BB 486 / BB 586 - Advanced Molecular Genetics
Spring 2017

(capstone class for Biochemistry and Molecular Biology degree)

Topics covered: Transmission genetics (Mendel's Laws, chromosome structure, gene linkage, mapping, mutation, drift, genes).
Regulation of gene expression, protein synthesis and protein processing.
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 (transcription, RNA metabolism, RNA transport, translation).
Recent and emerging techniques of molecular biology.

Instructor: Michael Freitag
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Teaching assistants: none

Class Hours: 11:00 – 11:50
Monday – Wednesday – Friday
STAG 211

Office Hours: Mo and 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 200 points; 400 points total).
Quizzes (unannounced, 50 points total).
Homework (twelve, ten count; 150 points total).
Graduate students (BB586) are required to write a term paper (200 points total).
*Total achievable points are 600 for undergraduates and 800 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 May 12th. 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: Friday, June 12th (11:59 pm; 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 – A reminder:

Please note: "Students with documented disabilities who may need accommodations, who have any emergency medical information the instructor should know, or who need special arrangements in the event of evacuation, should make an appointment with the instructor as early as possible, no later than the first week of the term. In order to arrange alternative testing, the student should make the request at least one week in advance of the test. Students seeking accommodations should be registered with the Office of Services for Students with Disabilities."

The University rules on civility and honesty can be found at: http://oregonstate.edu/admin/stucon/regs.html

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 phone call, texting, messaging and twitter functions is not permitted in the classroom during lectures. Feel free, however, to use phones to look up information during class.

"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** **Spring 2017**

Date	Meeting	Topic
4/3	1	Course Overview – The "Awe-full Power of Genetics" and the gene
4/5	2	*Discussion: DNA as the genetic material*
4/7	3	Methods: DNA sequencing technology and applications
4/10	4	*Paper discussion 1: The first (complete) genomes*
4/12	5	The RNA world – versatility of RNA
4/14	6	*Paper discussion 2: rRNA sequencing for phylogeny*
4/17	7	Regulatory RNA
4/19	8	Methods: Proteins and protein structure
4/21	9	*Paper discussion 3: Evolution of the genetic code*
4/24	10	Primer on DNA replication: The basics and PCR
4/26	11	Molecular Genetics: To be forward or reverse - that is the question.
4/28	12	*Paper discussion 4: A minimal genome*
5/1	13	Model organisms: *Neurospora crassa*
5/3	14	Chromosome, locus, gene – mapping of traits
5/5	15	*Paper discussion 5: Bulk segregant analysis and sequencing*
5/8		**First EXAM (covers first 14 meetings)**
5/10	16	Model organisms: *Saccharomyces cerevisiae*
5/12	17	*Paper discussion 6: Essential genes unmasked*
5/15	18	Model organisms: *Escherichia coli*
5/17	19	*Paper discussion 7: Prokaryotic transcriptional regulation*
5/19	20	Methods: Chromatin immunoprecipitation
5/22	21	*Paper discussion 8: Eukaryotic transcription – chromatin-based gene regulation*
5/24	22	Model organisms: *Arabidopsis thaliana*
5/26	23	*Paper discussion 9: Epigenetic gene regulation in plants by DNA methylation*
5/29		*Memorial Day (no class)*
5/31	24	Model organisms: *Caenorhabditis elegans*
6/2	25	*Paper discussion 10: RNA-based gene silencing by RNAi*
6/5	26	Model organisms: *Mus musculus* and *Homo sapiens [?]*
6/7	27	*Paper discussion 11: Systems biology: The circadian clock*
6/9	28	*Paper discussion 12: Genetic engineering of stem cells*

6/12 Monday Second EXAM (noon; covers meetings 15 to 28)

Reading for BB486 – Spring 2017

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):

Group 1 *Paper discussion: The first (complete) genomes*

The Genome Sequence of *Saccharomyces eubayanus* and the Domestication of Lager-Brewing Yeasts
EmilyClare Baker, Bing Wang, Nicolas Bellora, David Peris, Amanda Beth Hulfachor, Justin A. Koshalek, Marie Adams, Diego Libkind, Chris Todd Hittinger
Mol Biol Evol. 2015 Nov; 32(11): 2818–2831. Published online 2015 Aug 11. doi: 10.1093/molbev/msv168

Group 2 *Paper discussion: rRNA sequencing for phylogeny*

Phylogenetic structure of the prokaryotic domain: the primary kingdoms.
Woese CR, Fox GE.
Proc Natl Acad Sci U S A. 1977 Nov;74(11):5088-90.
Population-based metagenomics analysis reveals markers for gut microbiome composition and diversity.
Zhernakova A, Kurilshikov A, Bonder MJ, Tigchelaar EF, Schirmer M, Vatanen T, Mujagic Z, Vila AV, Falony G, Vieira-Silva S, Wang J, Imhann F, Brandsma E, Jankipersadsing SA, Joossens M, Cenit MC, Deelen P, Swertz MA; LifeLines cohort study., Weersma RK, Feskens EJ, Netea MG, Gevers D, Jonkers D, Franke L, Aulchenko YS, Huttenhower C, Raes J, Hofker MH, Xavier RJ, Wijmenga C, Fu J.
Science. 2016 Apr 29;352(6285):565-9. doi: 10.1126/science.aad3369. Epub 2016 Apr 28.

