CELLULAR BASIS OF DISEASE – BISC 479 – FALL 2019

Lecture: Tu & Th 1:30–2:45 pm SHOEMAKER Room 408
Instructor: Dr. Brian Doctor, 414 Shoemaker Hall
Email: rbdoctor@olemiss.edu
Office Phone: 662-915-1390

Communication:

E-Mail Is the most reliable means of getting me a message.

Social Media Nope

Phone Feel free to call but do NOT leave me a message. If I am free in my office I will gladly pick up but I do NOT replay my messages.

Office Hours

Monday	12:00 pm to 1:00 pm
Tuesday	3:00 pm to 4:00 pm
Wednesday	12:00 pm to 1:00 pm

Drop-in Feel free to drop by my office after 1:00 on M/W/F or after 3:00 on Tu/Th. If I am there and free I would be delighted to talk with you. If I am in the middle of something I will set up a time to talk.

Appointment Send me an e-mail with the dates/times you can come by and I will reserve you that time.

Mail Box Do NOT leave materials or assignments for me in the departmental mailboxes; I will not get them in a timely fashion. To drop off assignments when I am not in, slide the pages under my office door.

Blackboard I use Blackboard to communicate with the class as a whole. This includes messages, powerpoint lecture slides, homework assignments and test scores.

Course Description: This course is designed for upperclassmen from the basic science departments who have established a strong foundational understanding of the composition, structures and functions of mammalian eukaryotic cells. The primary intent of the course is to broaden and deepen each student's understanding and appreciation of the anatomy and physiology of mammalian eukaryotic cells. The secondary intent of the course is to learn what changes occur at the cellular level if the normal composition, structure or function is disrupted and how those cellular alterations lead to disease states at the tissue, organ and organism levels. While the diagnosis and treatment of some of the diseases being covered may be touched upon, those points are well beyond the scope of this course.

The course will predominantly utilize a READ-DESCRIBE-DISCUSS-RECALL format. Prior to each class its students will read articles about the physiology of a specific cellular structure, function or component and the pathophysiologic conditions or diseases that develop when the specific structure, function or component is disrupted. These will be primarily review articles and, occasionally, peer-reviewed primary research articles. Alternatively, a short list of topics will be provided. In these cases, students should investigate those topics prior to the next class.

The course will be segregated into three sections. The first section will explore the changes in cell behavior when the cellular physiology is altered and the diseases that arise within an individual after the cellular physiology is altered. The cellular alterations can come at different levels of organization., ranging from imbalances in trace elements to modification of macromolecules to altered cell-cell interactions.

The second section focuses on the cellular pathophysiology of obesity, cholesterol and coronary heart disease (CHD). CHD is the leading cause of death in the US. Consequently, the cellular factors responsible for CHD will be investigated. The spectrum of contributing factors include those that are genetic, epigenetic, environmental and immune in nature. This section seeks to understand the cellular underpinnings of CHD.

The third section turns to infectious diseases, how the immune system has evolved to counter the effect of pathogens and the self-inflicted diseases that develop when the immune system is errantly regulated.

Learning Objectives:
After completing this course a student should:

- have markedly elevated their working knowledge of the physiology of mammalian cells
- have gained an appreciation for how changes in the composition or structure of mammalian cells can result in altered cell function
- have gained an understanding for how modifications at the cellular level can produce changes at the tissue level and disease at the organism level
- have improved their scientific writing skills
- have practiced their *critical thinking* skills

Texts and Reading:
There is NO primary textbook that is required.

PDF files of review articles (main reading material), primary research articles from peer-reviewed journals &/or other reading materials will be posted on Blackboard a minimum of two days prior to the day that material is to be presented in class. To MAXIMIZE the value of our lecture time, reading materials should be read BEFORE class. You will be asked to self-report at the start of each lecture if you read the assigned reading material.

Access to a Cell and Molecular Biology text is very likely to increase the depth, rate and efficiency that the topics are studied and mastered. Examples of three excellent textbooks to consider are listed below; any one of the three will fit the bill. If you need to borrow a Cell/Molecular Biology textbook, I have some that you may use on a short term basis (so everyone can get access). Come by after class or during office hours to borrow one and return it in a day or two.

Molecular Biology of the Cell, 6th edition, Alberts et al. (ISBN 9780815344322)

Molecular Cell Biology 7th edition, Lodish et al.

Karp's Cell & Molecular Biology, 8th edition, Iwasa and Wallace.

