Molecular Genetics: Genes, Circuits, and Behavior

Matthew DeGennaro, Ph.D.

Deuxieme Maison 193
Tu/Th 12:30PM - 1:45PM

Fall 2017 office hours AHC1 319A Tuesday 3 to 6pm and by appointment

Objective: This course for senior undergraduate and graduate students is designed to give an understanding of the fundamentals of molecular genetics. Molecular genetics is a powerful way of seeing nature that has uncovered many mysteries about how living things function. You will learn how to interpret, present, and discuss data from the primary literature.

Overview: How we perceive and respond to our environment is governed by the nervous system. The task of understanding how this network of specialized cells functions is a daunting one. Over the past 30 years, molecular genetic analysis of neural function in model organisms has greatly expanded our knowledge. By using the primary literature, we will discuss classic experiments that have made important contributions to neuroscience. These fundamental works will serve as a foundation for our discussion of more current papers. Although this course will focus on neurobiology, the molecular genetic approaches and techniques discussed are applicable to many biological questions.

The primary goals of this course are to improve student's comprehension of the primary literature and ability to think critically about research. Each week we will discuss papers covering the topics listed below that will be posted on the course Blackboard. The papers will be presented by teams led by graduate students. The team is required to make a PowerPoint presentation for the paper that includes all the figures of the paper and a background slide or two at the beginning of the presentation. Undergraduates students will assist the graduate students with making the presentation and will present the figures of the paper with their group to the rest of the class. During the presentation, each member of the team will present figures to the class on a rotating basis. Two papers presentations will occur each class. Depending on enrollment, a team will likely make a least 6 presentations over the semester. The presentation needs to be emailed to me prior to each class or brought into class on a usb drive.

All students are required to read these papers and be prepared for a detailed discussion of the experiments presented within them. Review articles included in the syllabus will not be presented, they are provided to give you additional background. The recommended text book, <u>Decoding the Language of Genetics</u>, is a useful primer on both basic and advanced genetics concepts. Presentations will be graded by the instructor and will constitute 50% of the final grade. Class participation and attendance will count as 20% of the final grade.

There will be a take home midterm exam and an in-class final exam that will account for the remaining 30% of the final grade. The take home exam questions will be run through the Turn-it-in program to assure original answers. The exams will cover molecular genetic techniques and terminology as well as concepts presented in the paper presentations.

Recommended textbook: **Decoding the Language of Genetics by David Botstein**

Course codes:	Undergraduate	PCB 4133-U01 O (79994)
	Graduate	BSC 6936-U01 O (79995)

Grading Criteria for Presentations

Undergraduates: Undergraduate students must be able to demonstrate that they read the paper and have a general understanding of the discoveries being put forward. The in-class presentation of the paper must **include all main figures** and include some background information from the introduction to the paper (2 to 4 slides). Some guidelines:

- Use the Powerpoint files from class 2 & 3 as a model for their presentations. These files can be found on blackboard.
- Breakup the figures if necessary on to different slides to ensure legibility
- Identify the technique(s) used to produce the data in the figure
- identify the control and experimental data sets or images
- Discuss how the data leads to the conclusions the authors make
- Discuss potential problems with the approach used
- Assess whether the data supports the title of the article

Graduates: In addition to the undergraduate requirements, graduate students should include these elements in the presentation or discussion:

- Discuss alternative approaches to the ones used in the article if possible
- Discuss why these findings appeared in a high-profile journal
- Add a slide to the presentation at the end summarizing the findings
- Discuss the unanswered questions that the researchers could address next

Grading Criteria for Exams

Midterm: Students will be given a short research article and will be asked a series of short-answer questions about it. The exam will be a take home exam. The test is open book and open notes. Undergraduates and graduate students will be given different articles and asked different questions.

Final exam: All students will be asked 15 multiple choice questions about molecular genetics (30% of exam). They will also have to match 20 genetic terms or concepts with their definitions (40% of exam). The last part of the exam will be different for undergraduates and graduate students (30% of the exam). Undergraduates will choose between one of the two online lectures given by the HHMI investigators and be asked a series of 15 short-answer questions about them. Graduate students will have to answer questions about both online lectures.

