BB 486 / BB 586 - Advanced Molecular Genetics
Winter 2020

Topics covered: Transmission genetics (chromosomes, gene linkage, mapping, mutation, drift, genes).
Regulation of gene expression, protein synthesis and protein processing.
Foundation for epigenetics and epigenomics.
Model organisms for molecular biology.
General molecular biology techniques.

Advanced topics in: Nucleic acid and protein structure, genome structure, chromatin, nucleosomes, DNA replication; DNA mutation and DNA repair; recombination and DNA rearrangements; genome expression and epigenetics, emerging techniques of molecular biology.

Instructor: Michael Freitag
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Teaching assistants: none

Class Hours: Mo We Fr, 10:00 – 10:50
Class Location: 026 Milam Hall

Office Hours: Mo We, noon – 1 pm (or by appointment)

Resources: *Molecular Biology of the Gene*, 7th edition, Watson, Baker *et al.*
(***not required***) *Lewin's Genes X*, Krebs *et al.*
iGenetics, 3rd edition, Peter Russel
Essential Genetics – A Genomics Perspective, 6th edition, Dan Hartl

Evaluation:

Examinations	two, non-cumulative, each 100 points; 200 points total
Presentations (group)	design of presentation, delivery, Q&A; 100 points total
Quizzes	none
Homework	none

Graduate students (BB586) are required to write a term paper (100 points total)
*Total achievable points are 300 for undergraduates and 400 for graduate students.

Learning aids:
-Required reading will be available on Canvas (including primary and review papers).
-Recommended (indicated as "not required") reading will be on Canvas.
-Lecture notes will be posted on Canvas before lectures
(there may be some changes ***after*** each lecture has been given).
-Problem sets will be available on Canvas.
-Links to student exercises will be available on Canvas.

BB 586 Graduate Student Term Paper

The paper assignment entails a critical analysis of a ***recent***, ***full-length***, ***primary*** research publication, dealing with any topic covered this term. **The appropriateness of the article should be discussed with the instructor prior to the scheduled first midterm exam.** The paper should take the form of a written "Journal Club" presentation, in which the student presents a clear summary and critical analysis of the paper. For example, the following questions should be considered: Is the paper a significant contribution to knowledge? If so, why? Are experimental methods clearly described? Do the authors adequately consider alternative models? Are the experiments convincing? Are the conclusions drawn justified based on the reported results? What are the most important future directions for the work? *Please make sure to substantiate your opinions by citing from the literature.* Recommended length: <10 pages.

Due date: **At the beginning of the scheduled final exam (via Canvas).**
Earlier submission is strongly encouraged. Late delivery earns 0 points.

Contact Information: If you have any questions or problems, feel free to contact me. My office is located on the second floor of the Agricultural and Life Sciences building (ALS2045), my laboratory is in ALS2035. My phone number is 737-4845 and my e-mail address is freitagm@oregonstate.edu.

University Policies

Statement Regarding Students with Disabilities: Accommodations for students with disabilities are determined and approved by Disability Access Services (DAS). If you, as a student, believe you are eligible for accommodations but have not obtained approval please contact DAS immediately at 541-737-4098 or at http://ds.oregonstate.edu. DAS notifies students and faculty members of approved academic accommodations and coordinates implementation of those accommodations. While not required, students and faculty members are encouraged to discuss details of the implementation of individual accommodations."

Reminder of some additional university policies:

The University rules on student conduct can be found here: https://studentlife.oregonstate.edu/sites/studentlife.oregonstate.edu/files/code-of-student-conduct-102218.pdf

Diversity: The College of Science strives to create an affirming climate for all students including underrepresented and marginalized individuals and groups. Diversity encompasses differences in age, color, ethnicity, national origin, gender, physical or mental ability, religion, socioeconomic background, veteran status, sexual orientation, and marginalized groups. We believe diversity is the synergy, connection, acceptance, and mutual learning fostered by the interaction of different human characteristics.

Religious Holidays: Oregon State University strives to respect all religious practices. If you have religious holidays that are in conflict with any of the requirements of this class, please see me immediately so that we can make alternative arrangements.