GRADING

Attendance	**20%**	**or**	**20 pts**
Preparation	**10%**	**or**	**10 pts**
Participation	**20%**	**or**	**20 pts**
Lecture Leader	**20%**	**or**	**20 pts**
Journal	**20%**	**or**	**20 pts**
Final	**10%**	**or**	**10 pts**
TOTAL			**100 pts**

ATTENDANCE **Students will sign in at the start of class**
*** for the first 4 absences, 1 pt will be docked from the total points**
*** for each subsequent absence, 2 pts will be docked**
*** 10 absences = 20 points**
*** >10 absences: cannot earn a passing grade**
*** excused absences do not count as a missed class**
(students MUST attend at least one class in the first two weeks or be dropped from the class)

PREPARATION **Students will note on the sign in sheet if they read the assigned material**
Students will be on the Honor system
*** for the first 4 missed preparations, 1 pt will be docked from the total points**
*** a maximum of 10 pts can be lost**

PARTICIPATION **at the end of the semester the instructor will assign a *participation* score**
*** maximum of 20 pts**

LECTURE LEADER **Students will be paired up at random**
Pairs will submit (3) topics from the syllabus they would enjoy leading
- **dates may be movable**
- **they should be submitted in order of preference**

Pairs will meet with the instructor twice in the week prior to their leading
Student-Pairs will actively help lead the lecture they are assigned to
Each Student-Pair will lead the group once during the semester

*** the instructor will evaluate the total performance**
*** a maximum of 20 pts can be earned**

JOURNAL **Students will keep an Electronic Journal**
Entries will be made following each lecture period
Entries will include:
Abstract (150-250 words) reporting main story line and key points
Answer any questions that are specifically posed
Perform any project assigned
Journals will be e-mailed during the semester upon request
Completed journals will be submitted prior to the Final Exam
*** a maximum of 20 pts can be earned**

FINAL **Format: Read a manuscript/text that is provided**
Analyze the data and information
Write a report/Answer questions
*** a maximum of 10 pts can be earned**

CELLULAR BASIS OF DISEASE *(tentative schedule)*

Date	**Topic**
Tu 8/27 *WEEK 1-1*	Course Overview; Genesis of Disease States
Th 8/29 *WEEK 1-2*	Review of Mammalian Cell Structures and Functions
Tu 9/3 *WEEK 2-1*	Diseases arise during imbalance of specific Elements * Fe (iron): hemoglobin, binding O2 anemia and haemochromatosis * I (iodine) T3 and T4 thyroid hormones; regulating metabolism goiter; endemic cretinism
Th 9/5 *WEEK 2-2*	Diseases arise from errant or absent molecules *Essential amino acids* *Essential fatty acids* Vitamins (e.g. A, C, D, Folic Acid, K)
Tu 9/10 *WEEK 3-1*	Diseases arise from errant macromolecules: DNA and Genetic Diseases
Th 9/12 *WEEK 3-2*	Diseases arise from errant macromolecules: DNA and Cancer
Tu 9/17 *WEEK 4-1*	Diseases arise from errant macromolecules: Protein synthesis, QC, turnover
Th 9/19 *WEEK 4-2*	Diseases arise from errant macromolecules: Protein accumulation • beta-amyloidosis • Lewy bodies and Alzheimers • Alpha-synucleins and Parkinson's • PrP and prions
Tu 9/24 *WEEK 5-1*	Uptake and Delivery of Lipids and Cholesterol * Physiology of phosphoglycerides, sphingolipids and cholesterol o Enterocyte uptake: cholesterol transporter o Vascular transport: LDL and HDL micelles o Cellular uptake: LDL receptor (receptor mediated endocytosis) • Physiology of free FA, monoacyl glyderides, triacylglycerides
Th 9/26 *WEEK 5-2*	Diseases arise from errant macromolecules: Lipids and Cholesterol * Sphingolipids: Tay-Sachs, Niemann-Pick • Cholesterol: Coronary Heart Disease o Familial Hypercholesterolemia o Obesity
Tu 10/1	Diseases arise from Obesity

WEEK 6-1

* energy storage: biochemistry
- energy storage: cell Biology
- excess adipose tissue, chronic inflammation and tyoe II diabetes

Th 10/3 Diseases arise from errant transmembrane transport

WEEK 6-2

* ion channels,transporters and pumps
- driving forces, Nernst Eqn
- pulmonary fluid secretion: CFTR Cl- channels; cystic fibrosis

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Tu 10/8 Diseases arise from errant cell-cell contact; Adherens Junctions

WEEK 7-1

* Cell adhesion, cadherins, b-catenin and EMT
- B-catenin and colon cancer
- E-cadherin and EMT

Th 10/10 Diseases arise from errant cell-cell contact; Tight Junctions

WEEK 7-2

* 'Gate' and 'Fence' functions; claudins, jams, occludens
- claudins and hypomagnesemia
- claudins and deafness

