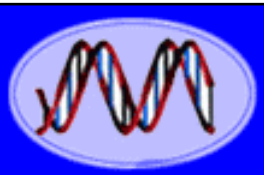
Plants of Tomorrow

Problem: Different Companies-Different Predictions-No Oversight!

TABLE 1: PREDICTIONS FOR DISEASE RELATIVE RISKS FOR FIVE INDIVIDUALS

Disease	Female A	Female B	Female C	Male D	Male E
Breast cancer	↑↑	↑↑	↓↓		
Coeliac disease	↓↓	↓↓	↓↓	↓↓	↓↓
Colon cancer	==	==	=↓	↑↑	=↓
Crohn's disease	↓↑	↓↑	↓↓	↓↓	↓=
Heart attack	↓↓	=↓	=↓	=↓	↑↑
Lupus	↑↓	↓↓	↓↓	↑=	↑=
Macular degeneration	↓↓	↓↓	↑=	↓↓	↓↓
Multiple sclerosis	↑↑		↓↓	↓↓	↓↓
Prostate cancer				↑↑	↓↑
Psoriasis	↓↑		↑↓	↑↑	↓↓
Restless legs syndrome	=↓	↑↑	↓=	↓↑	↑↑
Rheumatoid arthritis	↑↑	↑↑	↓↓	↓↓	↑↑
Type 2 diabetes	↓↓	=↓	↓↓	↑↓	=↓

↑ increased risk (RR > 1.05), ↓ decreased risk (relative risk (RR) < 0.95), = average risk (0.95 ≤ RR ≤ 1.05). First prediction is from 23andMe; second prediction is from Navigenics. Different predictions are highlighted in beige.



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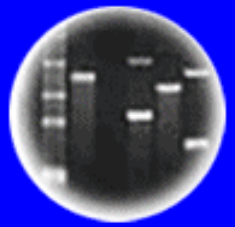