Reach Out for Success: University students encounter setbacks from time to time. If you encounter difficulties and need assistance, it's important to reach out. Consider discussing the situation with an instructor or academic advisor. Learn about resources that assist with wellness and academic success at oregonstate.edu/ReachOut. If you are in immediate crisis, please contact the Crisis Text Line by texting OREGON to 741-741 or call the National Suicide Prevention Lifeline at 1-800-273-TALK (8255)

Cheating or plagiarism by students is subject to the disciplinary process outlined in the Student Conduct Regulations. Students are expected to be honest and ethical in their academic work. Academic dishonesty is defined as an intentional act of deception in one of the following areas:

- Cheating-use or attempted use of unauthorized materials, information or study aids
- Fabrication-falsification or invention of any information
- Assisting-helping another commit an act of academic dishonesty
- Tampering-altering or interfering with evaluation instruments and documents
- Plagiarism-representing the words or ideas of another person as one's own

Behaviors disruptive to the learning environment will not be tolerated and will be referred to the Office of Student Conduct for disciplinary action.

Use of cellular phones is not permitted in the classroom during exams.

Cellular phones may, however, be used to look up material during class discussions and to find information that corrects potential or actual mistakes by the instructor.

"The goal of Oregon State University is to provide students with the knowledge, skill and wisdom they need to contribute to society. Our rules are formulated to guarantee each student's freedom to learn and to protect the fundamental rights of others. People must treat each other with dignity and respect in order for scholarship to thrive. Behaviors that are disruptive to teaching and learning will not be tolerated, and will be referred to the Student Conduct Program for disciplinary action. Behaviors that create a hostile, offensive or intimidating environment based on gender, race, ethnicity, color, religion, age, disability, marital status or sexual orientation will be referred to the Affirmative Action Office."

Prerequisites and Co-requisites

This is a capstone course to meet the requirements of majors in Biochemistry and Molecular Biology.
PREREQUISITES: BB 314, BB 315, BB 492 (can be waived with instructor permission).

Learner Outcomes

- Understand transmission genetics, ability to map genetic loci based on results from three-point crosses, explain the concept of a locus, cistron, gene, non-coding RNA.
- Acquire working knowledge of the molecular biology of DNA and RNA metabolism, and the transmission and expression of genetic information.
- Gain an understanding of how genetic processes are regulated at the gene and genome level.
- Demonstrate ability to explain and chose from appropriate methods to carry out molecular biology investigations.
- Display a measurable understanding of key concepts relevant to molecular biology via performance on written examinations, quizzes and homework assignments as outlined above in “Evaluation”.

Learner Expectations

- Student will come prepared for lectures by studying the assigned readings, handouts or lecture notes **prior** to class.
- Students will participate in lively class discussions. To do this you must have read the assigned paper.
- Students will be excellently prepared to serve as discussion leaders for the papers they have been assigned.
- Significant time is required for studying the assigned readings, lectures and notes throughout the term. ***Studying for exams at the last minute will likely result in a poor grade.***
- **The instructor is here to help you**! In turn, you are expected to arrange to come to office hours if help is needed. **DO NOT WAIT UNTIL THE LAST WEEK BEFORE EXAMS!**
- Graduate students: significant time and effort will be spent on preparing the term paper. Grades will be assigned relative to the scientific rigor evident in the final product.