For **5 points of extra credit on the final exam**, students will choose between one of two fictitious abstracts and outline 4 experiments that the paper supporting the abstracts conclusions might include.

No questions will be answered by the instructor during the final exam.

Groups:

Name	Group #
Joshua Raji	1
Bryan Alexander Solano	1
Elina Barredo	2
Kevin Dourado	2
John Castillo	3
Clara Karam George	3
Fredis Mappin	4
Nicholas Franco	4
Moises Camacho	5
Krystal Blanca Fernandez	5
Nirvan Ramphall	6
Andre Silva	6
Renata Gallegos	7
Hiram Anthony Duarte	7
Wissam Khalaf	8
Lilia Amel Curbelo Jalil	8
Robert Seitter	9
Sebastian Garcia-Umpierre	9
Mariluz Soula	10
Pamela Karina Bermudez	10
Jessica Blanco	11
Brian Garcia	11

Weekly meeting topics and readings:

Week 1 Aug 21st
Concepts in Molecular Genetics

Class 1: Tuesday
- Lecture on molecular genetic concepts and terms
- Organization of groups for paper presentations
- Chapter 1 of Decoding the Language of Genetics by David Botstein

Forward Genetics

Class 2: Thursday
Lehmann R & Nüsslein-Volhard C. Abdominal segmentation, pole cell formation, and embryonic polarity require the localized activity of oskar, a maternal gene in Drosophila. Cell. 1986 Oct 10;47(1):141–52. **(Presented by Instructor)**

Wang C, Lehmann R. Nanos is the localized posterior determinant in Drosophila. Cell. 1991 Aug 23;66(4):637–47. **(Presented by Instructor)**

Week 2 August 28th
Genome Editing

Class 3: Tuesday
Barrangou R, Fremaux C, Deveau H, Richards M, Boyaval P, Moineau S, et al. CRISPR provides acquired resistance against viruses in prokaryotes. Science 2007 Mar 23;315(5819):1709–12. **(Presented by Instructor)**

Kistler KE, Vosshall LB, Matthews BJ. Genome engineering with CRISPR-Cas9 in the mosquito Aedes aegypti. Cell Rep. 2015 Apr 7;11(1):51–60. **(Presented by Instructor)**

Transgenesis & Binary systems for cell manipulation

Class 4: Thursday
Coates CJ, Jasinskiene N, Miyashiro L, James AA. Mariner transposition and transformation of the yellow fever mosquito, *Aedes aegypti*. Proc Natl Acad Sci USA. 1998 Mar 31;95(7):3748–51. **Presented by Group #1**

Brand AH & Perrimon N. Targeted gene expression as a means of altering cell fates and generating dominant phenotypes. Development. 1993 Jun;118(2):401–15. **Presented by Group #2**

Week 3 September 4th
Initial molecular genetic approaches to neuroscience

Class 5: Tuesday
S. Benzer (1971) From the gene to behavior. *JAMA* 218 (7): 1015-22. *Background article*

S. Brenner (1974) The genetics of *Caenorhabditis elegans*. *Genetics* 77 (1): 71-94.
Presented by Group #3

Bargmann CI, Horvitz HR. Control of larval development by chemosensory neurons in Caenorhabditis elegans. Science. 1991 Mar 8;251(4998):1243–6.
Presented by Group #4

Class 6: Thursday
W. Quinn et al. (1974) Conditioned behavior in *Drosophila melanogaster*. *PNAS* 71 (3): 708-12. **Presented by Group #5**

Duerr JS, Quinn WG. Three Drosophila mutations that block associative learning also affect habituation and sensitization. Proc Natl Acad Sci. 1982 Jun;79(11):3646–50.
Presented by Group #6

Week 4 September 11th
Ion channels & synaptic transmission

Class 7: Tuesday
D. Papazian et al. (1987) Cloning of the genomic and complementary DNA from Shaker, a putative potassium channel gene from *Drosophila*. *Science* 237 (4816): 749-53.
Presented by Group #7

Wainger BJ, DeGennaro M, Santoro B, Siegelbaum SA, Tibbs GR. Molecular mechanism of cAMP modulation of HCN pacemaker channels. Nature. 2001 Jun 14;411(6839):805–10.
Presented by Group #8