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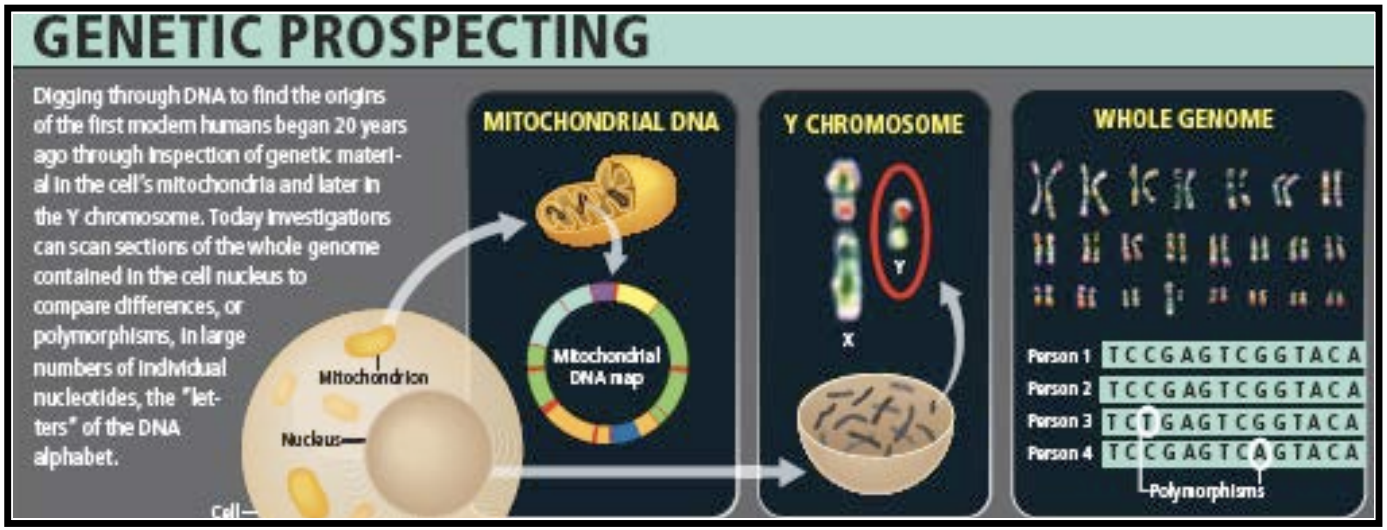
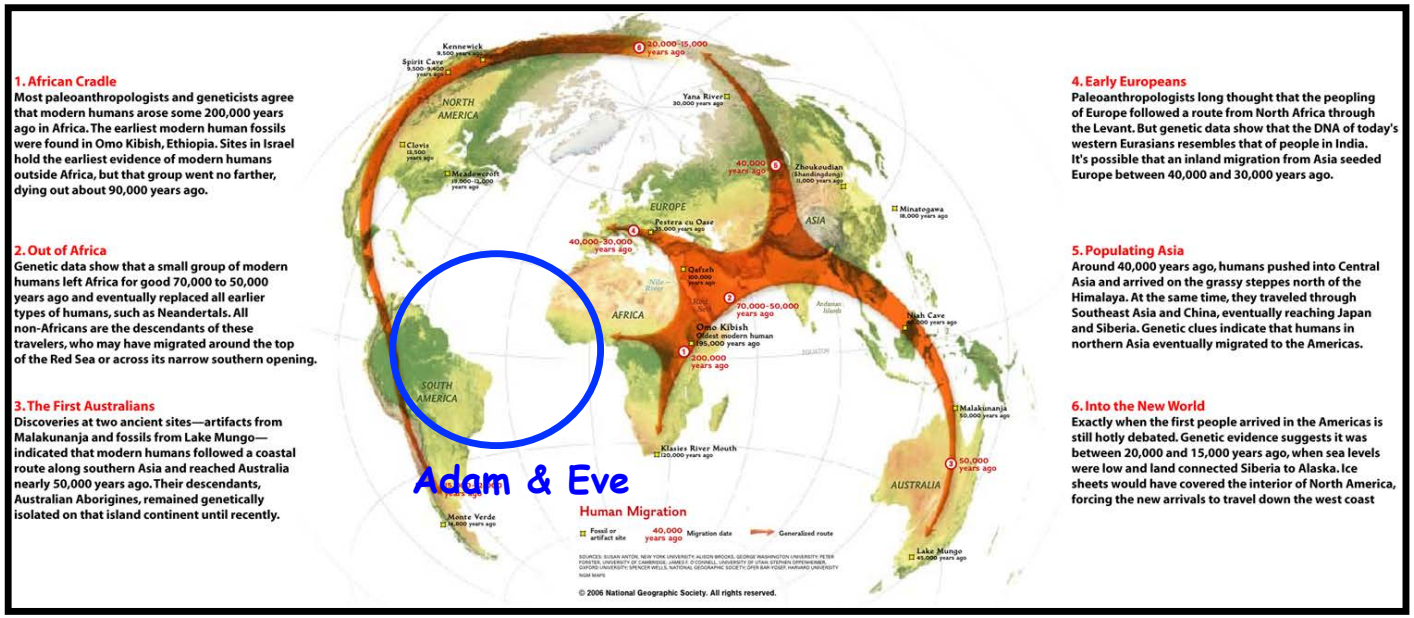
Finally….Nuclear DNA SNPS Can Be Used To Trace Human Populations & Origins



