Syllabus change

Skipping Coexistence
(for now?)

Readings for next 3 lectures:

Ch. 10.1-10.4, 11.1-11.5
Ch. 12.1-12.3, 13
Unique

Topic 12 – Variation & Map

Luck of the Draw

DNA and the blueprint for life
Genetic Information: a review

Cell Nucleus
Chromosomes
Gene (make protein)
Nucleotide bases (G-C, T-A)
Proteins are made of amino acids

http://publications.nigms.nih.gov/theneugenetics/images/ch1_dnagenes.jpg

http://www.accessexcellence.org/RC/VL/GG/images/dna2.gif
Genetic Information: a review

Physical structure of DNA

1953:
James Watson, Francis Crick
Rosalind Franklin
Genetic Information: a review

Haploid: half the genetic info needed for a full set (humans: 23 is haploid):
- 1 pair chromosomes

Diploid: full set of genetic information (humans: 46 is diploid)
- 2 pairs of chromosomes

Gametes: sex cells (sperm, egg)

Zygote: fertilized embryo (egg + sperm)

Mitosis: division for replication (most cells)

Meiosis: division for variation (sex cells, 2 steps)

Autosomal: non-sex chromosome
Making copies

How does the information (DNA) get used?

Transcription
Deoxyribonucleic acid (DNA) $\rightarrow$ Ribonucleic acid (RNA)

Translation
RNA $\rightarrow$ Amino acids (20) $\rightarrow$ Protein

Protein:

50% of the dry weight of organisms
Thousands of types
structural (muscles, cartilage)
signaling (insulin)
Enzymes (catalyze reactions)
Twins

Monozygotic twins (identical twins)
1 in every 250 live births
Fertilization of a single zygote that splits

Dizygotic twins (fraternal twins)
1 in every 80 live births
Fertilization of two eggs
New variation: Meiosis

Sources of Genetic Variation

1. Haploid cell production (gametes)
   Random combinations of sperm and egg

2. Recombination (Crossing Over)
   Exchange of genes among chromosomes

3. Independent assortment
   Genes are not linked to one another
Possible combinations = $2^n$
- $n$ is the haploid number
- $n = 2$
- $2^2 = 4$

In human, $n = 23$
$2^{23} = 8,388,608$ combinations

**Meiosis**

Diploid precursor

Haploid Gametes
### “n” and Gamete Variations

<table>
<thead>
<tr>
<th>Species</th>
<th>Chromosome Number &amp; Calculation</th>
<th>Genetic Variability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mosquito (<em>Culex pipiens</em>)</td>
<td>$n = 3; 2^3 = 8$</td>
<td></td>
</tr>
<tr>
<td>Toad (<em>Bufo americanus</em>)</td>
<td>$n = 11; 2^{11} = 2048$</td>
<td></td>
</tr>
<tr>
<td>Rice (<em>Oryza sativa</em>)</td>
<td>$n = 12; 2^{12} = 4096$</td>
<td></td>
</tr>
<tr>
<td>Frog (<em>Rana pipiens</em>)</td>
<td>$n = 13; 2^{13} = 8192$</td>
<td></td>
</tr>
<tr>
<td>Cat (<em>Felis domesticus</em>)</td>
<td>$n = 19; 2^{19} = 524,288$</td>
<td></td>
</tr>
<tr>
<td>Human (<em>Homo sapiens</em>)</td>
<td>$n = 23; 2^{23} = 8,388,608$</td>
<td></td>
</tr>
<tr>
<td>Potato (<em>Solanum tuberosum</em>)</td>
<td>$n = 24; 2^{24} = 16,777,216$</td>
<td></td>
</tr>
<tr>
<td>Dog (<em>Cani familiaris</em>)</td>
<td>$n = 39; 2^{39} = 549,755,813,888$</td>
<td></td>
</tr>
<tr>
<td>Water fly (<em>Nymphaea alba</em>)</td>
<td>$n = 80; 2^{80} = 1.2 \times 10^{24}$</td>
<td></td>
</tr>
</tbody>
</table>

Zygototice combinations vastly increase genetic variability!
Possible zygote combinations:

\[ Z = P \times M \]

\[ Z = \text{possible different zygotes} \]

\[ P = \text{possible different paternal gametes} \]

\[ M = \text{possible different maternal gametes} \]

\[ Z = (8.4 \times 10^6) \times (8.4 \times 10^6) \]

\[ = 70 \times 10^{12} \]

\[ 70,000,000,000,000 \]

Your uniqueness is guaranteed!