Class 8: Thursday
Special seminar at the University of Miami Medical School for EXTRA CREDIT

- Thursday, September 7th at noon at University of Miami Medical School, RMSB (Rosensteil Medical Sciences Building) room 6018
- if you attend and write a 1 paragraph synopsis you can get **up to 4 points added to your final grade for the course**
- If you have trouble getting to the University of Miami Medical school that day please contact me

Week 5 September 18th
Learning and memory

Class 9: Tuesday
E. Kandel (2009) The biology of memory: a forty-year perspective. *J. Neuroscience* 29 (41): 12748-56. *Review article*

S. Schacher et al. (1988) cAMP evokes long-term facilitation in *Aplysia* sensory neurons that requires new protein synthesis. *Science* 240 (4859): 1667-9.
Presented by Group #9

J. Sweatt & E. Kandel (1989) Persistent and transcriptionally-dependent increase in protein phosphorylation in long-term facilitation of *Aplysia* sensory neurons. *Nature* 339 (6219): 51-4.
Presented by Group #10

Class 10: Thursday
L. Levin et al. (1992) The *Drosophila* learning and memory gene rutabaga encodes Ca2+/calmodulin-responsive adenylyl cyclase. *Cell* 68 (3): 479-89.
Presented by Group #11

T. Zars et al. (2000) Localization of short-term memory in *Drosophila*. *Science* 288 (5466): 672-5. **Presented by Group #1**

Written take home exam questions given out, exam must be returned to me via email by September 25th (10% of final grade).

Week 6 September 25th
Visual perception

Class 11: Tuesday
G. Maimon et al. (2010) Active flight increases the gain of visual motion processing in *Drosophila*. *Nat Neuroscience* 13 (3): 393-9. **Presented by Group #2**

Siegel M, Buschman TJ, Miller EK. Cortical information flow during flexible sensorimotor decisions. Science. 2015 Jun 19;348(6241):1352–5. **Presented by Group #3**

Olfactory receptors

Class 12: Thursday
L. Buck & R. Axel (1991) A novel multigene family may encode odorant receptors: a molecular basis of odor recognition. *Cell* 65 (1): 175-87. **Presented by Group #4**

R. Benton et al. (2009) Variant ionotropic glutamate receptors as chemosensory receptors in *Drosophila*. *Cell* 136 (1): 149-62. **Presented by Group #5**

Week 7 October 2nd
Olfactory receptor expression

Class 13: Tuesday
Joseph RM, Carlson JR. Drosophila Chemoreceptors: A Molecular Interface Between the Chemical World and the Brain. Trends Genet. 2015 Dec;31(12):683–95. *Review article*

Vosshall LB, Wong AM, Axel R. An olfactory sensory map in the fly brain. Cell. 2000 Jul 21;102(2):147–59. **Presented by Group #6**

Matthews BJ, McBride CS, DeGennaro M, Despo O, Vosshall LB. The neurotranscriptome of the *Aedes aegypti* mosquito. BMC Genomics. 2016;17(1):32.
Presented by Group #7

Olfactory receptor evolution

Class 14: Thursday
Croset V, Rytz R, Cummins SF, Budd A, Brawand D, Kaessmann H, et al. Ancient protostome origin of chemosensory ionotropic glutamate receptors and the evolution of insect taste and olfaction. Stern DL, editor. PLoS Genet. 2010 Aug 27;6(8):e1001064.
Presented by Group #8

McBride CS, Baier F, Omondi AB, Spitzer SA, Lutomiah J, et al. Evolution of mosquito preference for humans linked to an odorant receptor. Nature. 2014 Nov 13;515(7526):222–7.
Presented by Group #9

Week 8 October 9th
Olfactory circuits

Class 15: Tuesday
C. Su et al. (2009) Olfactory perception: receptors, cells, and circuits. *Cell* 139 (1): 45-59.
Review article

C. Bargmann & H. R. Horvitz (1991) Control of larval development by chemosensory neurons in *Caenorhabditis elegans*. *Science* 251 (4998): 1243-6. **Presented by Group #10**

S. Chalasani et al. (2007) Dissecting a circuit for olfactory behavior in *Caenorhabditis elegans*. *Nature* 450 (7166): 63-70. **Presented by Group #11**