Schedule **BB 486/586** **Winter 2020**

Date	Meeting	Topic
1/6	1	Course Overview – The "Awe-full Power of Genetics" and the gene
1/8	2	Methods: DNA sequencing technology and applications
1/10	3	*Paper discussion 1: Evolution of the genetic code – it's a new world?*
1/13	4	The RNA world – versatility of RNA
1/15	5	Chromosome, locus, gene. What are essential genes?
1/17	6	*Paper discussion 2: Minimal genomes – bacteria and fungi*
1/20		*Martin Luther King Day – no classes*
1/22	7	Chromatin biology
1/24	8	*Paper discussion 3: Introduction of histones into bacteria and yeast*
1/27	9	Molecular Genetics: To be forward or reverse - that is the question.
1/29	10	Model organisms: *Escherichia coli*
1/31	11	*Paper discussion 4: Standing variation, mutagenesis, and selection*
2/3	12	Model organisms: *Neurospora crassa*
2/5	13	The rise of biochemical genetics – mapping and "one gene – one enzyme"
2/7	14	*Paper discussion 5: Self/Non-self recognition*
2/10		**First EXAM (covers first 14 meetings)**
2/12	15	Model organisms: *Saccharomyces cerevisiae*
2/14	16	*Paper discussion 6: One genome – one (or two) chromosome(s)*
2/17	17	Transformation – Complementation and gene deletions
2/19	18	Model organisms: *Agrobacterium tumefaciens*
2/21	19	*Paper discussion 7: The sliding scale from symbiont to pathogen*
2/24	20	Methods: Chromatin immunoprecipitation
2/26	21	Model organisms: *Arabidopsis thaliana*
2/28	22	*Paper discussion 8: Epigenetic switches – H3K27 methylation*
3/2	23	Mitosis and meiosis
3/4	24	Model organisms: *Caenorhabditis elegans*
3/6	25	*Paper discussion 9: Meiosis*
3/09	26	Gene therapy
3/11	27	*Paper discussion 10: CRISPR/Cas therapies*
3/13	28	Review and wrap-up
3/17	**Tuesday**	**Final exam (9:30; covers meetings 15 to 28)**

Reading for BB486 – Winter 2019

1. All background reading is posted on Canvas in the folder for each week. This includes reviews and copies of textbook chapters that complement the lectures and discussions. Highly recommended reading.

2. Papers for discussions (<u>absolutely required reading</u> for all students):

Papers that are the basis for the mid-term exam:

Groups 1+2 *Paper discussion: Evolution of the genetic code*

Groups 1 and 2: A semi-synthetic organism that stores and retrieves increased genetic information.
Zhang Y, Ptacin JL, Fischer EC, Aerni HR, Caffaro CE, San Jose K, Feldman AW, Turner CR, Romesberg FE.
Nature. 2017 Nov 29;551(7682):644-647. doi: 10.1038/nature24659.
Assigned tasks:
Group 1: Background on new basepairs (introduction), Fig. 1, SI as necessary
Group 2: Fig. 2, Fig. 3, SI as necessary

Groups 3+4 *Paper discussion: Minimal genomes*

Group 3: Design and synthesis of a minimal bacterial genome.
Hutchison CA 3rd, Chuang RY, Noskov VN, Assad-Garcia N, Deerinck TJ, Ellisman MH, Gill J, Kannan K, Karas BJ, Ma L, Pelletier JF, Qi ZQ, Richter RA, Strychalski EA, Sun L, Suzuki Y, Tsvetanova B, Wise KS, Smith HO, Glass JI, Merryman C, Gibson DG, Venter JC.
Science. 2016 Mar 25;351(6280):aad6253. doi: 10.1126/science.aad6253.

Group 4: Precise control of SCRaMbLE in synthetic haploid and diploid yeast.
Jia B, Wu Y, Li BZ, Mitchell LA, Liu H, Pan S, Wang J, Zhang HR, Jia N, Li B, Shen M, Xie ZX, Liu D, Cao YX, Li X, Zhou X, Qi H, Boeke JD, Yuan YJ.
Nat Commun. 2018 May 22;9(1):1933. doi: 10.1038/s41467-018-03084-4.
Erratum in: Nat Commun. 2019 Feb 14;10(1):839.

Groups 5+6 *Paper discussion: Histones wrap DNA – how conserved are they?*

Group 5: Chromatinization of *Escherichia coli* with archaeal histones.
Rojec M, Hocher A, Stevens KM, Merkenschlager M, Warnecke T.
Elife. 2019 Nov 6;8. pii: e49038. doi: 10.7554/eLife.49038.

Group 6: Resetting the Yeast Epigenome with Human Nucleosomes.
Truong DM, Boeke JD.
Cell. 2017 Dec 14;171(7):1508-1519.e13. doi: 10.1016/j.cell.2017.10.043. Epub 2017 Nov 30.

Groups 7+8 *Paper discussion: Standing variation, mutagenesis, selection for antibiotic resistance*

Group 7: Historical contingency in the evolution of antibiotic resistance after decades of relaxed selection.
Card KJ, LaBar T, Gomez JB, Lenski RE.
PLoS Biol. 2019 Oct 23;17(10):e3000397. doi: 10.1371/journal.pbio.3000397. eCollection 2019 Oct.

