

The Intersection of Genetics & Genealogy

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Topics of Interest

- Medical Genealogy
 - Sources of ancestral medical information
 - Legal aspects of obtaining medical records
- Genetic Genealogy
 - Overview of genetics
 - Tracing the paternal lineage
 - Tracing the maternal lineage

Medical Genealogy

- Use of ancestral medical information to predict increased risk for diseases.

Sources of Information

- Family prescriptions, doctor's instructions or medical bills among family papers
- Family photos
- Family members
- Diaries and letters
- Death records
- Funeral records
- Obituaries
 - Google News Archives, www.genealogybank.com, ancestry.com, footnote.com, ProQuest Obituaries

Sources of Information

- Census records
 - www.archives.gov, www.ancestry.com, Ancestry Library Edition, Heritage Quest Online, pilot.familysearch.org
 - 1850, 1860, 1870, 1880—mortality schedules
 - 1880—DDD schedules—
www.familytreemagazine.com/cheatsheets
- Hospital records
- Insurance records
- Military records
 - archives.gov/research/guide-fed-records/groups/094.html
(WWI or earlier)
 - archives.gov/veterans/military-service-records/medical.html
(recent veterans)
 - Footnote, Heritage Quest Online (confederate and revolutionary war)

Other Helpful Websites

- www.antiquusmorbus.com
 - Provides long list of definitions for medical terms and causes of death
- bjhughes.org/epidemic.html
 - Provides information on epidemics
- en.wikipedia.org/wiki/List_of_epidemics#North_America
 - Provides information on epidemics in North America

Obtaining medical records

- In NC, it is suggested that providers retain medical records for 10 years after the last treatment date or until age 21 for minors; diagnostic images should be kept for at least 5 years
 - May vary by state to state
- Providers are required to provide a copy of the patient's health records at the written request of the patient, his attorney, or authorized representative
- Providers can charge for medical records including cost per page, research fees, handling fees or related costs, and the cost of postage
- Requestor must specifically ask for psychiatric/psychological records and genetic testing results

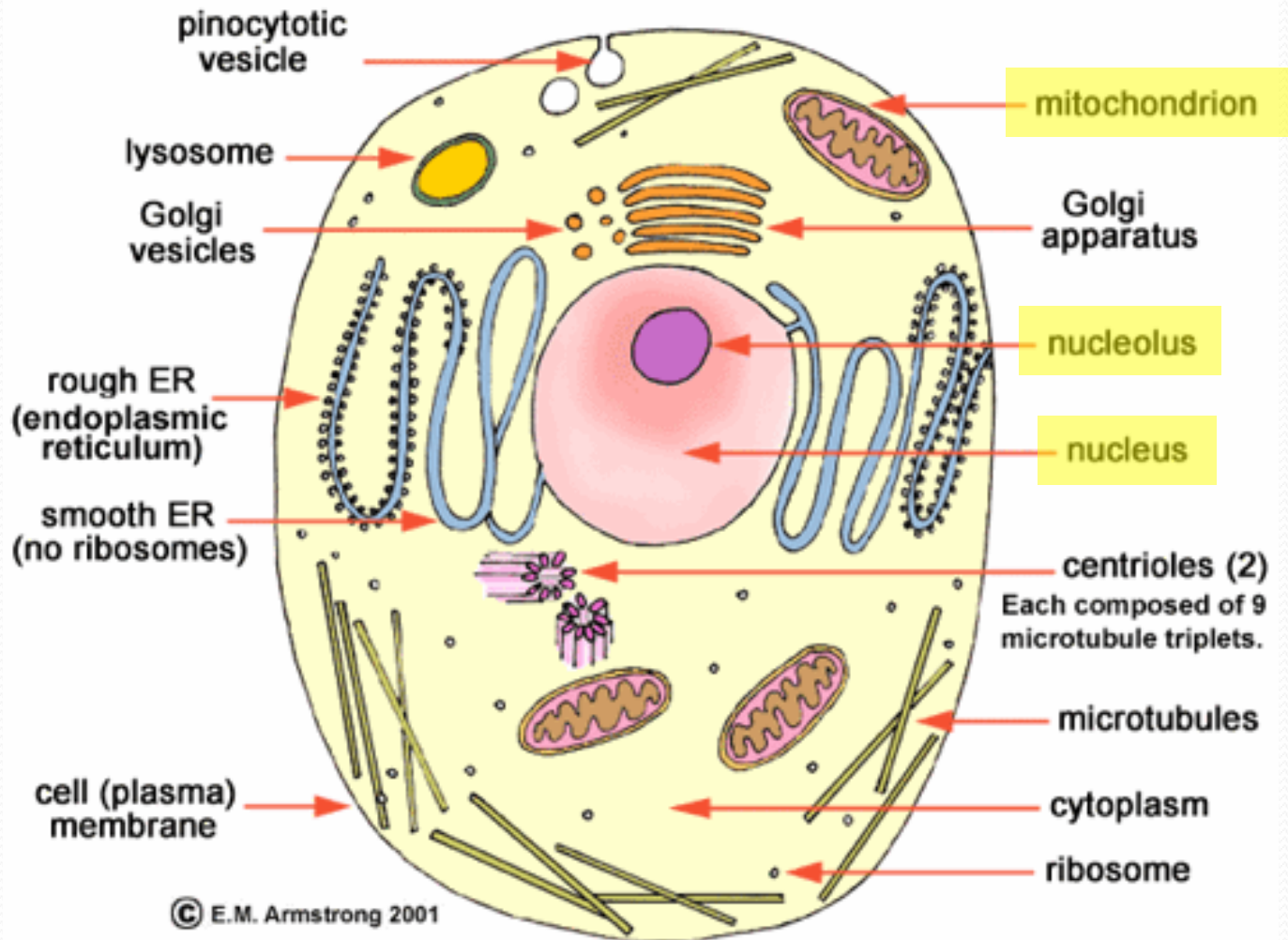
Documenting Your Family's Medical History

- Serves as a useful records of information to discuss with your primary care physician
- If a genetic disorder is identified in the family, you can request a referral to a genetic counselor to review the implications to yourself
 - www.nsgc.org
 - www.geneticalliance.org
- Surgeon General's My Family Health Portrait
 - familyhistory.hhs.gov/fhh-web/home.action