Class 16: Thursday
V. Ruta et al. (2010) A dimorphic pheromone circuit in *Drosophila* from sensory input to descending output. *Nature* 468 (7324): 686-690. **Presented by Group #1**

Shirasu M, Yoshikawa K, Takai Y, Nakashima A, Takeuchi H, Sakano H, et al. Olfactory receptor and neural pathway responsible for highly selective sensing of musk odors. Neuron. 2014 Jan 8;81(1):165–78. **Presented by Group #2**

Week 9 October 16th
Gustation

Class 17: Tuesday
J. Chandrashekar et al. (2006) The receptors and cells for mammalian taste. *Nature* 444 (7117): 288-94. *Review article*

K. Scott et al. (2001) A chemosensory gene family encoding candidate gustatory and olfactory receptors in *Drosophila*. *Cell* 104 (5): 661-73. **Presented by Group #3**

G. Zhao et al. (2003) The receptors for mammalian sweet and umami taste. *Cell* 115 (3): 255-66. **Presented by Group #4**

Appetite

Class 18: Thursday
B. Al-Anzi et al. (2009) Obesity-blocking neurons in *Drosophila*. *Neuron* 63 (3): 329-41.
Presented by Group #5

C. Pérez et al. (2011) Molecular annotation of integrative feeding neural circuits. *Cell Metab* 13 (2): 222-232. **Presented by Group #6**

Week 10 October 23rd
Patterning the nervous system

Class 19: Tuesday
T. Kidd et al. (1999) Slit is the midline repellent for the robo receptor in *Drosophila*. *Cell* 96 (6): 785-94. **Presented by Group #7**

K. Brose et al. (1999) Slit proteins bind Robo receptors and have an evolutionarily conserved role in repulsive axon guidance. *Cell* 96 (6): 795-806. **Presented by Group #8**

Class 20: Thursday
D. Schmucker et al. (2000) *Drosophila* Dscam is an axon guidance receptor exhibiting extraordinary molecular diversity. *Cell* 101 (6): 671-84. **Presented by Group #9**

B. Matthews et al. (2007) Dendrite self-avoidance is controlled by Dscam. *Cell* 129 (3): 593-604. **Presented by Group #10**

Week 11 October 30th
Fear

Class 21: Thursday
G. Suh et al. (2004) A single population of olfactory sensory neurons mediates an innate avoidance behavior in *Drosophila*. *Nature* 431 (7010): 854-9.
Presented by Group #11

W. Haubensak et al. (2010) Genetic dissection of an amygdala microcircuit that gates conditioned fear. *Nature* 468 (7321): 270-6. **Presented by Group #1**

Class 22: Thursday
No in-class presentation, view two online seminars on Molecular genetics
These videos will also be available for download on BlackBoard along with their transcripts.
Content presented in lectures will be asked about in the final exam

Sizing up the Brain Gene by Gene: http://www.hhmi.org/biointeractive/sizing-brain-gene-gene

Unwinding Clock Genetics: http://www.hhmi.org/biointeractive/unwinding-clock-genetics

Week 12 November 6th

Circadian Rhythm & Sleep

Class 23: Tuesday

Vosshall LB, Price JL, Sehgal A, Saez L, Young MW. Block in nuclear localization of period protein by a second clock mutation, timeless. Science. 1994 Mar 18;263(5153):1606–9.
Presented by Group #2

Rogulja D, Young MW. Control of sleep by cyclin A and its regulator. Science. 2012 Mar 30;335(6076):1617–21.
Presented by Group #3

Social behavior

Class 24: Thursday

M. de Bono et al. (2002) Social feeding is *Caenorhabditis elegans* is induced by neurons that detect aversive stimuli. *Nature* 419 (6910): 899-903. **Presented by Group #4**

Yan H, Opachaloemphan C, et al. An Engineered *orco* Mutation Produces Aberrant Social Behavior and Defective Neural Development in Ants. Cell. 2017 Aug 10;170(4):736–9.
Presented by Group #5

Week 13 November 13th

Imaging neurons

Class 25: Tuesday

Tian L, Hires SA, Mao T, Huber D, Chiappe ME, et al. Imaging neural activity in worms, flies and mice with improved GCaMP calcium indicators. Nat Methods. 2009 Dec;6(12):875–81.
Presented by Group #6

