Cell Cycle Researchers Receive 2001 Nobel Prize in Medicine

• Dr. Leland Hartwell
  Fred Hutchinson Cancer Research Center, Seattle, WA
  Discovered and Determined the Function of the >100 Cell Division Cycle (cdc) Genes (includes cyclins, cdks)
  Which Drive the Cell Cycle

• Dr. Tim Hunt
  • Imperial Cancer Research Fund, London, UK
  • Discovered & Determined the Function of Cyclins

• Dr. Paul Nurse
  • Imperial Cancer Research Fund, London, UK
  • Discovered & Determined the Mechanism & Function of Cyclin-Dependent Kinases

What Makes a Model Organism – Especially for Genetics?

<table>
<thead>
<tr>
<th>ORGANISM</th>
<th>GENERATE MUTANTS</th>
<th>GENERATION TIME</th>
<th>BIOCHEM</th>
<th>CELLBIO</th>
<th>GENE TRANSFER</th>
<th>DEV</th>
</tr>
</thead>
<tbody>
<tr>
<td>YEAST &amp; S. cerevisiae</td>
<td>YES</td>
<td>V. SHORT</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>NEMATODE &amp; C. elegans</td>
<td>YES</td>
<td>V. SHORT</td>
<td>LIMITED</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>FRUIT FLY &amp; D. melanogaster</td>
<td>YES</td>
<td>V. SHORT</td>
<td>LIMITED</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>MUSTARD &amp; A. thaliana</td>
<td>YES</td>
<td>SHORT</td>
<td>LIMITED</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>FROG &amp; X. laevis</td>
<td>LIMITED</td>
<td>V. LONG</td>
<td>YES</td>
<td>YES</td>
<td>LIMITED</td>
<td>YES</td>
</tr>
<tr>
<td>MOUSE &amp; M. domestica</td>
<td>LIMITED</td>
<td>LONG</td>
<td>LIMITED</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>HUMAN &amp; H. sapiens</td>
<td>NO</td>
<td>V. LONG</td>
<td>LIMITED</td>
<td>YES</td>
<td>NO</td>
<td>NO</td>
</tr>
</tbody>
</table>
Mendel Experimentally Utilized Phenotypic Diversity, Large # of Progeny, Ease of Manipulation & Short Generation Time in *Pisum sativum* To Elucidate Principles of Inheritance & Establish Genetics as a Science 1st Use of a Model Experimental Organism

### 10.1 Mendel’s Results from Monohybrid Crosses

<table>
<thead>
<tr>
<th></th>
<th>Dominant</th>
<th>Reccessive</th>
<th>Total</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spherical seeds × Wrinkled seeds</td>
<td>5,474</td>
<td>1,850</td>
<td>7,324</td>
<td>2.96:1</td>
</tr>
<tr>
<td>Yellow seeds × Green seeds</td>
<td>6,022</td>
<td>2,001</td>
<td>8,023</td>
<td>3.01:1</td>
</tr>
<tr>
<td>Purple flowers × White flowers</td>
<td>705</td>
<td>224</td>
<td>929</td>
<td>3.15:1</td>
</tr>
<tr>
<td>Inflated pods × Constricted pods</td>
<td>882</td>
<td>299</td>
<td>1,181</td>
<td>2.95:1</td>
</tr>
<tr>
<td>Green pods × Yellow pods</td>
<td>428</td>
<td>152</td>
<td>580</td>
<td>2.82:1</td>
</tr>
<tr>
<td>Axial flowers × Terminal flowers</td>
<td>651</td>
<td>207</td>
<td>858</td>
<td>3.14:1</td>
</tr>
<tr>
<td>Tall stems × Dwarf stems</td>
<td>787</td>
<td>277</td>
<td>1,064</td>
<td>2.84:1</td>
</tr>
</tbody>
</table>

**Characters = Genes:** Seed morphology, color; Flower color, Pod morphology etc.  
**Traits = Alleles:** Spherical vs wrinkled; Yellow vs green; Purple vs white; Infl. vs constr. etc.

