

Biology 41: Cells into Organs: Assembly, Function and Disease
Fall 2019
LSC Room 105

Instructor: Bing He
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Office Hours: Tue 11 AM – 12 PM, Thurs 2 PM – 3 PM
Meeting times: MWF, 11:30 am – 12:35 pm

Course Description:

How do cells organize into the myriad forms of tissues, and how do they work together to perform specific physiological functions? In this course, we will use epithelial tissues as an example to explore these fundamental questions. Epithelia are among the most common types of tissue organization in animals. They line the cavities, ducts and surfaces of all the major organ systems and provide a variety of functions such as secretion, protection and sensing. During development, epithelial tissues also function in morphogenetic processes that guide the formation of body patterns. Defects in epithelial growth control and function play a major role in human diseases such as cystic fibrosis and cancer. The goal of this course is to understand the form, dynamics and function of epithelial tissues, and how dysregulation of epithelia can lead to various human diseases.

Pre-Requisites: Biol 012 or permission of instructor

Learning Objectives:

1. Gain a working knowledge of the general principles of tissue organization and function.
2. Understand the mechanisms underlying epithelial reorganization in morphogenesis.
3. Learn about how dysregulation of epithelia leads to human diseases.
4. Become familiar with the experimental methods used to study tissue organization, function and morphogenesis.
5. Become comfortable reading research papers from the primary literature that investigate fundamental aspects of epithelial organization and function.

Teaching Approach:

Class period will be a combination of lectures, discussions of the assigned reading (see below), and question-based exercises completed in small groups. The exercises are designed to help reinforce the lecture material and master skills for data interpretation and problem solving.

Reading Materials:

- There is no required textbook for this course. Instead, I will post selected review articles to supplement the lecture material. These readings are intended to reinforce and contextualize material covered in class.
- We will read several primary literature articles throughout the term. These articles will provide a basis for in-class, small-group discussions.
- This syllabus, power point presentations, additional readings, and in-class assignments will be posted to Dartmouth's Canvas site (<http://canvas.dartmouth.edu>).
- Optional textbook readings for further independent study (will not be covered on the exams):
Epithelial Organization and Development. Edited by Tom P. Fleming
Epithelial Morphogenesis in Development and Disease. Edited by Walter Birchmeier and Carmen Birchmeier

TOPICS AND SCHEDULE:

Part 1 (week 1-3): Epithelial organization, cell polarity and tumorigenesis

Week 1: Basic principles of epithelial organization

- (9/16 M) 1. From cell in solitary to cell aggregates – Self-organization of tissue architecture
(9/18 W) 2. How do cells glue together? – The nuts and bolts of cell-cell adhesions
(9/20 F) 3. How do cells talk to each other? – Chemical communication between cells
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Week 2: Cell polarity and epithelial integrity

- (9/23 M) 4. Epithelial polarity and tumorigenesis – Lessons from model organisms
(9/25 W) 5. Paper discussion 1:
Cooperative regulation of cell polarity and growth by Drosophila tumor suppressors. Bilder et al. Science. 2000
(9/27 F) 6. Epithelial-mesenchymal transition in development and metastasis
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Week 3: Cell polarity and epithelial integrity (cont.)

- (9/30 M) 7. Paper discussion 2:
The transcription factor Snail controls epithelial-mesenchymal transitions by repressing E-cadherin expression. Cano et al. Nat Cell Biol. 2000
(10/2 W) 8. Review session 1
(10/4 F) 9. Midterm Exam 1

Part 2 (week 4-6): Regulation of tissue size and shape

Week 4: Cell proliferation and organ size control

- (10/7 M) 1. Coordination of cell proliferation and cell death in organ size control
(10/9 W) 2. Control of cell growth by ECM and integrin signaling
(10/11 F) 3. Paper discussion 3:

Role of YAP/TAZ in mechanotransduction. Dupont et al Nature 2011.