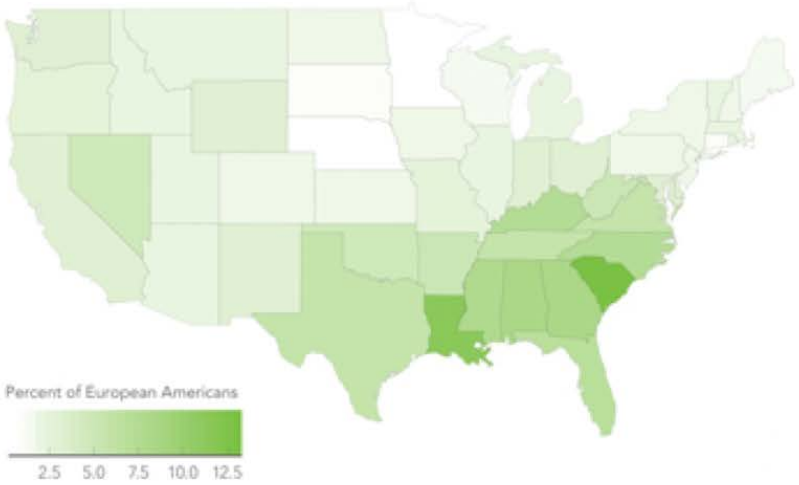


Genetic Analysis Reveals the U.S. is Truly a Melting Pot

By Carl Engelking | December 19, 2014 3:10 pm

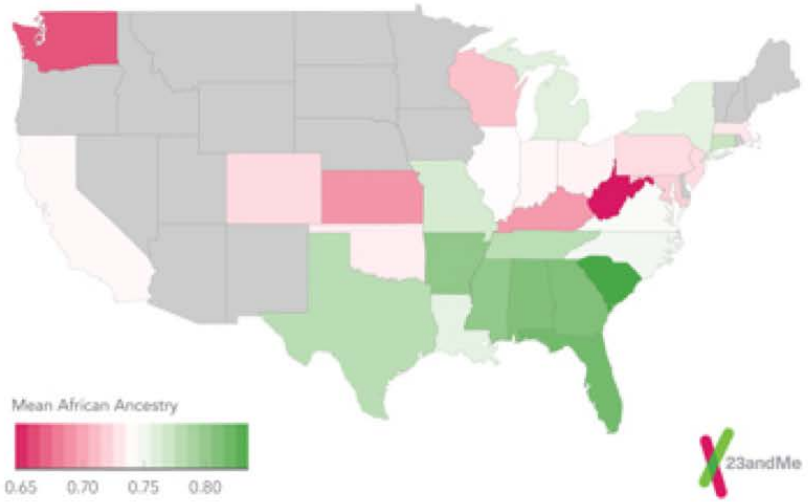
Self-Identified White Americans With African Ancestry

Percent of self-identified European (white) Americans who have one percent or more African ancestry.



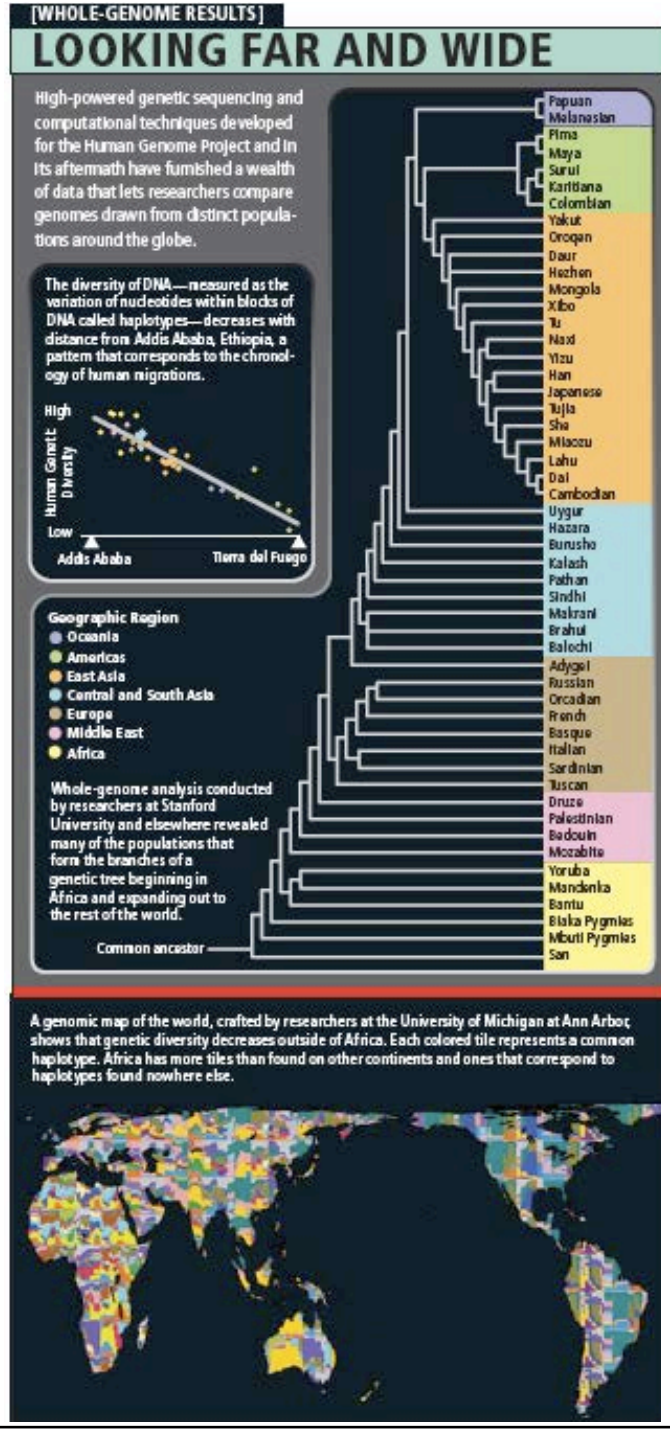
African Ancestry Among African Americans