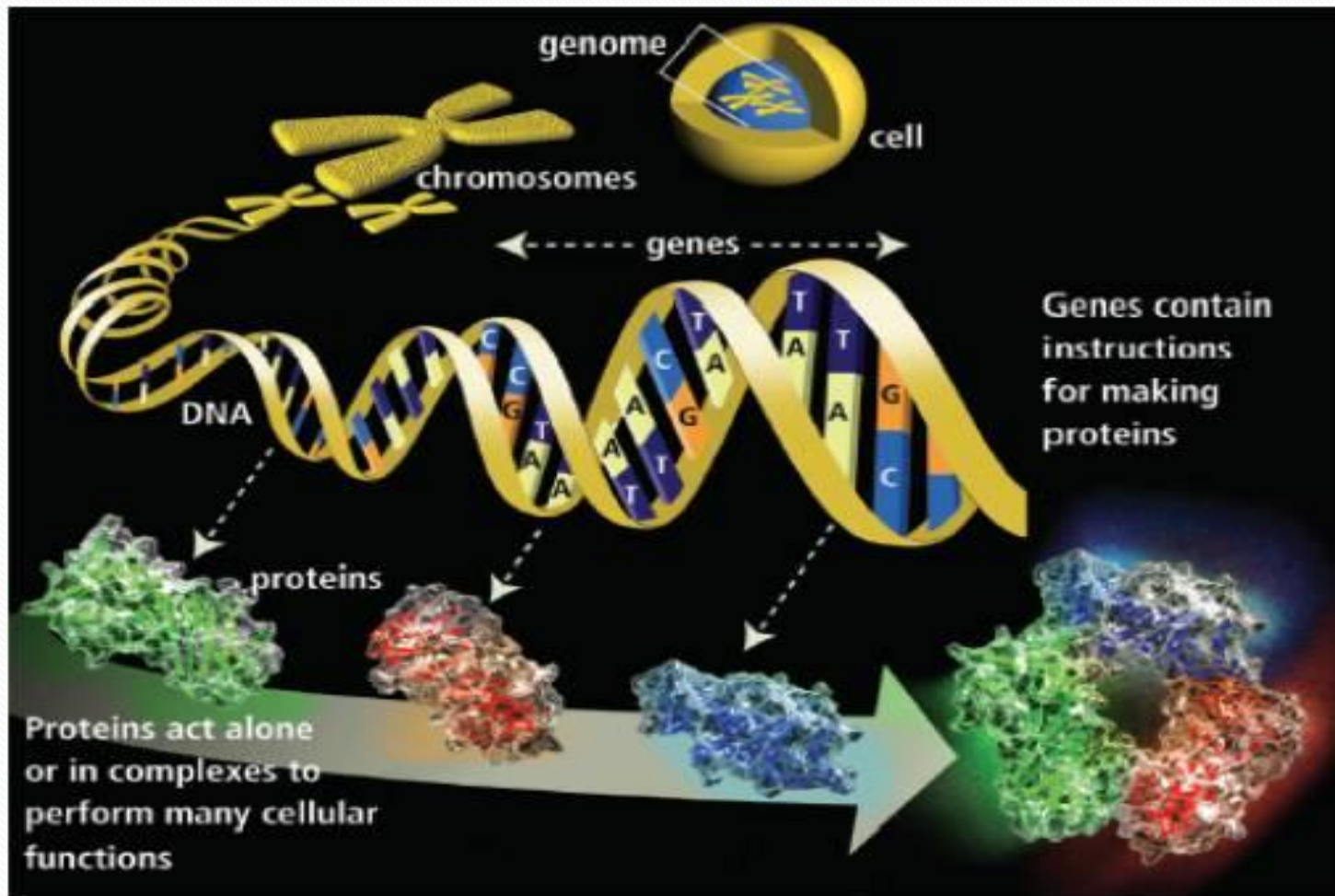
Genetic Genealogy

- Application of genetics to traditional genealogy
- Use of genealogical DNA testing to determine the level of genetic relationship between individuals