Tu 10/15 Diseases arise from errant cell-cell contact: Desmosomes

WEEK 8-1

* tethers and mechanically links mechanical
- epidermis pemphigus vulgaris (auto-immune)

Th 10/17 Diseases arise in the cytoskeleton: Intermediate Filaments

WEEK 8-2

* keratins Bullosa Simplex *Butterfly children* (genetic)
- lamins *laminopathies*

Tu 10/22 Diseases arise in the cytoskeleton: Actin

WEEK 9-1

* structural support of the plasma membrane
- tracks for motor proteins
- myosins: actin motor proteins
- myosin mutations, Hair Cells, deafness
- Wiscot-Aldridge Syndrome protein

Th 10/24 Diseases arise in the cytoskeleton: Microtubules

WEEK 9-2

* Motile and Primary Cilia
- Ciliopathies: *inversin*
- Ciliopathies: *ADPKD, ARPKD*
- Ciliopathies: *Kartagner's Disease*

Tu 10/29 Apooptosis

WEEK 10-1

* Programmed cell death
- Syndactyly
- Canale-Smith syndrome

Th 10/31 Cell Signaling: coordinating the responses to *hypoxia*

WEEK 10-2 * Immediate-local: nitric oxide

*long-term-local: HIF1a – VEGF – increased neo-vascularization
*immediate-systemic: increased lung tidal volumes and rates
increased cardiac ouotput
*long term systemic increased hematocrit
*lifetimes-systemic: Andes adaptations vs Himalayas adaptations

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Tu 11/05 Erythrocytes
WEEK 11-1 * Hemoglobin: Sickle Cell Anemia
* Spectrin cytoskeleton: Spherocytosis & Elliptocytosis

Th 11/07 Retina: Pigmented Epithelial Cells
WEEK 11-2 Support the rods and cone cells
- Retinitis Pigmentosa: blindness following loss of RPE cells
- Stem cell therapy

Tu 11/12 Infectious Diseases
WEEK 12-1 * Viruses ex *influenza*
- Bacteria ex. *Heliobacter pylori*
- Parasites (helminthes or worms): ex. Hook worm
- Parasites (protozoa): ex. Giardia
- Fungi, yeasts, mold ex.
- Prions ex. PrP

- Toxins and Poisons
- Cancer cells

Th 11/14 Immune responses vs alternative infectious agents
WEEK 12-2 * Innate immune responses
  - macrophage
  - neutrophils
  - eosinophils
  - mast cells
  - basophils
  - natural killer cells
  - dendritic cells
- Adaptive immune responses
  - B cells
  - T cells

Tu 11/19 Diseases due to Inappropriate Immune Responses
WEEK 13-1 * Excessive responses
    - Hypersensitivity responses
    - Chronic inflammatory responses
    - Auto-immune responses
- Insufficient responses (immune deficiencies)
    - Primary (inherited) >150 identified
    - Secondary (acquires)

Th 11/21 Diabetes (root: siphon or pass through)
WEEK 13-2 Mellitis (root: honeyed or sweet)
Insipidus (root: without taste)

- Diabetes Mellitis (Type I) auto-immunity vs pancreatic beta cells
  (Type II) loss of insulin receptor signaling
- Diabetes Insipidus loss of ADH receptor signaling

Tu 11/26 Thankgiving Break

- Pursue the elusive whitetail

Th 11/28 Thanksgiving Day

- Eat turkey, Beat State

Tu 12/3 Diseases of Development
WEEK 14-1

Th 12/5 Cellular basis of AGING
WEEK 14-2

Th 12/10 **FINAL EXAM**

Disability Access and Inclusion: The University of Mississippi is committed to the creation of inclusive learning environments for all students. If there are aspects of the instruction or design of this course that result in barriers to your full inclusion and participation, or to accurate assessment of your achievement, please contact the course instructor as soon as possible. Barriers may include, but are not necessarily limited to, timed exams and in-class assignments, difficulty with the acquisition of lecture content, inaccessible web content, and the use of non-captioned or non-transcribed video and audio files. If you are approved through SDS, you must log in to your Rebel Access portal at **https://sds.olemiss.edu** to request approved accommodations. If you are NOT approved through SDS, you must contact Student Disability Services at **662-915-7128** so the office can: 1. determine your eligibility for accommodations, 2. disseminate to your instructors a Faculty Notification Letter, 3. facilitate the removal of barriers, and 4. ensure you have equal access to the same opportunities for success that are available to all students.

Academic Integrity: Any form of misconduct -- cheating, plagiarism, fabrication -- will not be tolerated and may subject violators to a failing grade in the course.

This syllabus is subject to change at the discretion of the instructor to accommodate instructional, and/or student needs.