Group 8: Spatiotemporal microbial evolution on antibiotic landscapes.
Baym M, Lieberman TD, Kelsic ED, Chait R, Gross R, Yelin I, Kishony R.
Science. 2016 Sep 9;353(6304):1147-51. doi: 10.1126/science.aag0822.

Groups 9+10 *Paper discussion: Self/Non-self recognition*

Groups 9 and 10: Characterization of Greenbeard Genes Involved in Long-Distance Kind Discrimination in a Microbial Eukaryote.
Heller J, Zhao J, Rosenfield G, Kowbel DJ, Gladieux P, Glass NL.
PLoS Biol. 2016 Apr 14;14(4):e1002431. doi: 10.1371/journal.pbio.1002431. eCollection 2016 Apr 14.
Assigned figures:
Group 9: Background on self/non-self recognition in *Neurospora*, Figs. 1, 2, and 3, movies as necessary
Group 10: Figs. 4, 5, 6, and 7; movies as necessary

Papers that are the basis for the final exam:

Groups 11+12 *Paper discussion: One genome – one chromosome*

Group 11: Creating a functional single-chromosome yeast.
Shao Y, Lu N, Wu Z, Cai C, Wang S, Zhang LL, Zhou F, Xiao S, Liu L, Zeng X, Zheng H, Yang C, Zhao Z, Zhao G, Zhou JQ, Xue X, Qin Z.
Nature. 2018 Aug;560(7718):331-335. doi: 10.1038/s41586-018-0382-x

Group 12: Karyotype engineering by chromosome fusion leads to reproductive isolation in yeast.
Luo J, Sun X, Cormack BP, Boeke JD.
Nature. 2018 Aug;560(7718):392-396. doi: 10.1038/s41586-018-0374-x. Epub 2018 Aug 1.

Groups 13+14 *Paper discussion: From symbionts to pathogens*

Groups 13 and 14: Evolutionary transitions between beneficial and phytopathogenic *Rhodococcus* challenge disease management.
Savory EA, Fuller SL, Weisberg AJ, Thomas WJ, Gordon MI, Stevens DM, Creason AL, Belcher MS, Serdani M, Wiseman MS, Grünwald NJ, Putnam ML, Chang JH.
Elife. 2017 Dec 12;6. pii: e30925. doi: 10.7554/eLife.30925. Erratum in: Elife. 2018 Mar 13;7:.
Assigned figures:
Group 13: Background on *Rhodococcus*; Figs. 1, 2, 3, and 4. Defenders of the authors.
Group 14: Figs. 5, 6, 7, 8, and 9. Defenders of Randall and Vereecke.

Groups 15+16 *Paper discussion: Epigenetic gene regulation in plants by histone methylation*

Group 15: EBS is a bivalent histone reader that regulates floral phase transition in Arabidopsis.
Yang Z, Qian S, Scheid RN, Lu L, Chen X, Liu R, Du X, Lv X, Boersma MD, Scalf M, Smith LM, Denu JM, Du J, Zhong X.
Nature Genet. 2018 Sep;50(9):1247-1253. doi: 10.1038/s41588-018-0187-8

Group 16: Dual recognition of H3K4me3 and H3K27me3 by a plant histone reader SHL.
Qian S, Lv X, Scheid RN, Lu L, Yang Z, Chen W, Liu R, Boersma MD, Denu JM, Zhong X, Du J.
Nat Commun. 2018 Jun 21;9(1):2425. doi: 10.1038/s41467-018-04836-y.

Groups 17+18 *Paper discussion: Meiosis in worms*

Groups 17 and 18: Synaptonemal Complex Central Region Proteins Promote Localization of Pro-crossover Factors to Recombination Events During *Caenorhabditis elegans* Meiosis.
Cahoon CK, Helm JM, Libuda DE.
Genetics. 2019 Oct;213(2):395-409. doi: 10.1534/genetics.119.302625. Epub 2019 Aug 20.
Assigned figures:
Group 17: Background on meiosis in *C. elegans*; Figs. 1, 2, 3, and 4.
Group 18: Figs. 5, 6, 7, and 8.

Groups 19+20 *Paper discussion: CRISPR/Cas therapies*

Group 19: to be announced

Group 20: to be announced