Genetics 101



Chromosomes, Genes, Proteins

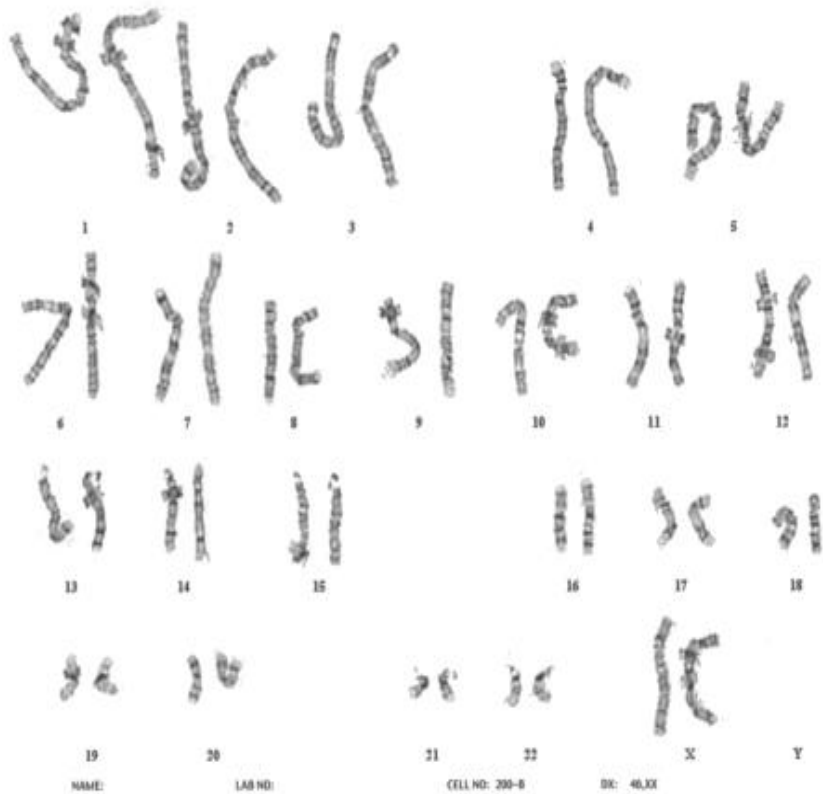


Chromosomes



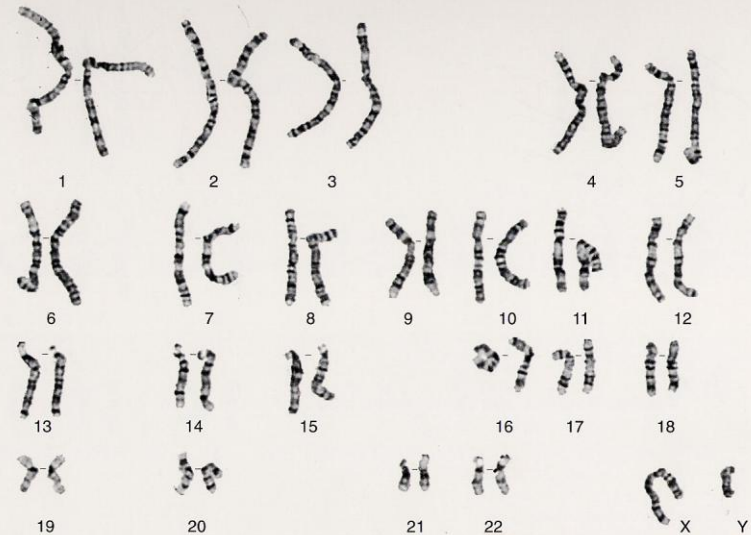
Normal Chromosome Complement

UNIVERSITY OF NORTH CAROLINA HOSPITALS CYTOGENETICS



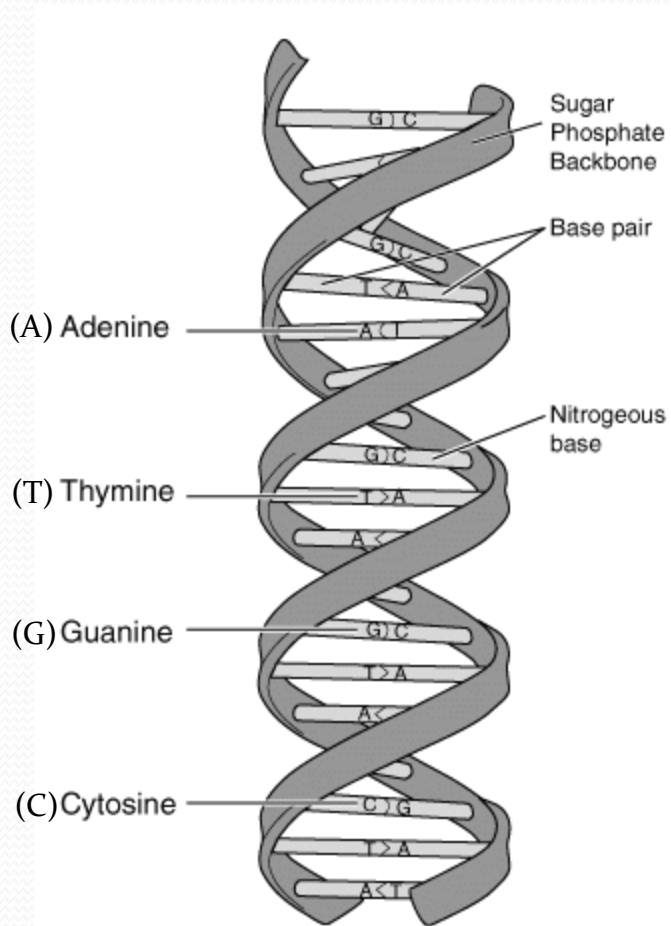
Normal female

NORMAL MALE
46,XY



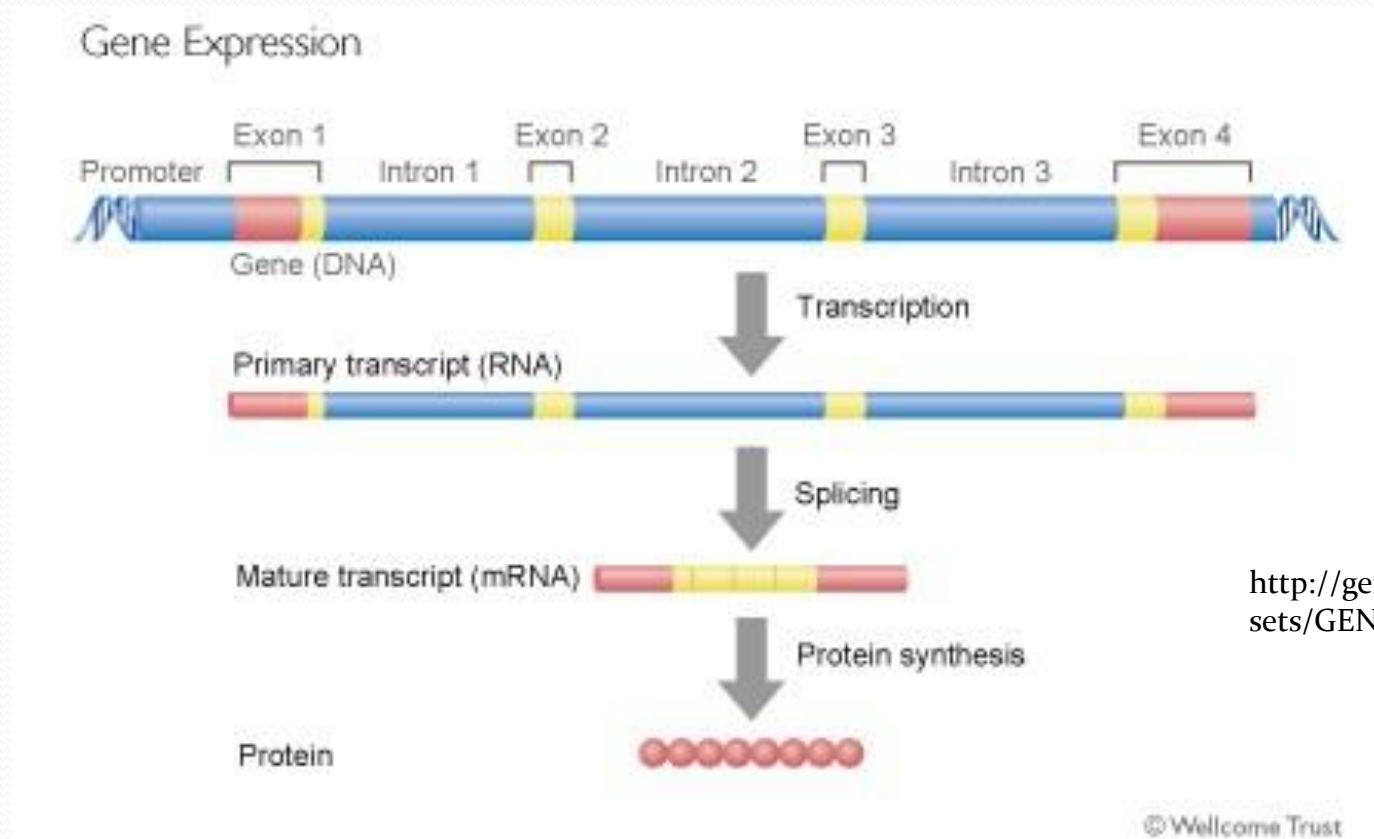
Normal male

DNA



- Human Genome Project
 - Started in 1990, finished 2003
 - Collaborative project
- Human genome has ~3 million base pairs
- 99.9% of DNA identical

Genes and Proteins



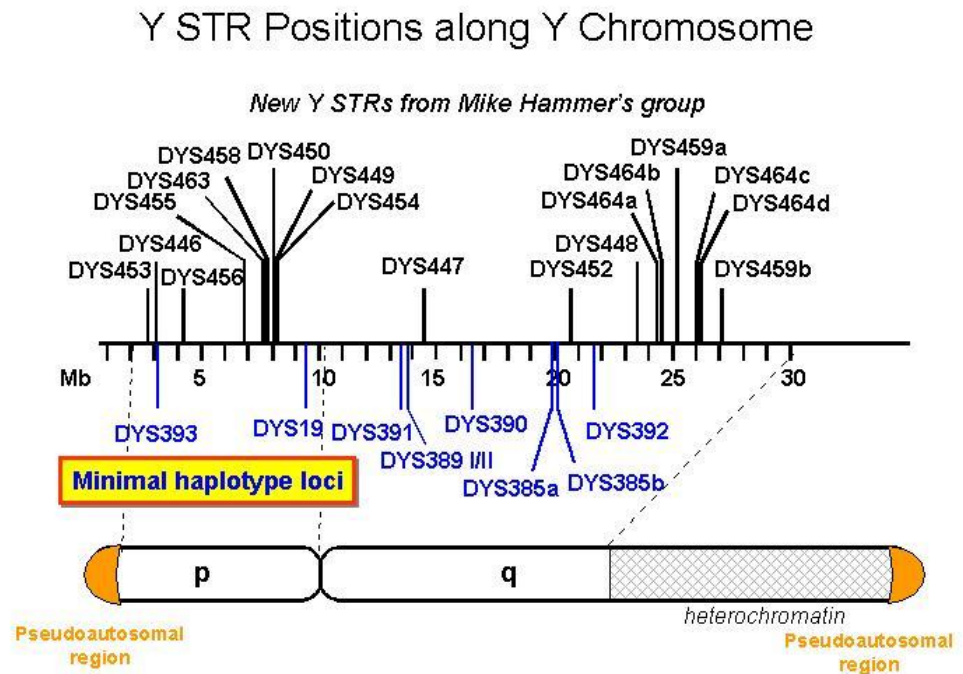
- Genes are the basic units of heredity
- ~20,000 to 25,000 genes
- ~95% of the human genome is non-coding, this non-coding DNA provides a record of ancestral history

Tracing the Paternal Lineage

- STRs
- Haplotypes
- SNPs
- Haplogroups

STRs

- Short tandem repeat
- Short pattern is repeated a number of times in a row (i.e., CAG may be repeated CAGCAGCAGCAG)
- Pattern can range in length from 2 to 16 base pairs
- Typically in the non-coding intron region
- Currently over 10,000 published STR sequences in the human genome



<http://www.cstl.nist.gov/biotech/strbase/ystrpos1.htm>

Haplotypes and Testing

- Complete set of results from multiple sites on a chromosome inherited from one parent
- Y-DNA tests generally examine 10-67 STR markers on the Y chromosome (most labs recommend at least 25 markers)
- Testing results typically provided as number of repeats at certain points on the Y chromosome
 - DYS# --DNA Y-chromosome segment number
 - Number of repeats at this number (e.g., 24)

Example Results

Kit	Surname	Haplo	3 9 3	3 9 0	1 9	3 9 1	3 8 5 a	3 8 5 b	4 2 6	3 8 8	4 3 9	3 8 9 - 1	3 8 9 - 2	3 9 2
1111	Fuller	Q	12	23	13	10	16	17	12	12	13	14	31	14
11178	Fuller	Q	12	23	13	10	16	17	12	12	13	14	31	14

Testing for STRs in the Y chromosome

- Finding connections among anyone names X
- Proving that families of the same surname are related
- Ruling out others with same name as related
- Finding proof of surname modifications
- Proving that everyone name X is related
- Uncovering connections hidden by adoption, illegitimacy, and other circumstances
- Discovering if family tales of famous relatives are true
- Putting traditional genealogical research to the test
- Trying to discover geographic origins in other continent or country

