BIOL4410 3.0 "ADVANCED DROSOPHILA GENETICS"

Lectures: Fridays 2:30 pm – 5:30 pm; HNE 030

Instructor: Dr. Vladimir (Kyle) Belozerov

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Office hours: Mon 1 pm – 2 pm, Wed 1 pm – 2 pm. Also by appointment.

Prerequisites: SC/BIOL 2020 3.00, SC/BIOL 2021 3.00, SC/BIOL 2040 3.00, SC/BIOL2070 3.00

Calendar description: A study of recent advances in Drosophila genetics. The course addresses techniques such as chromosomal analysis, lethal tagging, genetic dissection, mosaic analysis, genetic screens, transposon tagging, enhancer trapping, methods for manipulating genes in transgenic flies and genetic ablation. Three lecture hours. One term. Three credits.

Textbooks: None. Original articles and reviews will be extensively used in this course. Pdf's of these articles will be posted on Moodle, and will also be available through York University library.

Evaluation: *Midterm* (October 24, 90 min) **25%**

Reading assignment #1 (paper assigned on Oct 15; due in class on Oct 17) **10%**

Reading assignment #2 (paper assigned on Nov 12; due in class on Nov 14) **10%**

Reading assignment #3 (paper assigned on Nov 19; due in class on Nov 21) **10%**

Reading assignment #4 (paper assigned on Nov 26; due in class on Nov 28) **10%**

Final (cumulative) **35%**

Learning objectives:

By the end of the course you should be able to:

1. Comfortably and rapidly read original scientific articles in the general area of Drosophila molecular genetics, summarize the central findings of a study, and critically analyze the experimental designs and methods chosen by the authors.

2. Clearly explain the advantages of using Drosophila as a model organism in biomedical research.

3. Design a forward genetic screen to isolate novel recessive alleles of a given gene and a similar screen to isolate recessive mutations with a specific phenotype. Define and explain complementation group analysis. Be able to provide a complete experimental protocol, including the rationale for the use of markers and balancers, for these screens.

4. Explain P-element transgenics in Drosophila: (1) how are transgenes introduced into the germline? (2) what is the genetic scheme used to mobilize existing P-element transgenes? (3) what is enhancer trapping and how is it used in biomedical research?

5. Fully explain the UAS-Gal4 binary system, and articulate the advantages of this system compared to single-transgene approaches.

6. Explain the molecular mechanism of RNA interference, including names and functions of key enzymes and protein complexes in the Drosophila RNAi pathway. Be able to compare and contrast a reverse genetic screen and a forward genetic screen.

7. Explain somatic mosaics: (1) what are they and how are they different from germline mutations? (2) what are the advantages of somatic mosaics? (3) what transgenes are required to generate a somatic mosaic? Be able to design molecular genetic experiments utilizing four techniques: Flp-Out, TARGET, MARCM, and twin-spot generator.

8. Explain phenomenology of meiotic recombination in Drosophila, and predict F1 progeny ratios from chromosomal linkage maps. Define the differences between linkage maps, physical maps, and molecular maps. Explain the molecular mechanism of gene conversion, including key enzymes and Holliday junction intermediates. How does gene conversion result in non-Mendelian allele frequencies?

9. Explain every step in a homologous recombination experiment in Drosophila, including the structure of targeting and auxiliary transgenes, and their specific functions. Compare and contrast homologous recombination with classical mutagenesis and reverse genetic gene targeting.

Major topics covered in the course:

1. Genes, mutations, alleles, chromosomes, balancers
2. Classical mutagenesis (EMS, X-rays)
3. Complementation analysis
4. Hybrid dysgenesis
5. P-elements
6. Transgenic flies
7. P-element mediated mutagenesis (gene disruption, imprecise excision)
8. P-element hopping
9. Enhancer trapping
10. UAS/Gal4 binary system
11. RNAi
12. Gal80, Gal80TS, TARGET
13. Recombinases
14. Flippase
15. FLPout
16. Conventional FRT mosaics
17. MARCM
18. Twin-spot generator
19. Inverse PCR, and regular PCR for transgene localization
20. Deletion mapping
21. PCR to find classical mutations
22. Cytogenetic, linkage, and molecular maps
23. Meiotic recombination
24. Gene conversion
25. Genetic engineering by homologous recombination

Course policies:

1. Makeup exams will only be offered to those students who missed a test with a legitimate documented reason. Only a "York Attending Physician`s Statement Form" or a similarly detailed doctor`s note (i.e. not a form stating that you visited a clinic) will be accepted for medical excuses. Booking holiday airfare coinciding with exam dates will not be considered a legitimate excuse. Please make sure that all documentation supporting your legitimate excuse is received by me within 1 week of the missed test.

2. The midterm must be written to pass the course. There will be no transferring of weight between different assignments/tests.

3. The exams and reading assignments will include written questions. If you believe that an answer was marked incorrectly, please contact me within 1 week of getting your graded work back. Remarking is only possible if you wrote in ink. Please keep in mind that re-marking can result in your score being raised, confirmed, or lowered. Second round of re-marking will not be offered.

4. Standard accommodation policies as set by the university will be followed in the course.

5. All students in the course must be familiar with York University's policies on academic integrity. Please consult the following website for more detail: http://www.yorku.ca/academicintegrity/students/index.htm