BB 486 / BB 586 - Advanced Molecular Genetics
Spring 2018

(capstone class for Biochemistry and Molecular Biology degree)

Topics covered: Transmission genetics
(Mendel's Laws, chromosomes, 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: Mo We Fr, 11:00 – 11:50
Class Location: 2018 ALS Building (BB classroom)

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 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 11th. 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 8th (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 2018**

<u>**Date**</u>   <u>**Meeting**</u>   <u>**Topic**</u>

Date	Meeting	Topic
4/2	1	Course Overview – The "Awe-full Power of Genetics" and the gene
4/4	2	*Discussion: DNA as the genetic material*
4/6	3	Methods: DNA sequencing technology and applications
4/9	4	*Paper discussion 1: A minimal genome*
4/11	5	The RNA world – versatility of RNA
4/13	6	*Paper discussion 2: rRNA sequencing for phylogeny*
4/16	7	Regulatory RNA
4/18	8	Methods: Proteins and protein structure
4/20	9	*Paper discussion 3: Evolution of the genetic code – it's a new world!*
4/23	10	Primer on DNA replication: The basics and PCR
4/25	11	Molecular Genetics: To be forward or reverse - that is the question.
4/27	12	*Paper discussion 4: Human histones in yeast*
4/30	13	Model organisms: *Neurospora crassa*
5/2	14	Chromosome, locus, gene – mapping of traits
5/4	15	*Paper discussion 5: Bulk segregant analysis and sequencing*

5/7		**First EXAM (covers first 14 meetings)**
5/9	16	Model organisms: *Saccharomyces cerevisiae*
5/11	17	*Paper discussion 6: Essential genes unmasked*
5/14	18	Model organisms: *Escherichia coli*
5/16	19	*Paper discussion 7: Prokaryotic genome defense*
5/18	20	Methods: Chromatin immunoprecipitation
5/21	21	*Paper discussion 8: Eukaryotic transcription – chromatin-based gene regulation*
5/23	22	Model organisms: *Arabidopsis thaliana*
5/25	23	*Paper discussion 9: Epigenetic gene regulation in plants by DNA methylation*
5/28		*Memorial Day (no class)*
5/30	24	Model organisms: *Caenorhabditis elegans*
6/1	25	*Paper discussion 10: RNA-based gene silencing by RNAi*
6/4	26	Model organisms: *Drosophila melanogaster and Mus musculus*
6/6	27	*Paper discussion 11: Systems biology: The circadian clock*
6/8	28	*Paper discussion 12: Genetic engineering of stem cells*

6/13   **Wednesday**   **Second EXAM (2 pm; covers meetings 15 to 28)**

Reading for BB486 – Spring 2018

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*

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 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.
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.

Group 4   *Paper discussion: Histones wrap DNA – how conserved are they?*

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.

Group 1   *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 2   *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 3   *Paper discussion: Prokaryotic genome defense – the origin of CRISPR/Cas9*

CRISPR provides acquired resistance against viruses in prokaryotes.
Barrangou R, Fremaux C, Deveau H, Richards M, Boyaval P, Moineau S, Romero DA, Horvath P.
Science. 2007 Mar 23;315(5819):1709-12.

Group 4   *Paper discussion: Eukaryotic transcription – chromatin-based gene regulation*

SNF2 Family Protein Fft3 Suppresses Nucleosome Turnover to Promote Epigenetic Inheritance and Proper Replication.
Taneja N, Zofall M, Balachandran V, Thillainadesan G, Sugiyama T, Wheeler D, Zhou M, Grewal SI.
Mol Cell. 2017 Apr 6;66(1):50-62.e6. doi: 10.1016/j.molcel.2017.02.006. Epub 2017 Mar 16.

Group 1   *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 2   *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 3   *Paper discussion: Systems biology: The circadian clock – Nobel Prize Topic*

Restoration of circadian behavioural rhythms by gene transfer in Drosophila.
Bargiello TA, Jackson FR, Young MW.
Nature. 1984 Dec 20-1985 Jan 2;312(5996):752-4.
The Neurospora clock gene frequency shares a sequence element with the Drosophila clockgene period.
McClung CR, Fox BA, Dunlap JC.
Nature. 1989 Jun 15;339(6225):558-62.
DNA Replication Is Required for Circadian Clock Function by Regulating Rhythmic Nucleosome Composition.
Liu X, Dang Y, Matsu-Ura T, He Y, He Q, Hong CI, Liu Y.
Mol Cell. 2017 Jul 20;67(2):203-213.e4. doi: 10.1016/j.molcel.2017.05.029. Epub 2017 Jun 22.

Group 4   *Paper discussion: Genetic engineering by CRISPR systems*

One-step generation of mice carrying reporter and conditional alleles by CRISPR/Cas-mediated genome engineering.
Yang H, Wang H, Shivalila CS, Cheng AW, Shi L, Jaenisch R.
Cell. 2013 Sep 12;154(6):1370-9. doi: 10.1016/j.cell.2013.08.022. Epub 2013 Aug 29.