Group 3 *Paper discussion: Evolution of the genetic code*

A co-evolution theory of the genetic code.
Wong JT.
Proc Natl Acad Sci U S A. 1975 May;72(5):1909-12.
Coevolution theory of the genetic code at age thirty.
Wong JT.
Bioessays. 2005 Apr;27(4):416-25. Review.

Group 4 *Paper discussion: A minimal genome*

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. Erratum in: ACS Chem Biol. 2016 May 20;11(5):1463.

Group 5 *Paper discussion: Bulk segregant analysis and sequencing*

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.

Group 6 *Paper discussion: Essential genes unmasked*

Systematic exploration of essential yeast gene function with temperature-sensitive mutants.
Li Z, Vizeacoumar FJ, Bahr S, Li J, Warringer J, Vizeacoumar FS, Min R, Vandersluis B, Bellay J, Devit M, Fleming JA, Stephens A, Haase J, Lin ZY, Baryshnikova A, Lu H, Yan Z, Jin K, Barker S, Datti A, Giaever G, Nislow C, Bulawa C, Myers CL, Costanzo M, Gingras AC, Zhang Z, Blomberg A, Bloom K, Andrews B, Boone C.
Nat Biotechnol. 2011 Apr;29(4):361-7. doi: 10.1038/nbt.1832. Epub 2011 Mar 27.

Group 1 *Paper discussion: Prokaryotic transcriptional regulation*

The SOS response controls integron recombination.
Guerin E, Cambray G, Sanchez-Alberola N, Campoy S, Erill I, Da Re S, Gonzalez-Zorn B, Barbé J, Ploy MC, Mazel D.
Science. 2009 May 22;324(5930):1034. doi: 10.1126/science.1172914.

Group 2 *Paper discussion: Eukaryotic transcription – chromatin-based gene regulation*

An allosteric PRC2 inhibitor targeting the H3K27me3 binding pocket of EED.
Qi W, Zhao K, Gu J, Huang Y, Wang Y, Zhang H, Zhang M, Zhang J, Yu Z, Li L, Teng L, Chuai S, Zhang C, Zhao M, Chan H, Chen Z, Fang D, Fei Q, Feng L, Feng L, Gao Y, Ge H, Ge X, Li G, Lingel A, Lin Y, Liu Y, Luo F, Shi M, Wang L, Wang Z, Yu Y, Zeng J, Zeng C, Zhang L, Zhang Q, Zhou S, Oyang C, Atadja P, Li E.
Nat Chem Biol. 2017 Apr;13(4):381-388. doi: 10.1038/nchembio.2304. Epub 2017 Jan 30.

Group 3 *Paper discussion: Epigenetic gene regulation in plants by DNA methylation*

Live-cell analysis of DNA methylation during sexual reproduction in Arabidopsis reveals context and sex-specific dynamics controlled by noncanonical RdDM.
Ingouff M, Selles B, Michaud C, Vu TM, Berger F, Schorn AJ, Autran D, Van Durme M, Nowack MK, Martienssen RA, Grimanelli D.
Genes Dev. 2017 Jan 1;31(1):72-83. doi: 10.1101/gad.289397.116. Epub 2017 Jan 23.

Group 4 *Paper discussion: RNA-based gene silencing by RNAi*

Early Developmental Exposure to dsRNA Is Critical for Initiating Efficient Nuclear RNAi in C. elegans.
Shiu PK, Hunter CP.
Cell Rep. 2017 Mar 21;18(12):2969-2978. doi: 10.1016/j.celrep.2017.03.002.

Group 5 *Paper discussion: Systems biology: The circadian clock*

Circadian rhythms of hedonic drinking behavior in mice.
Bainier C, Mateo M, Felder-Schmittbuhl MP, Mendoza J.
Neuroscience. 2017 Mar 10;349:229-238. doi: 10.1016/j.neuroscience.2017.03.002. [Epub ahead of print]

Group 6 *Paper discussion: Genetic engineering of stem cells*

Small Molecules Modulate Chromatin Accessibility to Promote NEUROG2-Mediated Fibroblast-to-Neuron Reprogramming.
Smith DK, Yang J, Liu ML, Zhang CL.
Stem Cell Reports. 2016 Nov 8;7(5):955-969. doi: 10.1016/j.stemcr.2016.09.013. Epub 2016 Oct 27.