Figure 1-1: Example of a pedigree or ancestral chart

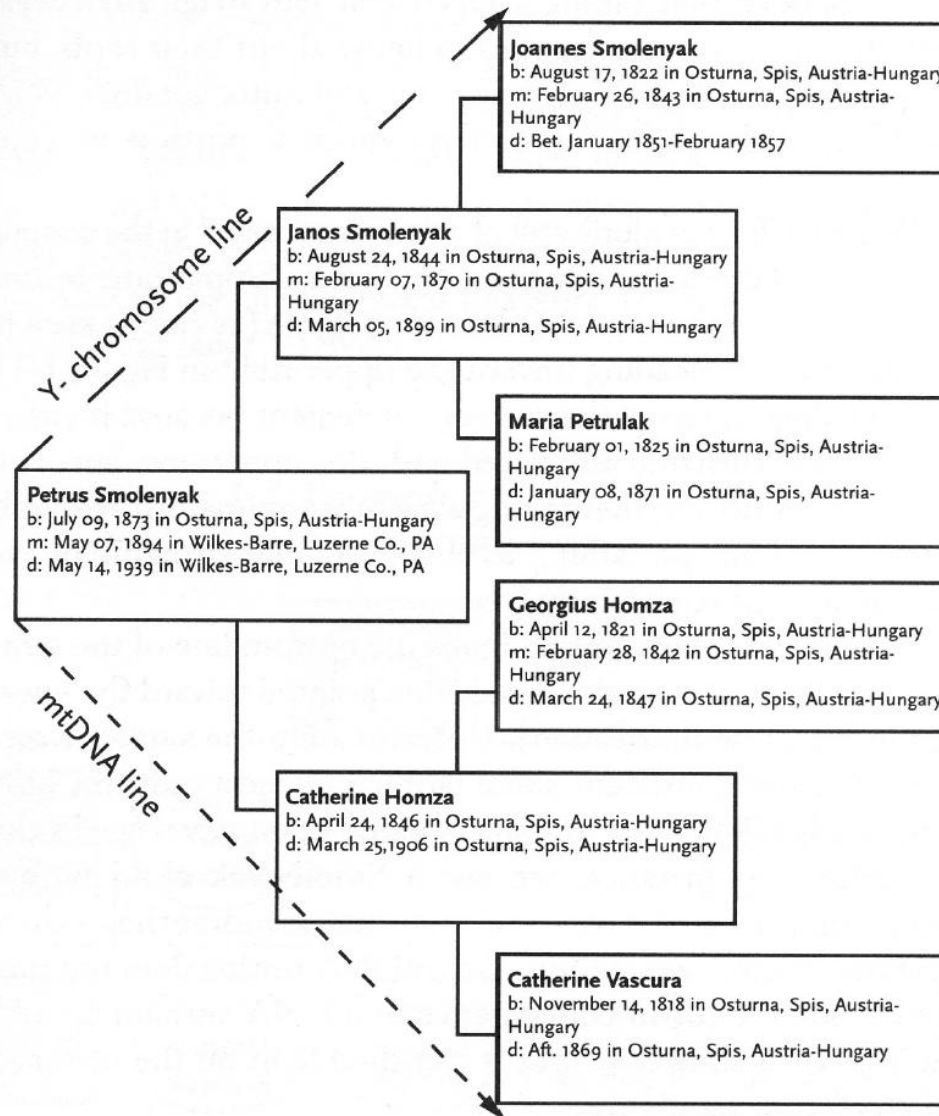
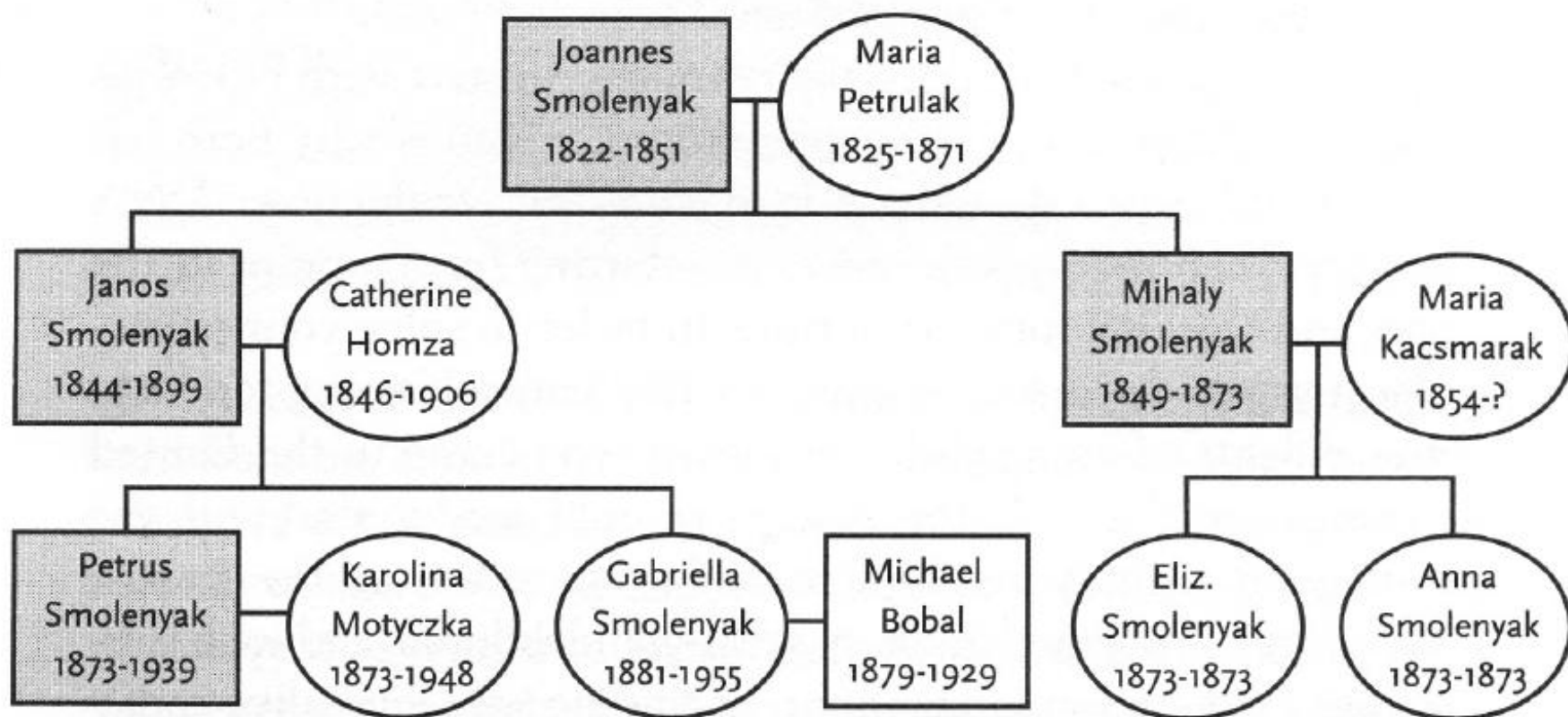


Figure 1-2: Example of a descendency chart or descendant tree



SNPs/UEPs

- Single nucleotide polymorphism/unique event polymorphisms
- Occurs when one base replaces another base (i.e., C>T)
 - Most are benign = not associated with disease
- Humans differ from one another in ~1 in 1000 base pairs (nucleotides) of DNA
- Mutations happen less frequently than in STRs

