SEP 1995
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GRANDE PRAIRIE REGIONAL COLLEGE

SCIENCE AND TECHNOLOGY DEPARTMENT
BIOLOGY INSTRUCTIONAL GROUP

Course : **Biology 2070 - Molecular Genetics and Heredity**

Prerequisites : Biology 1070 (Note: Students may not obtain credit for Genetics 1970 and Biology 2070)

Sections : One lecture section and one lab section will be offered in the winter term.

Lecture Section	A3	MWF	- 14:00-14:50
Lab Section	L1	T	- 15:00-17:50

Transferability :
U of A - Biology 207
U of C - TBA
U of L - TBA

Instructor :
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Description : Biology 2070 is a course dealing with both classical and molecular genetics. The chromosomal and molecular basis for the transmission and function of genes will be covered as well as the construction of genetic and physical maps of genes and genomes. Molecular biology strategies for isolation of specific genes and examples of regulatory mechanisms for the expression of the genetic material in both prokaryotes and eukaryotes will also be discussed

Requirements :
i) Attendance of lectures/labs and completion of course work as outlined in the Academic Guidelines of the College.
ii). Midterm Exam
iii). Final Lecture Exam
iv) Final Lab Exam
v). Lab Reports and Problem Sets

Evaluation :

Lab Assignments/Problem Sets	- 20%
Midterm Exam	- 30%
Final Lab Exam	- 10%
Final Exam	- 40%

Resources :

Textbook	- TBA (Note: The textbook will be chosen after consulting the BI 207 course instructors at U of A.)
Lab Manual	- U of A Biology 207 Lab Manual

Lecture 1. Introduction, evidence that genes encode proteins.

Concepts:

1. Genes encode proteins that often function in a pathway whose end-product is useful to the cell.
2. Beadle and Tatum demonstrated the relationship between genes and proteins by studying biochemical mutants in Neurospora.
3. Complementation analysis is useful to determine if the same genes are affected in different mutant organisms.

Lecture 2. DNA

Concepts:

1. DNA exists primarily as a double helical structure. The strands in the helix have sugar-phosphate backbones that are held together by hydrogen bonds between correctly paired bases.
2. A very et al., demonstrate that DNA is the genetic material.
3. Meselson and Stahl show that DNA replicates by a semi-conservative mechanism.

Lecture 3. DNA replication I.

Concepts:

1. Kornberg isolates DNA polymerise I and shows that DNA can be synthesized in vitro.
2. Several DNA polymerases exist in the cell. These usually have specialized functions and contain several different enzymatic activities.
3. Replication of DNA proceeds in a semi-discontinuous fashion.

Lecture 4. DNA replication II.

Concepts:

1. DNA replication must be primed by short RNA oligonucleotides
2. DNA replication involves many other factors including single-stranded DNA binding proteins, helicase, and gyrase.

Lecture 5. Mutation I.

Concepts.

1. Various mutagenic agents damage DNA in different ways. Mutations can affect a single base-pair of DNA or large segments of DNA.
2. There are different pathways to the establishment of heritable mutations in DNA.
3. Mutations and evolution.

Lecture 6. Mutation II.

Concepts:

1. Cells have the ability to undergo DNA repair in order to counteract damage done to DNA.
2. There are many different enzymatic pathways for reversing damage done to DNA.

Lecture 7. Mutation III.

Concepts:

1. Mutations in genes often result in non-functional gene products.
2. Mutations that affect genes encoding proteins can be classified as missense, nonsense, or frameshift mutations depending on the affect they have on the protein.
3. The phenotypic affect of some mutations can be suppressed by mutations in other genes.

Lecture 8. Chromosome structure and genome organization.

Concepts:

1. Chromosome number is specific for a given species. Chromosomes have different structures in different organisms. In organisms with a diploid phase in their life cycle, the chromosomes exist in homologous pairs.
2. Chromosomes can be classified according to their physical structure.

Lecture 9. Meiosis I.

Concepts.

1. During meiosis the amount of genetic material and the number of chromosomes are reduced to the haploid amount.
2. The process of meiosis occurs in distinct phases which can be observed and described.
3. The occurrence of crossing-over and the random segregation of chromosomes during meiosis insures genetic diversity

Lecture 10. Meiosis II.

Concepts

1. Genes exist on chromosomes and their behaviour during meiosis can thus be related to the behaviour of chromosomes
2. Tetrad analysis in certain fungi is an important tool for the analysis of the behaviour of chromosomes and genes during meiosis

Lecture 11. Monohybrid and dihybrid crosses.

Concepts:

1. The behaviour of genes and chromosomes through meiosis can be used to explain the ratios of offspring observed in genetic crosses.
2. When organisms are crossed, the alleles found in the parents may be found in different combinations in the offspring due to random segregation of chromosomes into gametes during meiosis.
3. Dominant alleles of genes mask the affect of recessive alleles even if both occur in the same cell or organism.