Week 5: Epithelial morphogenesis

- (10/14 M) 4. Planar cell polarity: from hair orientation to body axis elongation
(10/16 W) 5. From 2D to 3D: epithelial folding and the role of actin-myosin contractility
(10/18 F) 6. Paper discussion 4:

Pulsed contractions of an actin-myosin network drive apical constriction. Martin et al., Nature. 2009.

Week 6: Epithelial morphogenesis (cont.)

(10/21 M) 7. Human neural tube defects

(10/23 W) 8. Review session 2

(10/25 F) 9. Midterm exam 2

Part 3 (week 7-9): Tissue malfunction, repair and regeneration

Week 7: Defects in molecule transport

(10/28 M) 1. Molecule transport across the epithelium – What causes Cystic Fibrosis?

(10/30 W) 2. Polarized protein targeting in epithelial cells

(11/1 F) 3. Paper discussion 5:

A revised airway epithelial hierarchy includes CFTR-expressing ionocytes. Montoro et al., Nature. 2018

Week 8: Defects in signal sensing and transduction

(11/4 M) 4. Autosomal Dominant Polycystic Kidney Disease (ADPKD) – Part I (primary cilium and signal sensing)

(11/6 W) 5. Autosomal Dominant Polycystic Kidney Disease (ADPKD) – Part II (what drives cyst formation?)

(11/8 F) 6. Paper discussion 6:

Polycystins 1 and 2 mediate mechanosensation in the primary cilium of kidney cells. Nauli et. al., Nat Genet. 2003

Week 9: Tissue repair and regeneration

(11/11 M) 7. How do injured tissues heal themselves? – Mechanisms of wound repair

(11/13 W) 8. Tissue engineering and regenerative medicine

(11/15 F) 9. TBD

Week 10: Review

(11/18 M) 10. Review session 3

Final Exam (Exam 3) 11/24 Sun 3:00 PM – 5:00 PM

ASSESSMENT:

Midterm exams (20% each)

Final exam (20%)

Paper evaluations (6% for each of the 5 papers; 30% in total)

Class participation (10%)

(1) Exams:

- Exams will focus on material covered in lecture, emphasizing data interpretation and problem-solving. Material from the readings that are not discussed in lecture will not be tested. Students taking the exams are expected to abide by the Dartmouth Honor principle. The use of electronic devices or any type of supplemental information (verbal or written) during the exam is prohibited unless otherwise instructed by the teacher.
- Graded exams will be returned to the students approximately one week after they are taken. Exams are graded not only for content but also for clarity and conciseness.
- The exam key will be posted on the course Canvas site. If, after reading the key, you feel there was an error in the scoring of your exam, you may submit an error correction request. Include a typewritten explanation stapled to your exam detailing the mistake made in the grading. Do not write or alter the exam prior to handing it in for error correction. The error correction request must be submitted within one week of the distribution of the graded exam.

(2) Paper Evaluations:

- We will read and discuss 6 research papers from the primary literature. Each student will pick 5 of the 6 papers to write a brief summary (one page or less, typed, see below for a detailed instruction of page format), focusing on (i) hypotheses being tested, (ii) experimental design, (iii) results, and (iv) interpretation of the results (a guideline for the summary will be provided for each paper).
- The summary should be submitted electronically (Canvas) before the beginning of class on the day we discuss the paper.
- After our in-class discussion, students will have the option to revise and resubmit their summary the next class period. The grades for the original and revised summaries will be averaged.
- One-page paper summary format:
 - Recommended fonts: Arial (NOT Arial Narrow), Georgia, Helvetica, Palatino Linotype
 - Font size: must be 11 points or larger
 - Line spacing: single
 - Margins must measure at least 0.5 inch (top, bottom, and sides)
 - File format: Word

(3) Class Participation:

- Your active participation in this course is essential and will be evaluated through your attendance at lectures (5%) and active engagement during the in-class exercises and discussions (5%) throughout the term.