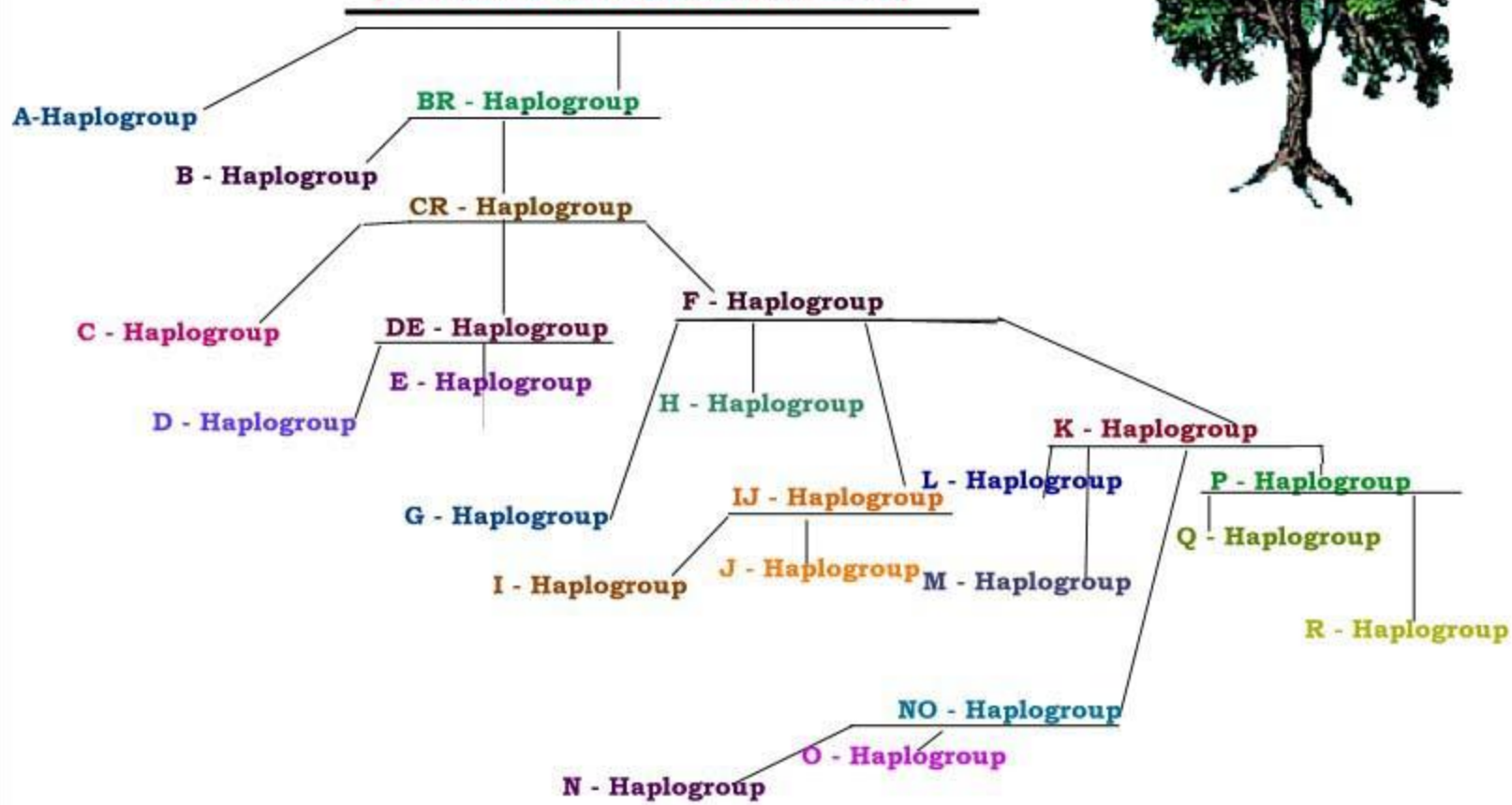
Haplogroups

- Cluster of people who share the same unique polymorphism
- Y-DNA haplogroup is defined as all of the male descendants of the single person who first showed a particular SNP mutation
- Characterize the early migrations of population groups
- Identify a group of people over a period of tens of thousands of years
- A haplogroup assignment indicates which part of the phylogenetic tree of male Homo Sapiens you descend from

Naming of haplogroups

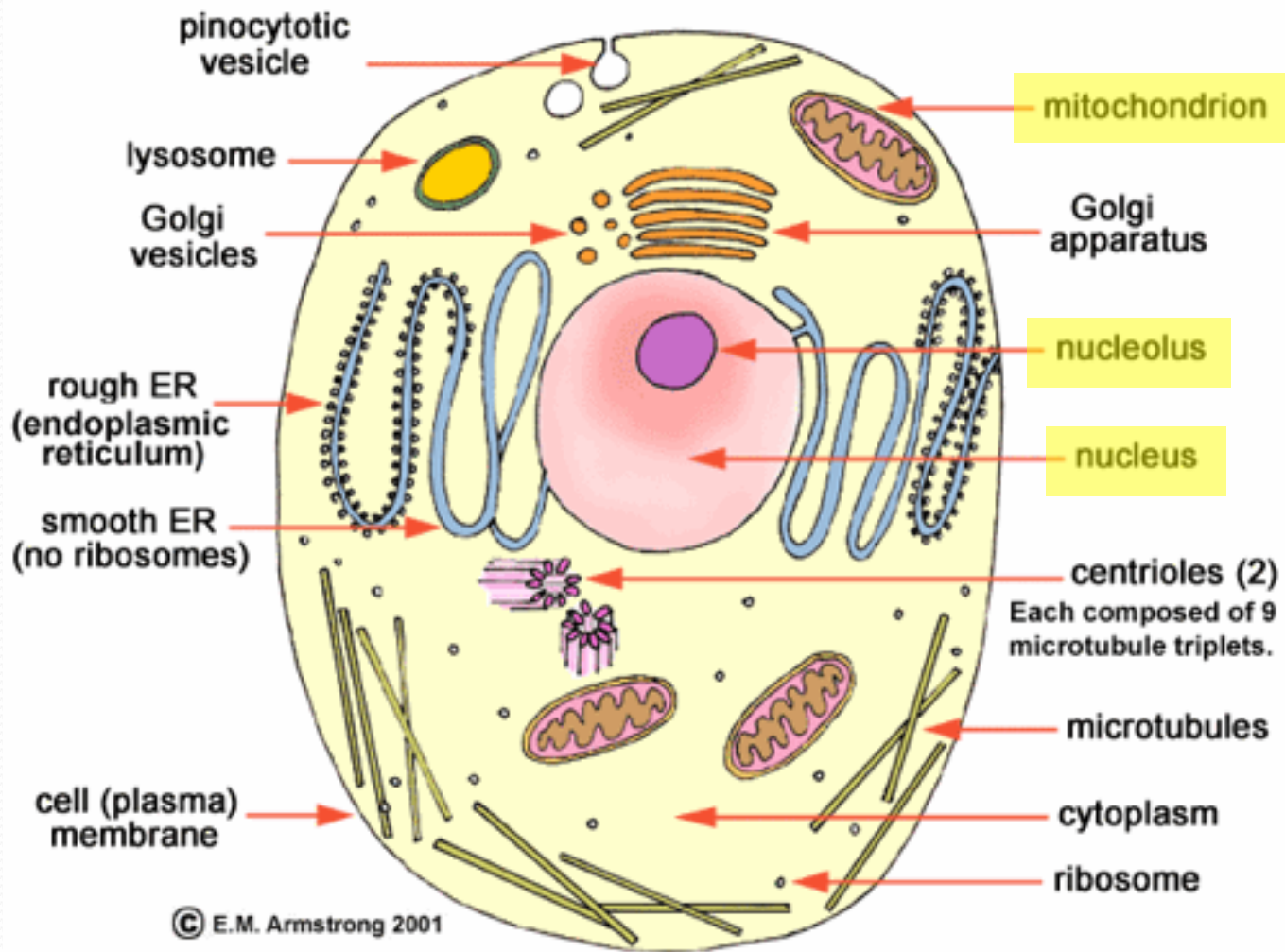
- Named according to capitalized letters of the alphabet
- Subgroups have a numeric name which follows the haplogroup name
- Y Chromosome Consortium (YCC) developed a naming system for the Y-DNA
- Defined 20 major haplogroups, called A through T, which represent the major divisions of human diversity based on SNPs on the Y-chromosome.