This is why no two humans are/were/will be alike.
Mendel’s Law

Gregor Mendel (1822-1844)
Austrian Monk, “Father of Genetics”

Studied pea plants
made scientific investigations of plant crosses
Observations led to Mendel’s Law (2)

Law of Segregation
Each gamete receives one copy of gene (confirmed by meiosis)

Law of Independent Assortment
Genes assort independent of each other (eye and hair color not linked)
Recombination at Meiosis I

- Replication of DNA
- Condensation of chromatin
- Recombinant chromatins
- A1/A2 hybrid

Recombination
Cystic Fibrosis

Genetic disease
1: 3,900 births
Respiratory infections
Average lifespan 36 years
Carrier 1 in 31 (Caucasian)
Cystic Fibrosis

Caused by a mutation (copying error) in sequence of a gene (base, G,C,A,T)
Defective gene leads to defective protein (CFTR)
Defective protein allows for excessive mucus production in lungs

Gene 170,000 bases → encodes for a protein of 1,480 amino acids
Cystic Fibrosis: 3 base deletion → protein different
Autosomal recessive disease
Sickle Cell Disease

Genetic disease
1:400 African America births
Carriers
12% in African Americas
0.01% in Caucasian America population

Anemia (low blood cells) and pain
Sickle Cell Disease

Mutation in a single base pair → one amino acid change in protein

Defective gene does not lead to a defective protein (carries oxygen)

Mutation involved with shape of the hemoglobin protein under low oxygen

Autosomal recessive disease
Sickle Cell Disease: Benefit?

Individuals with Sickle Cell trait:
Natural resistance to Malaria (mosquito-borne disease)

Process:
Infected mosquito bites a human
Parasite enters blood cells
The acid produced by the parasite causes blood cell to sickle
Sickle cells are destroyed by body
Sickle Cell Disease: Selection

Individuals with one copy of the gene:
Resistance to Malaria

Individuals with both copies:
Sickle cell Disease

Distributions of malaria and Sickle Cell Disease

http://mathildasanthropologyblog.files.wordpress.com/2008/08/malaria_distribution.jpg
Human Genome Project

Virus genome (1975)
  Fred Sanger
  5,386 bases
  Took 5 years!

Human genome (1991 to 2003)
Goal was to identify all the base pairs and genes in the human genome
Find origins of disease

Two teams: US Government
           Celera (private), Dr. Craig Venter
<table>
<thead>
<tr>
<th>Organisms</th>
<th>Genome</th>
<th>Gene Size</th>
<th>Predicted Gene No.</th>
<th>Actual Gene No.</th>
<th>Coding %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Archeae</td>
<td>1.6 Mb</td>
<td>1 kb</td>
<td>1,660</td>
<td>1,738</td>
<td>100%</td>
</tr>
<tr>
<td><em>E. coli</em></td>
<td>4.6 Mb</td>
<td>1 kb</td>
<td>4,200</td>
<td>4,100</td>
<td>93%</td>
</tr>
<tr>
<td>Yeast</td>
<td>13.5 Mb</td>
<td>2 kb</td>
<td>6,750</td>
<td>6,034</td>
<td>89%</td>
</tr>
<tr>
<td>Worm</td>
<td>97 Mb</td>
<td>2 kb</td>
<td>48,000</td>
<td>19,900</td>
<td>39%</td>
</tr>
<tr>
<td>Arabidopsis</td>
<td>100 Mb</td>
<td>2 kb</td>
<td>50,000</td>
<td>25,000</td>
<td>50%</td>
</tr>
<tr>
<td>Fruit Fly</td>
<td>165 Mb</td>
<td>2 kb</td>
<td>82,500</td>
<td>13,601</td>
<td>16%</td>
</tr>
<tr>
<td>Human</td>
<td>3,000 Mb</td>
<td>2 kb</td>
<td>1,650,000</td>
<td>30,000</td>
<td>1.5%</td>
</tr>
</tbody>
</table>

Non-coding size increases with Evolutionary lineages (evidence of common descent)
Non-coding genes: Interruption mechanisms

Without interruption - **Exons**

I had fun with my friends. It was a great summer.