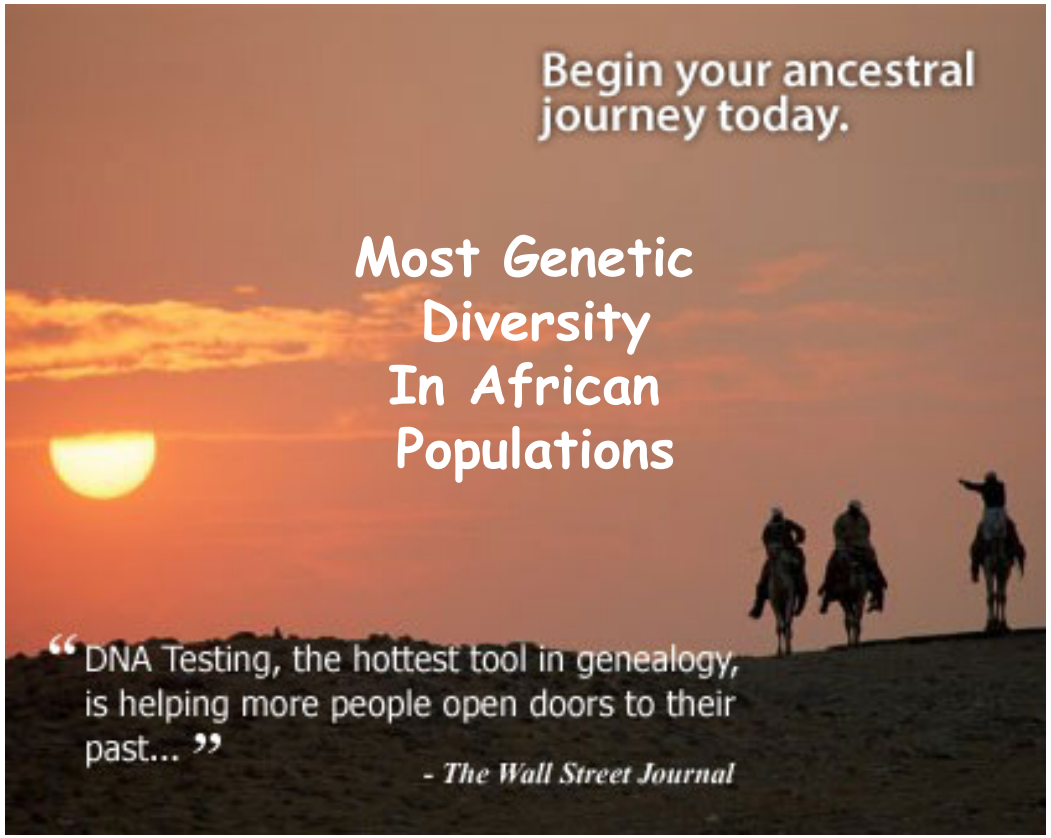
The mean proportion of African ancestry for African Americans across the United States. African Americans in Georgia and South Carolina have the highest average percentage of African ancestry among African Americans in the US.

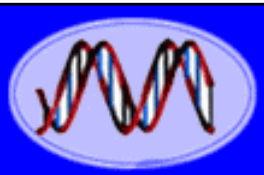


http://blogs.discovermagazine.com/d-brief/2014/12/19/genetic-melting-pot/#1

Human Population Relationships and Origins Using Whole-Genome Comparisons







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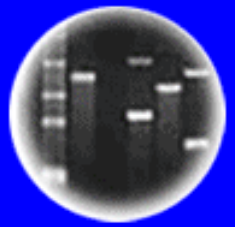

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HUMAN DIVERSITY

RICHARD LEWONTIN

Scientific American Library
1982 ISBN 07167-14698

There is More Genetic Diversity Within Populations than Between Populations!! So Much for the Concept of Racial "Purity"!!!!

More Genetic Diversity Within Any Population Than Between Polulations

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).

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.

Within Population Differences Account For 95% of Human Genetic Variation

Genetic Structure of Human Populations

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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)	2.5 (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!

Conclusions

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%

Variation That Occurs in Ancestral Population

85% Within Population genetic variability

8% Between Populations of Same "Race"

7% Between "Race" Genetic Variability

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

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 few 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 representation 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