**Y chromosome Adam
who belonged to an unknown haplogroup
(Sometimes called Y for Y chromosome)**

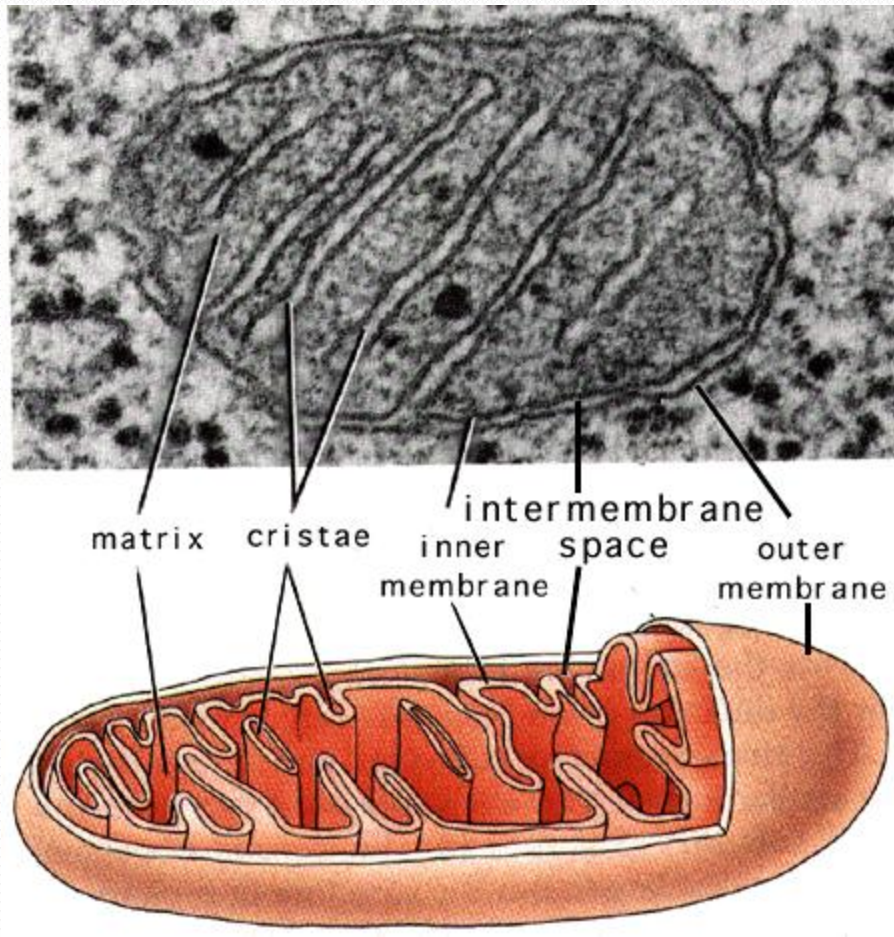


Summary of mutation features

	STRs	SNPs
Mutation rate	Fast	Slow
Historical occurrence	Multiple times	One time (unique event)
Time frame	Genealogical	Archaeological
Application	Connections to specific individuals	Connections to broad geographical areas
Results define the....	Haplotype	Haplogroup
Number of people who share the same results	Small	Large



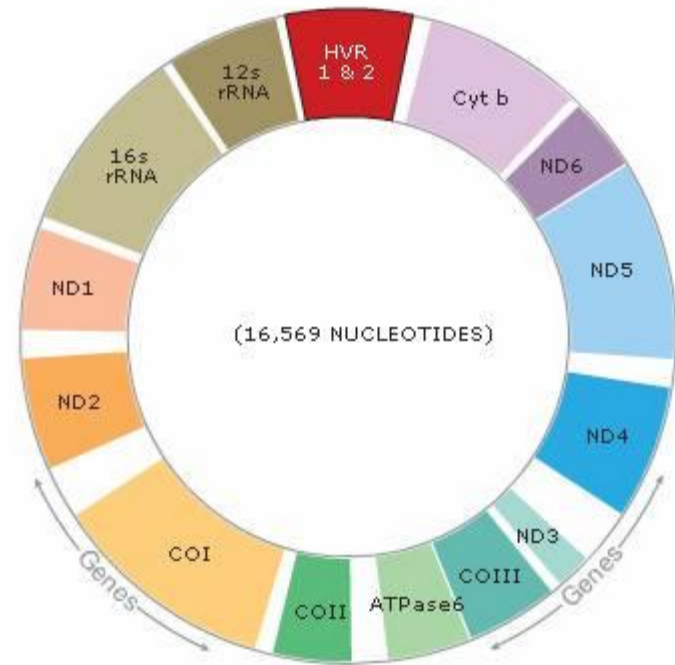
Mitochondria



- Hundreds to thousands of mitochondria in each cell
- Provides the cell with energy
- Also called the “powerhouses” of the cell

Mitochondrial DNA

- Contains 37 genes
- 16,569 bases
- Mitochondria inherited almost exclusively through maternal line during egg formation
- Almost all of the genetic material is coding material

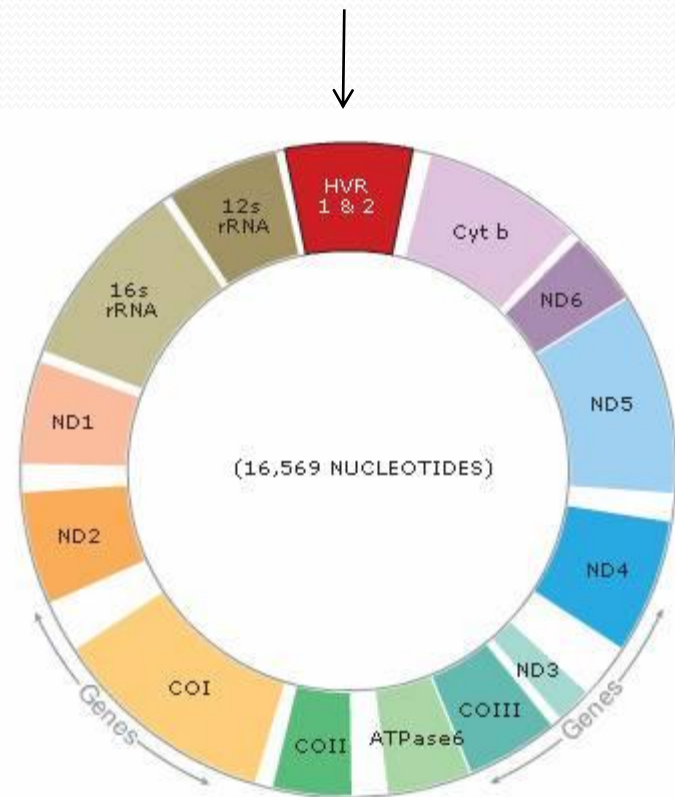


Tracing the Maternal Lineage

- Hypervariable Regions 1 and 2
- Haplotypes
- RFLPs
- Haplogroups

Hypervariable Regions 1 and 2

- ~1100 bases
- Changes in this area of the mitochondrial DNA are not associated with disease
 - Subject to polymorphisms
- Labs sequence several 100 bases in the HVR
 - Typically study HVR1 first to place in broad group
 - 16024-16569
 - Testing HVR2 reduces the number of coincidental markers
 - 00001-00576



<http://clanhaley.com/dna/mtdna.jpg>

Mitochondrial Haplotypes

- Some labs will list actual sequence, while others show differences from the CRS (Cambridge Reference Sequence)

Example Results

Region	HVR ₁	HVR ₂
Differences from CRS	111T,223T,259T,290T,319A,362C	073G,146C,153G