Lecture 12. Trihybrid crosses and testcrosses.

Concepts:

1. Genetic crosses can be analyzed with respect to any number of traits.
2. The number of different genotypes and phenotypes can be predicted for crosses involving a known number of genes.
3. Testcrosses are useful in genetic analysis.

Lecture 13. Multiple alleles, co-dominance.

Concepts:

1. Genes may have many more than two alleles.
2. Alleles of genes do not always exhibit simple dominance/recessiveness relationships. Sometimes the phenotype of both alleles are expressed in the same cell or organism.
3. The ABO blood system in humans provides an example of both multiple alleles and co-dominance.

Lecture 14. Gene interactions.

Concepts:

1. Different alleles of genes may have complex interactions in a cell or organism.
2. The ratio of different phenotypes in a dihybrid cross may be affected if the two genes examined in the cross affect the same pathway. The concept of epistasis explains how the affect of one gene can mask the affect of another.
3. Epistasis can be observed in biochemical pathways or single transduction pathways.

Lecture 15. Sex chromosomes and sex linkage.

Concepts:

1. Sex-determination in higher eukaryotic organisms is associated with a pair of non-homologous chromosomes, the sex chromosomes.
2. Genes found on the sex chromosomes exhibit distinctive behaviour in genetic crosses.

Lecture 16. Karyotype variation I.

Concepts:

1. Errors during meiosis can result in non-disjunction of chromosomes so that the distribution of chromosomes is not equitable in the gametes. This results in gametes carrying more or fewer than the normal complement of chromosomes.
2. Fertilization events involving abnormal gametes results in zygotes with abnormal chromosome numbers.
3. In humans and other organisms, abnormal chromosome number can result in incomplete development of the embryo or phenotypically altered individuals.

Lecture 17. Karyotype variation II.

Concepts:

1. Chromosomes can undergo physical rearrangements of DNA.
2. Rearranged chromosomes may not pair properly during meiosis.
3. Chromosome rearrangements and their phenotypic consequences in humans.

Lecture 18. Genetic linkage

Concepts:

1. Genes that are located on the same chromosome are sometimes separated during meiosis as the result of crossing-over.
2. Genes that are located in close proximity to each other exhibit genetic linkage. This was demonstrated by the work of Bateson, Punnet, and Morgan.
3. Sturtevant developed methods for mathematically describing the physical relationships between linked genes using recombination frequencies.

Lecture 19. Genetic mapping, 3-point cross

Concepts:

1. A testcross involving three linked genes serves as an example for the construction of a genetic map using recombination frequencies.

Lecture 20. Fine structure mapping, intragenic recombination.

Concepts:

1. Analysis of genetic crosses involving large number of progeny can result in very refined genetic maps and reveal linkage relationships between genes that are very close together on a chromosome.
2. Using bactyeriophage, Benzer shows that crossing-over can occur between mutations in the same gene.
3. Crossing-over occurs between adjacent nucleotides in the DNA.

Lecture 21. Physical maps of genes.

Concepts:

1. Using restriction enzymes a physical map of a segment of DNA can be developed.
2. It is relatively easy to construct physical maps of small DNA molecules such as bacterial plasmids or discrete fragments of DNA.

Lecture 22. Isolation of genes.

Concepts:

1. Discrete pieces of DNA isolated from any organism are replicated in bacteria if they are inserted into a bacterial plasmid.
2. Genes encoding specific functions can often be isolated by complementation of a mutant phenotype using a library or bank of wild-type genes. Mutant cells are transformed with the entire library of genes and plated on a selective medium so that only cells receiving the wild-type version of the mutant gene will grow.

Lecture 23. Structure of eukaryotic genes

Concepts:

1. Hybridization studies between eukaryotic mRNAs and the genes encoding those mRNAs revealed that the genes contain extra sequences that intervene between regions found in the mature mRNA
2. Genes in eukaryotes are usually not present as contiguous coding sequence. Rather, they contain exons of coding sequence separated by regions of non-coding sequence called introns
3. Complex enzymatic mechanisms exist to remove introns prior to translation of eukaryotic mRNAs.

Lecture 24. Isolation of non-selectable genes I.

Concepts:

1. Some genes cannot be isolated by complementation of a mutant phenotype.
2. The isolation of such genes usually proceeds from examination of libraries containing the gene of interest.
3. Gene libraries can be constructed in a variety of vectors. Different vectors are characterized by the amounts of foreign DNA that is contained in a single clone. Plasmid vectors typically contain 1 to 10 kb of foreign DNA, phage vectors up to 25 kb, cosmid vectors up to 45 kb, and YAC vectors up to and exceeding 1000 kb.