**Interruption Between Genes**

Non-coding intervening sequence

I had fun with my friends. It was a great summer.

**Interruptions Within Genes**

Non-coding sequences - **Introns**

I had fun with my friends. It was a great summer.

**Interruptions Between and Within Genes**

I had fun with my friends. It was a great summer.
Different Genome Structures

- **E. Coli** - 4.6 Mb; 4100 genes; 93%
- **Yeast** - 13.5 Mb; 6000 genes; 89%
- **Fly** - 165 Mb; 13,600 genes; 16%
- **Human** – 3,300 Mb; 30,000 genes; 2%
Non-coding DNA Puzzle

1.5% of genes code for protein
What about the other 98.5%?
Some are remnants of old inactive genes (Pseudogenes)
Some are short repeats (TATATATA)
Mobile genetic elements (transposons, “jumping genes”) (50% of genome): parasites

Their function?

gene regulation
faulty DNA replication known as gene duplication
functions yet to be discovered
The Punnett Square

<table>
<thead>
<tr>
<th></th>
<th>H</th>
<th>h</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>HH</td>
<td>Hh</td>
</tr>
<tr>
<td>H</td>
<td>Hh</td>
<td>hh</td>
</tr>
</tbody>
</table>

Dominant
Recessive

Homozygous

Eye color (E):
Dominant = brown
Recessive = blue

EE = brown
Ee = brown
ee = blue
Types of Genetic Disorders

Single gene disorders
- Autosomal: both parents give a copy of the defective gene
- Sex-linked: defective gene on one sex chromosomes
  - XX female
  - XY male

Chromosomal disorders
- extra/missing entire chromosome
Single-Gene Disorders

**Autosomal Disorders**
- Huntington disease
- Hereditary colorectal cancer
- Cystic fibrosis
- Tay-Sachs disease
- Spinal muscular atrophy
- Sickle cell anemia

**Sex-linked Disorders**
- Hemophilia A
- Duchene muscular dystrophy
- Color blindness
<table>
<thead>
<tr>
<th>Chromosome Disorders</th>
<th>Chromosome Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Down Syndrome</td>
<td>Trisomy 21</td>
</tr>
<tr>
<td>Triple X Syndrome</td>
<td>Trisomy X</td>
</tr>
<tr>
<td>Kleinfelters Syndrome</td>
<td>XXY</td>
</tr>
<tr>
<td>Turner Syndrome</td>
<td>XO (only one sex chromosome)</td>
</tr>
</tbody>
</table>
Timing of Genetic Disorders

Early Onset disorders
Occur early in life
Usually shorten life-span
Many autosomal recessive
example: Tay-Sachs

Late Onset Disorders
Occur late in life
Some autosomal dominant
example: Familial Alzheimer’s
Tay-Sachs

Autosomal recessive (25% chance of infected child)
Symptoms start about 1 year
Very rare
Single base pair error, causes malformed protein (enzyme)
Missing enzyme: breaks down fatty tissue in brain
Build-up of fatty tissue causes neuron death
At-risk groups (1 in 30 carrier):
  Ashkenazi Jews ("German Jews")
  Cajun
  French Canadian
General public: 1 in 300
Tay-Sachs Screening

Carrier testing: detect whether an individual is a carrier (high risk groups)

Prenatal testing: has the fetus inherited two copies?

Success?

Highest at-risk group: Ashkenazi Jews ("German Jews")

Since screening was possible, 90% reduction in Tay-Sachs cases
Next time: Development

Read: 197-199
   597
   29.4