Figure 1-1: Example of a pedigree or ancestral chart

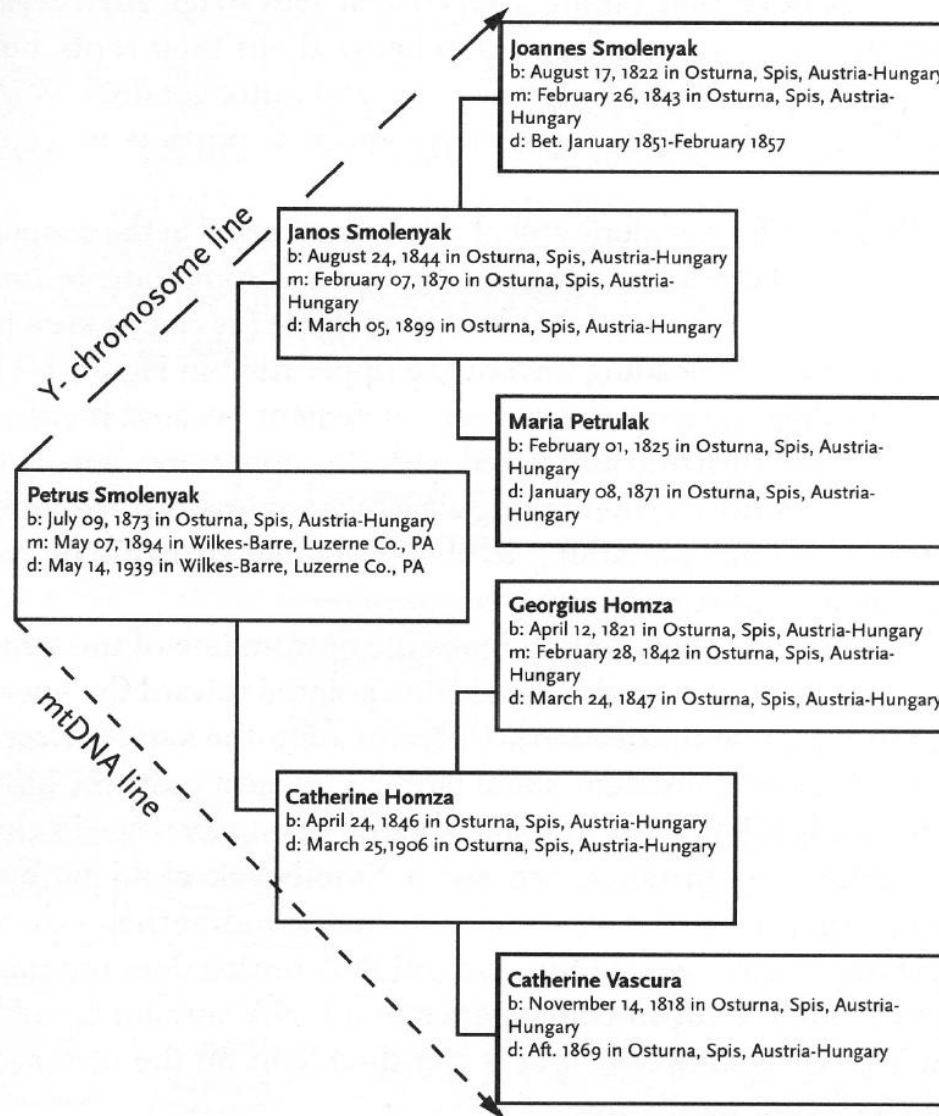
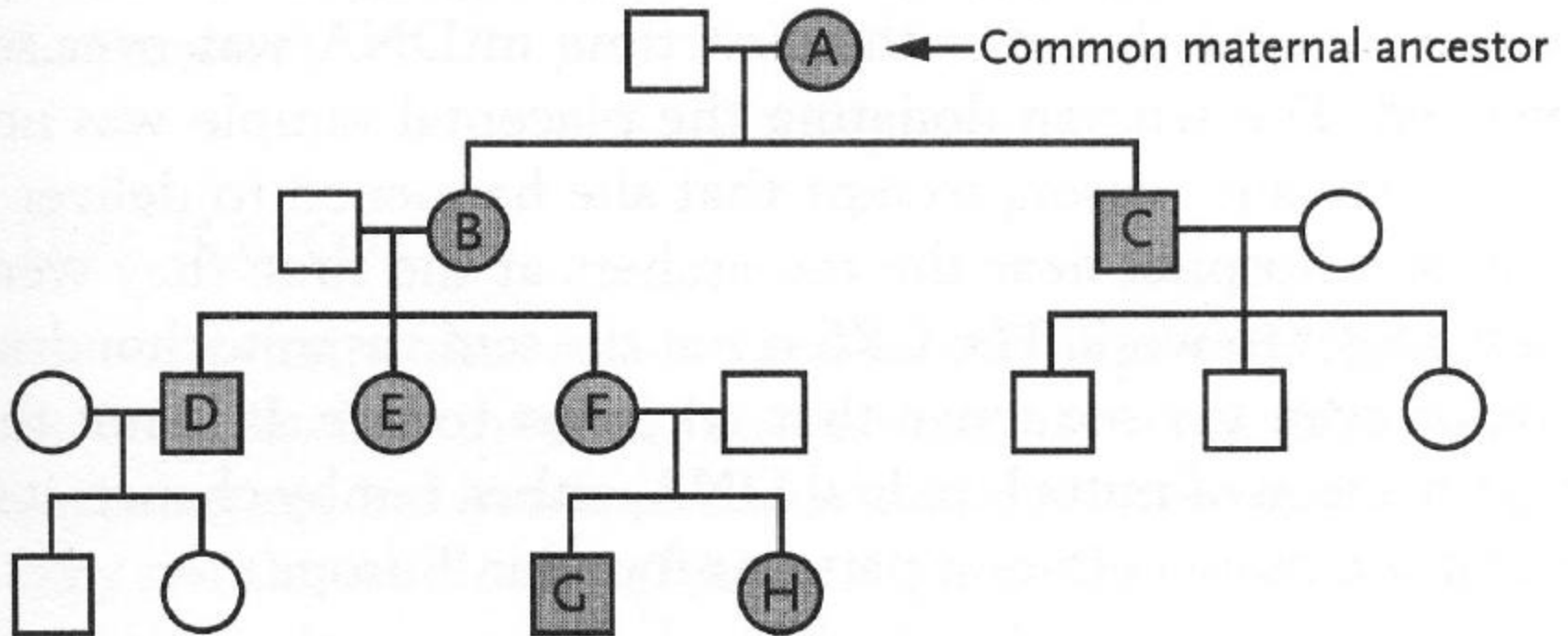


Figure 4-1: Path of descent for A's mitochondrial DNA (mtDNA)



RFLPs

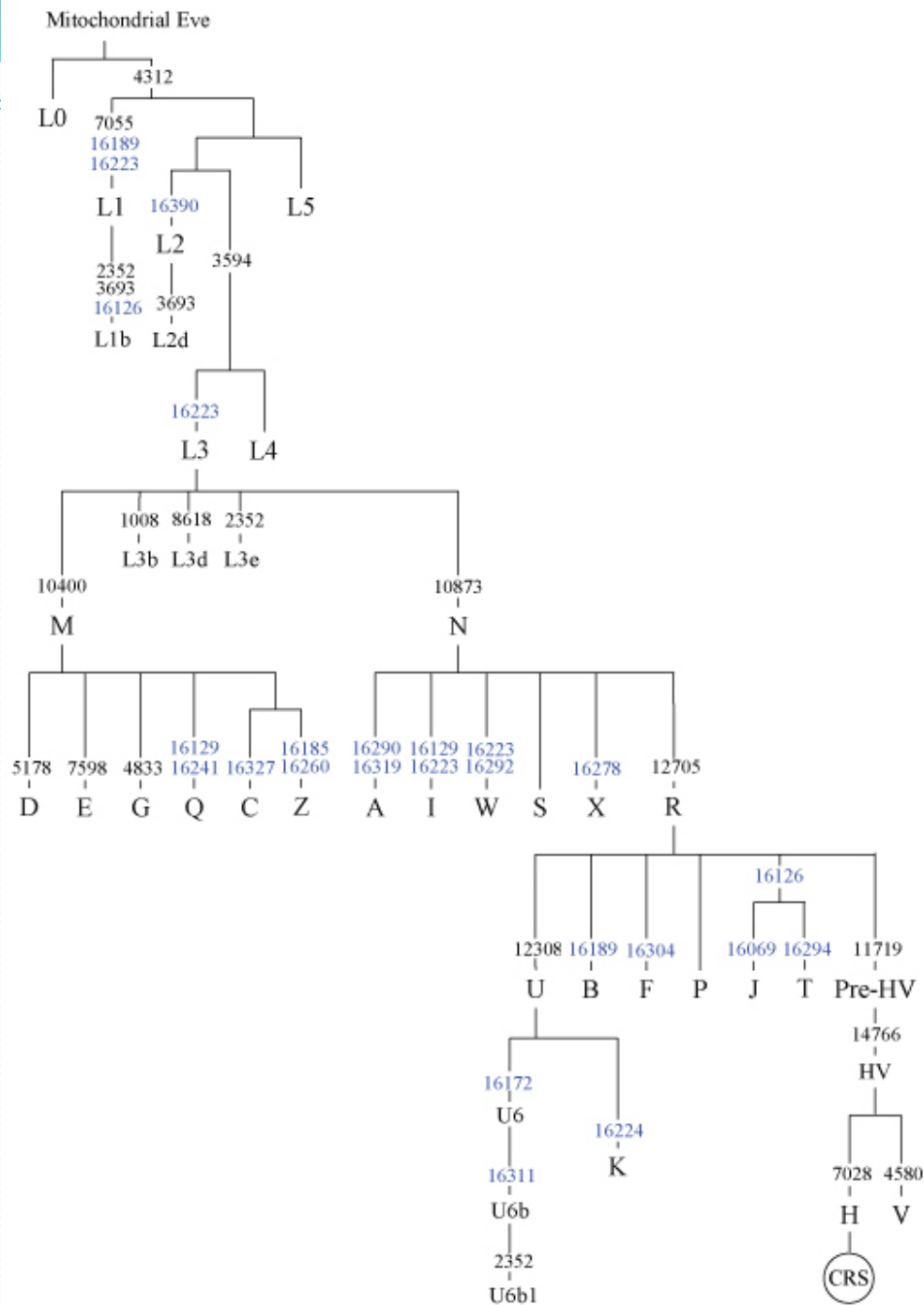
- Restriction fragment length polymorphisms
- Uses series of enzymatic reactions to break the coding region of the mitochondrial DNA into small fragments according to the sequence of the DNA
- If a person happens to have a change at the place the enzyme would normally cut the DNA, this individual will have a bigger size piece or fragment of DNA