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**Mendel’s 1st – The Monohybrid Cross**

**Question:** When two strains with contrasting traits breed, are their characteristics irreversibly blended in succeeding generations?

**Method:**
- P seeds
- P plants
- Growth
- Pollen
- Maturation
- F1 seeds from P plant
- F1 plant
- Growth
- Pollen
- F2 seeds from F1 plant
- F2 100% Spherical
- F2 75% Spherical
- 25% wrinkled

**Results:**

**Conclusion:** There is no irreversible blending of characteristics. A trait can reappear in succeeding generations.
"True-Breeding" Individuals
Homozygous SS or ss
Always exhibit same phenotype when “selfed” or “self-crossed”

Units of Inheritance
Present as Discrete Particles = Gene
Units Occur in Pairs = Alleles

F₁ Individuals are Heterozygous Ss
Do not breed true

Mendel’s 1st law
Law of Segregation
Alleles Segregate Independently
Each Gamete Receives 1 Allele
Alleles Are Combined Randomly
In Zygote

Phenotype = Trait
e.g., Spherical vs wrinkled 3:1

Genotype = Genetic Constitution
e.g., SS, Ss, ss
1 : 2 :1

Meiosis Explains Independent Segregation Of Alleles

Locus = Chromosomal
Location of the Seed gene
S & s are the 2 alleles of this gene

Homologous Chromosomes
Separate in Meiosis I
Alleles Segregate SS & ss

Sister Chromatids
Separate in Meiosis II
Each Haploid Gamete
Receives 1 allele S or s
**Test Cross aka Back Cross**
Distinguishes Between Homozygous and Heterozygous Genotypes for Dominant Phenotypes

A recessive phenotype Can only arise from a Homozygous genotype

**Mendel's 2nd law: The Dihybrid Cross**

- **Parental (P1) generation**: Sy/Yy
- **F1 generation**: SsYy

**Segregation of S from s is Independent from Segregation of Y from y**

- **F2 generation**:
  - 2 Parental: Sphere/Yellow (9)
  - Wrinkled/Green (1)
  - 2 Recombinant: Sphere/Green (3)
  - Wrinkled/Yellow (3)

**F2 Ratio of 9:3:3:1**

**Mendel's 2nd law:**

- **Law of Independent Assortment**
  - Alleles of Different Genes
  - *Almost always assort Independently of one another*

**Note**: This applies To genes on Different Chromosomes but Not necessarily to genes On the Same chromosome Genes on the same Chromosome are linked And subject to Recombination in meiosis I
Meiosis Explains Independent Assortment Of Alleles (On Different Chromosomes) – Caveat Emptor

Chromosome w/ S or s allele Does not determine where Chromosome w/ Y or y allele goes

Chromosome w/ Y or y allele Does not determine where Chromosome w/ S or s allele goes

Non-homologous Chromosomes Behave Independently

Four haploid gametes

D. melanogaster – An Ideal Genetic System to Illustrate:

• Genes on the Same Chromosome Are Physically Linked & May Not Sort Independently

• Genes on Homologous Chromosomes Can Recombine During Meiosis I

• Genetic Maps Can be Derived from Recombination Frequencies
If Linkage Were Absolute
i.e. B/b & Vg/vg "co-localized" to the same locus, then no Recombinant progeny would be observed as below

This is not the outcome!
Instead, one observes recombinant phenotypes 17% of time - Recall
50% expected if unlinked & 0% if Absolutely Linked
Recombination between linked genes on homologous chromosomes during Meiosis I explains why they do not sort independently.

Recombination between a given pair of linked genes occurs at a consistent, reproducible frequency.

Distance Determines Recombination Frequency
The further apart 2 linked genes are located, the greater the likelihood that a crossover event will occur between them. (up to a limit)

Conversely, 2 genes which are located close together have a reduced likelihood that a crossover event will occur between them.

Therefore, can use recombination frequencies to map relative positions of genes on a given chromosome.