ACADEMIC HONOR:

The Dartmouth College Student Handbook (page iii) states “Fundamental to the principle of independent learning are the requirements of honesty and integrity in the performance of academic assignments, both in the classroom and outside. Dartmouth operates on the principle of academic honor, without proctoring of examinations. Students who submit work which is not their own or who commit other acts of academic dishonesty forfeit the opportunity to continue at Dartmouth.” The complete text of the Dartmouth Academic Honor Principle is given in the Dartmouth College Student Handbook.

There are a number of situations in which a student in Biology 41 might be tempted to violate the Academic Honor Principle. These situations include (but are not limited to) the following:

- a) Examinations must be completed without reference to written materials other than those provided with the exam paper and must be completed without communication with anyone else (the only permissible exception is that students may request clarification of any exam question from the course faculty and staff who are present expressly for that purpose). The answers that you provide must be entirely your own work.
- b) Class policy permits the re-submission of exams for potential re-evaluation by the professor. Any alteration of the answers between the time when the graded papers were returned to the student and the time when the paper was submitted for re-grading constitutes a breach of the Academic Honor Principle.

Honesty is the foundation of the academic pursuit of knowledge. In recognition of this, the faculty of Biology 41 will not overlook any violations of the Academic Honor Principle. Indeed, the Faculty Handbook of Dartmouth College states explicitly that College Faculty members are obligated to report potential violations of the Academic Honor Principle to the Dartmouth College Committee on Standards. Should the Committee on Standards find the student to be in violation of the Academic Honor Principle, punishments usually involve suspension for multiple terms or separation of the student from the College.

NOTE TO STUDENTS WITH PHYSICAL OR LEARNING DISABILITIES:

I encourage students who may need disability-related academic adjustments to see me privately as early as possible in the term, preferably before the end of the first week. Students requiring disability-related academic adjustments or services must consult the Student Accessibility Services (SAS) office (Carson Suite 125, student.accessibility.services@dartmouth.edu). Once SAS has authorized adjustments or services, I will need to view the originally signed SAS Services and Consent form and/or a letter on SAS letterhead. If you have questions about whether you qualify to receive academic adjustments or services, please contact the SAS office directly. All discussions will remain confidential.

RELIGIOUS OBSERVANCES:

Some students may wish to take part in religious observances that occur during this academic term. If you have a religious observance that conflicts with your participation in this course, please speak with me as soon as possible to discuss appropriate accommodations.

MENTAL HEALTH:

I recognize that the academic environment at Dartmouth is challenging, that our terms are intensive, and that classes are not the only demanding part of your life. There are a number of resources available to you on campus to support your wellness, including:
your undergraduate dean (<http://www.dartmouth.edu/~upperde/>),
Counseling and Human Development (<http://www.dartmouth.edu/~chd/>),
and the Student Wellness Center (<http://www.dartmouth.edu/~healthed/>).

I want you to be aware of these resources and encourage you to use them as needed.

TITLE IX:

At Dartmouth, we value integrity, responsibility, and respect for the rights and interests of others, all central to our Principles of Community. We are dedicated to establishing and maintaining a safe and inclusive campus where all have equal access to the educational and employment opportunities Dartmouth offers. We strive to promote an environment of sexual respect, safety, and well-being. In its policies and standards, Dartmouth demonstrates unequivocally that sexual assault, gender-based harassment, domestic violence, dating violence, and stalking are not tolerated in our community.

The Sexual Respect Website (<https://sexual-respect.dartmouth.edu>) at Dartmouth provides a wealth of information on your rights with regard to sexual respect and resources that are available to all in our community. Please note that, as a faculty member, I am obligated to share disclosures regarding conduct under Title IX with Dartmouth's Title IX Coordinator. Confidential resources are also available, and include licensed medical or counseling professionals (e.g., a licensed psychologist), staff members of organizations recognized as rape crisis centers under state law (such as WISE), and ordained clergy (see <https://sexual-respect.dartmouth.edu/reporting-support/all-resources/confidential-resources>). Should you have any questions, please feel free to contact Dartmouth's Title IX Coordinator (Kristi.Clemens@Dartmouth.edu) (and deputies if appropriate).