Hampel S, Chung P, McKellar CE, Hall D, Looger LL, Simpson JH. Drosophila Brainbow: a recombinase-based fluorescence labeling technique to subdivide neural expression patterns. Nat Methods. 2011 Mar;8(3):253–9. **Presented by Group #7**

Optogenetics & Chemogenetics

Class 26: Thursday

O. Yizhar et al. (2011) Optogenetics in neural systems. *Neuron* 71 (1): 9-34. *Review article*

Lin D, Boyle MP, Dollar P, Lee H, Lein ES, Perona P, et al. Functional identification of an aggression locus in the mouse hypothalamus. Nature. 2011 Feb 10;470(7333):221–6.
Presented by Group #8

Gomez JL, Bonaventura J, Lesniak W, Mathews WB, Sysa-Shah P, Rodriguez LA, et al. Chemogenetics revealed: DREADD occupancy and activation via converted clozapine. Science. 2017 Aug 4;357(6350):503–7. **Presented by Group #9**

Week 14 November 20th
Mating behavior

Class 27: Tuesday
E. Demir & B. Dickson (2005) Fruitless splicing specifies male courtship behavior in *Drosophila*. *Cell* 121 (5): 785-94. **Presented by Group #10**

Haga-Yamanaka S, Ma L, He J, Qiu Q, Lavis LD, et al. Integrated action of pheromone signals in promoting courtship behavior in male mice. eLife. 2014 Jul 29;3:e03025.
Presented by Group #11

Week 15 November 27th
Addiction & Thirst

Class 28: Tuesday
K. Kaun et al. (2011) A *Drosophila* model for alcohol reward. *Nat. neuroscience* 14 (5): 612-9.
Presented by Group #1

Jourjine N, Mullaney BC, Mann K, Scott K. Coupled Sensing of Hunger and Thirst Signals Balances Sugar and Water Consumption. Cell. 2016 Aug 11;166(4):855–66.
Presented by Group #2

Class 29: Thursday
Review Session

In-class final exam (20% of final grade): *December 5th from 12 to 2pm*

Final Grade calculations:

Attendance & class participation: 20%
Presentations: 50%
Midterm and final exam: 30%

Grading Scale: A 100-94 A- 93-90 B+ 89-87 B 86-84 B- 83-80 C+ 79-77 C 76-74 C- 73-70 D+ 69-67 D 66-64 D- 63-60 F < 60

Academic Misconduct: Florida International University is a community dedicated to generating and imparting knowledge through excellent teaching and research, the rigorous and respectful exchange of ideas, and community service. All students should respect the right of others to have an equitable opportunity to learn and honestly demonstrate the quality of their learning. Therefore, all students are expected to adhere to a standard of academic conduct, which demonstrates respect for themselves, their fellow students, and the educational mission of the University. All students are deemed by the University to understand that if they are found responsible for academic misconduct, they will be subject to the Academic Misconduct procedures and sanctions, as outlined in the Student Handbook.

Full handbook and information can be found at:
http://www.fiu.edu/~oabp/misconductweb/1acmisconductproc.htm

DEFINITION OF ACADEMIC MISCONDUCT: Academic Misconduct is defined as the following intentional acts or omissions committed by any FIU student:

1.01 Cheating: The unauthorized use of books, notes, aids, electronic sources; or assistance from another person with respect to examinations, course assignments, field service reports, class recitations; or the unauthorized possession of examination papers or course materials, whether originally authorized or not. Any student helping another cheat may be found guilty of academic misconduct.

1.02 Plagiarism: The deliberate use and appropriation of another's work without any indication of the source and the representation of such work as the student's own. Any student who fails to give credit for ideas, expressions or materials taken from another source, including internet sources, is guilty of plagiarism. Any student helping another to plagiarize may be found guilty of academic misconduct.

1.08 Academic Dishonesty: In general, by any act or omission not specifically mentioned above and which is outside the customary scope of preparing and completing academic assignments and/or contrary to the above stated policies concerning academic integrity.

If found cheating, YOU WILL RECEIVE AN “F” FOR THE CLASS, NO EXCEPTIONS.

Syllabus subject to change