Lecture 25. Isolation of non-selectable genes II.

Concepts:

1. If a gene from a well-conserved gene family has been cloned in one organism, this clone can often be used as a heterologous probe to isolate the related gene form a library containing the DNA of another organism.
2. Probes for specific genes can also be constructed by reverse translation of the amino acid sequence of a protein.

Lecture 26. Isolation of non-selectable genes III.

Concepts:

1. Non-selectable genes in the genome of an organism can be isolated by chromosome "walking" if a nearby gene has been cloned. This requires probing a library with the cloned gene and proceeding in steps from clones identified with each previous probe

Lecture 27. Locating genes in large genomes.

Concepts:

1. Restriction fragment length polymorphisms (RFLPs) can be used to map genomes.
2. RFLPs and pedigrees can be used to map genes when no crosses can be performed.

Lecture 28. Gene regulation in prokaryotes 1.

Concepts.

1. Genes of the trytophan (trp) operon in E. coli encode proteins required for the biosynthesis of tryptophan.
2. The synthesis of trp biosynthetic enzymes is controlled by the presence of tryptophan in the medium.
3. Mutations in certain genes result in altered regulation of the synthesis of trp enzymes.

Lecture 29. Gene regulation in prokaryotes II.

Concepts:

1. In E. coli, genes are transcribed by RNA polymerase, which recognizes a promoter sequence upstream of the genes to be transcribed. Transcription and translation are coupled. Transcription terminates at a specific sequence downstream of the coding sequences.
2. The major level of control of trp biosynthetic enzyme synthesis occurs at the level of transcription. This is achieved by the binding of a regulatory protein that is active only when bound to tryptophan. Binding of the protein at the trp operator site prevents RNA polymerase binding.
3. Mutations can affect the site of RNA polymerase binding or the site of binding of the regulatory protein.

Lecture 30. Gene regulation in prokaryotes III.

Concepts:

1. There are secondary levels of control in the trp operon.
2. Attenuation controls trp enzyme synthesis by utilizing ribosomes and RNA. Secondary structures in the mRNA leader sequence to respond to changing levels of charged tRNA-tryptophan.

Lecture 31. Gene expression in prokaryotes.

Concepts:

1. Nonsense mutations that occur in the early genes of an E. coli operon often decrease expression of downstream genes. This phenomenon has been called polarity.
2. Polarity can be explained by the premature termination of transcription once transcription and translation are uncoupled.

Lecture 32. Regulation of eukaryotic genes, the globin system I.

Concepts:

1. Human adult hemoglobin consists of two different subunt is assembled as a tetramer with the structure $alpha_2beta_2$
2. Hemoglogins vary through development. The early human embryo contains only a hemoglobin with the structure $zeta_2epsilon_2$, where zeta and epsilon are related to alpha and beta, respectively. The embryonic form is soon replaced by the fetal form which has the structure $alpha_2gamma_2$, where gamma is different beta-like subunit.

Lecture 33. Regulation of eukaryotic genes, the globin system II.

Concepts:

1. Human hemoglobin genes are arranged in two developmentally ordered clusters. The genes specifying the alpha- and beta-like subunits in mammals form two different gene clusters on separate chromosomes.
2. The expression of the specific genes required at a certain point in development is achieved through temporal and tissue specific regulation.

Lecture 34. Regulation of eukaryotic genes, the globin system III.

Concepts:

1. Specific DNA sequences, usually located upstream of the coding sequence, control the expression of genes in eukaryotes.

Lecture 35. Genetic control of spatial patterns.

Concepts:

1. The controlled expression of genes during development of a single fertilized egg results in a diverse array of specialized tissues even though all cells contain the same complement of genes.
2. The segmentation of Drosophila embryos can be explained by differential expression of known genes during development.

LAB

1. Introduction to the lab.

2. Biochemical pathways.
   - methionine auxotrophs of E. coli and growth on intermediates of the pathway.

3. Mutation.
   - UV Mutagenesis.

4. Meiosis.
   - observation and description of stages of meiosis.

5 Monohybrid cross.
   - scoring C. elegans phenotypes and hypothesis testing.

6. Dihybrid cross.
   - scoring D. melanogaster phenotypes and hypothesis testing.

7. Genetic mapping and sex-linkage.
   - scoring D. melanogaster from a three point cross.

8. Problem solving.

9. Plasmid isolation, transformation.
   - Isolation of an ampicillin resistance plasmid and transformation of sensitive strain.

10. Restriction Mapping.
    - digestion of isolated plasmid with restriction enzymes, agarose gel electrophoresis.

11 Gene Regulation.
   - Induction of trp operon enzymes.

12. Segmentation mutants.
    - description of mutant D. melanogaster embryos.