Mitochondrial Haplogroups

- All of the female descendants of the single person who first showed a particular polymorphism, or SNP mutation
- Identifies a group who share a common ancestor far back in time

Naming of Mitochondrial Haplogroups

- Named according to capitalized letters of the alphabet
- Named as researchers differentiate different population groups rather than in a hierarchical order
- Mitochondrial haplogroups do not necessarily correlate with Y haplogroups



<http://www.genebase.com/image/mtdnaSnpBackboneChart01.jpg>

Summary of mutation features

	Hypervariable Region (HVR ₁ &2)	Coding Region
Mutation rate	Fast	Slow
Historical occurrence	Multiple times	One time (unique event)
Time frame	Genealogical	Archaeological
Application	Connections to specific individuals	Connections to broad geographical areas
Results define the...	Haplotype	Haplogroup
Number of people who share the same results	Small	Large

Summary of Y-chromosome and mitochondrial features

Compare and Contrast	Y Chromosome	Mitochondrial DNA
Where found	Males only	Males and females
Size	About 60,000,000 bases; only 23,000,000 sequenced	16,569 bases, all sequenced
Inheritance	From father	From mother
Function	Determines gender	Generates energy
Laboratory technique	Length of STRs	Actual sequence
Cost	Less expensive	More expensive
Polymorphism	Number of repeats	Base substitution
Mutation rate/generation	0.002 per STR	0.00001 per base
Sample haplotype format	14-24-12-11-13-13	16192T, 16270T
Haplotype diversity	High	High
Longevity of haplotype	Pattern can last hundreds of years	Pattern can last thousand of years

Genetic Genealogy Testing Companies

Name of Company	Website	Phone Number
Ancestry DNA	dna.ancestry.com	1-800-ANCESTRY
DNA Consultants	dnaconsultants.com	505-473-5155
DNA Heritage	dnaheritage.com	866-736-2362
Family Tree DNA	familytreedna.com	713-868-1438
Family Builder	familybuilder.com	
Gene Tree	genetree.com	866-740-6362
National Geographic Genographic Project	www3.nationalgeographic.com/genographic*	
Oxford Ancestors	oxfordancestors.com	+44 -186-584-7549

*only tests for 12 Y-DNA markers

Questions to Ask When Picking a Testing Company

- What is the turnaround time?
- How responsive is the company to your questions by email or phone?
- What type of report does the company give you? Just your matches? Access to analysis programs?
- Does the company provide a matchmaking service?
- What is the cost and payment options?
- How long will the company retain the samples that are submitted?
- Does the company offer any additional services?

What to do with testing information?

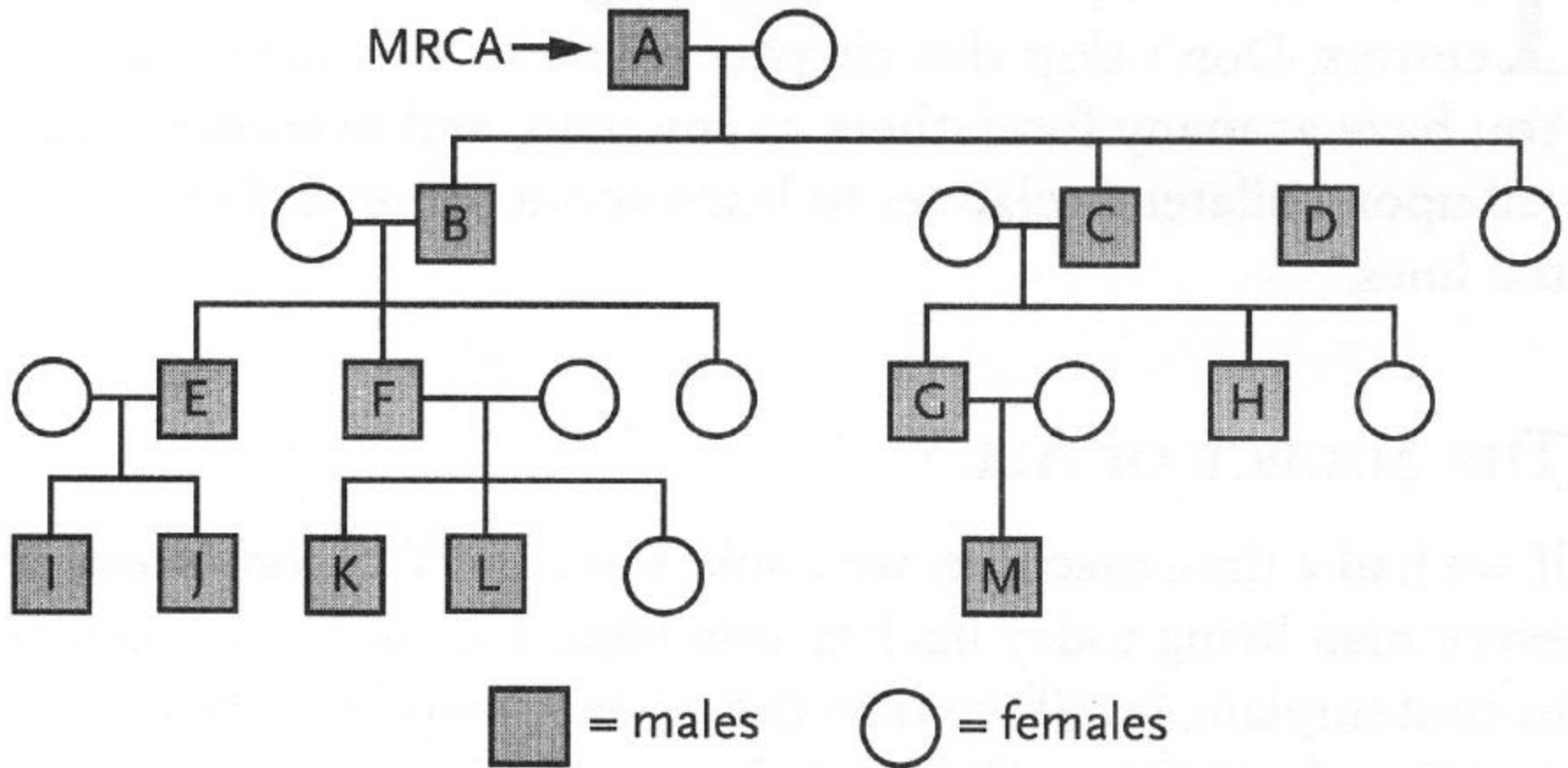
- Find a surname project
 - >1000 projects underway
 - National Genealogical Society's *NewsMagazine*, www.dnalist.net, surname websites
- Launch your own surname project
- Reverse genealogy
 - Identifying possible common ancestors to trace lines from the past to the present
- Broadcasting
 - Locating people and information of interest by making it easier for others to find him/her

Analysis Options

Level of Analysis

	Basic	Intermediate	Advanced
Within Study/Testing Company	Test results/website for your study—seek perfect and close matches only and compare pedigrees; review ready-made reports	Test results/website for your study—cluster all participants; combine with genealogical data; MRCA calculations	Determine ancestral haplotype; display results in network diagrams or genetic distance grids
Beyond Study/Testing Company	N/A	Public access databases/websites	Research technical literature for information pertaining to your haplotype, haplogroup, etc. (i.e., Google, PubMed)

Figure 3-1: Coalescence to the Most Recent Common Ancestor (MRCA)



Suggested Resources to Interpret Testing Results

- Maternal lineage
 - www.mitosearch.org
 - <http://www.kerchner.com/cgi-bin/mtdna.cgi>
- Paternal lineage
 - www.ysearch.org
 - <http://ybase.org>
 - <http://www.yhrd.org/>
 - <http://www.smgf.org/>

Drawbacks of genealogical testing

- Cost
- Privacy issues—what protections does the company have in place?
- Difficulty in interpreting the data
- Identification of non-paternity or undisclosed adoption
- Knowledge of possible medical associations (i.e., correlation between lack of DYS464 markers and infertility)

Suggested Resources to Learn More About Medical/Genetic Genealogy

- Family Tree Magazine (www.familytreemagazine.com)
- The International Society of Genetic Genealogy (www.isogg.org)
- Smolenyak MS & Turner A. (2004). Trace Your Roots with DNA: Using Genetic Tests to Explore Your Family Tree.