

**COURSE TITLE:** Experimental Biology

**COURSE NUMBER:** G302

**CREDITS:** 5

**COURSE DIRECTOR:** Mary Baylies, Ph.D.

**COURSE PREREQUISITES:** None; Open to first year PhD students

**GRADING POLICY:** Pass/Fail

## **COURSE DESCRIPTION AND LEARNING OBJECTIVES**

Experimental Biology teaches conceptual and practical aspects of four different research disciplines: imaging, genetics, genomics, and biochemistry. Each topic will be covered for one week through a combination of workshops, research paper discussions, and lectures. The purpose of this course is to hold discussions about different research disciplines and their methods, but not to teach each topic comprehensively. Each week will introduce new concepts and may not connect directly to the previous week. Questions that will be considered in the course include:

- How is imaging performed at different length scales, and what can be learned through different techniques?
- How have imaging technologies pushed the boundaries of knowledge?
- How are genetic principles and applied technologies used to make new discoveries?
- What techniques allow for the experimental manipulation of DNA, RNA and protein, and how do they work?
- How do the “kits” on my research bench actually work?

## **COURSE STRUCTURE**

This course meets four to five days a week for four weeks. Each day includes a 2 hour lecture/discussion followed by a 2 hour afternoon session. Total in-class time includes approximately 75 hrs. Students are also expected to spend considerable time reading the pre-assigned articles and background assignments prior to class.

### *Teaching Fellows*

Each topic will have a teaching fellow, who is an advanced GSK Student. The teaching fellow's responsibilities will include setting up for the course, helping organize group projects, creating and evaluating student problem sets and reflection papers.

## **ASSIGNMENTS AND METHODS FOR ASSESSING STUDENT ACHIEVEMENT**

The course is structured so that each morning lecture/discussion is followed by a group presentation or assignment that will test the students' knowledge of the topics discussed in the morning. Projects will include paper discussions, problem sets, and explanations of how certain biological research tools work. Students will receive real-time feedback from the faculty director during their presentations.

In addition, some weeks will have either a reflection paper or problem sets assigned, which will be reviewed by the teaching fellows. These assignments will be due during the week following that section.

## **BASIS FOR GRADE DETERMINATION**

Students will receive a pass/fail grade for this course. To receive a passing grade, students must attend all morning and afternoon sessions, actively participate in class discussions, and complete all group and individual assignments outlined by each week's faculty leader. Students are permitted to miss one morning and afternoon session. Any more absences will be brought to the attention to the Dean to determine how this will impact the final grade.

## **COURSE EVALUATION**

Students will be encouraged to complete anonymous post course surveys that will evaluate the effectiveness of the course. This survey is used to improve future course offerings.

## **COURSE SCHEDULE**

The following schedule shows planned activities for each week. Please take note of assignments for paper introductions and a small group project in week 2.

### **Week 1: Introduction/Imaging**

**8/25/2025; 9/2/2025 – 9/5/2025**

- Lectures each morning (10am-12pm)
- Discussion sessions each afternoon (1-3pm)

Teaching Fellow: Achuth Nair

#### **Monday 8/25**

**Morning Breakfast session: Dr. Selwyn Vickers, lecture: “The impact of Research on the Mission of MSK” – This session will meet from 9:00-11:00 am**

#### **Tuesday 9/2**

**Morning Session: Introduction to the Year – From Basic Biology to Cancer**

**Afternoon Session: Group Paper discussion**

Cheung KJ, Padmanaban V, Silvestri V, Schipper K, Cohen JD, Fairchild AN, Gorin MA, Verdone JE, Pienta KJ, Bader JS, Ewald AJ. Polyclonal breast cancer metastases arise from collective dissemination of keratin 14-expressing tumor cell clusters. Proc Natl Acad Sci U S A. 2016 Feb 16;113(7):E854-63. doi: 10.1073/pnas.1508541113. Epub 2016 Feb 1. PMID: 26831077; PMCID: PMC4763783.

**Student Presenter:** Lange, Matthew

## Wednesday 9/3

### **Morning session: Rich Hite, lecture**

*Introduction to imaging at different scales*

1. What types of imaging are useful in biological sciences?
  - a. Start small with electrons
  - b. Light has diverse roles in imaging
  - c. How to image whole organisms?
2. How can information at different scales be combined to better understand complex biological questions?
  - a. Dynamic vs. static images
  - b. Time-resolved effect of perturbations
  - c. Steady-state vs non-equilibrium

### **Afternoon session: Rich Hite, lecture**

*Electron microscopy*

1. Electron optics viewed through the lens of light optics
2. Physics of converting a 3D object into a 2D image
  - a. Central section theorem
  - b. Fourier transforms
3. Practical applications of electron microscopy in biological sciences
  - a. Traditional electron microscopy
  - b. Single-particle cryo-EM
  - c. Cryo-ET
  - d. Electron crystallography (micro-ED)
4. Limitations of electron microscopy
  - a. Static structures
  - b. Heterogeneity

## Thursday 9/4

### **Morning session: Christina Pyrgaki, lecture**

*Light microscopy: Visualization of cells and cellular components*

**Afternoon session: Instrument Tours – meet in Z668**

**Group 1:**

Afroz, Jalwa  
Beattie, Kai  
Cherkas, Shelby  
Hanselman, Olivia  
Li, Ruofei

**Group 3:**

Ahmed, Nibras  
Levin, Bailey  
Mutaher, Mohammed  
Perea del Angel, Ana  
Pope, Eleanor

**Group 2:**

Illouz, Sylvia  
Lange, Matthew  
Magnus, Karina  
McIlhenny, Lauren  
Tarrab, Stephanie

**Group 4:**

Prabakaran, Adithya  
Styers, Hannah  
Sussman, Carleigh  
Ta, Christina  
Volpe, Christina

**Friday 9/5 (10:00-12:00 and 1:00-4:00)**

**Morning session: Jason Lewis, lecture**

*Whole body imaging*

**Afternoon session (1:00-4:00): Organized visits to imaging facilities at MSK – meet in Z138 at 12:45.**

Tours will be organized in 3 groups, each group visiting 3 of the imaging facilities for 1 hour, beginning at 1:00 pm.

Groups as follows:

**Group 1:**

Afroz, Jalwa  
Ahmed, Nibras  
Beattie, Kai  
Cherkas, Shelby  
Hanselman, Olivia  
Illouz, Sylvia

**Group 2:**

Lange, Matthew  
Levin, Bailey  
Li, Ruofei  
Magnus, Karina  
McIlhenny, Lauren  
Mutaher, Mohammed  
Perea del Angel, Ana

**Group 3:**

Pope, Eleanor  
Prabakaran, Adithya  
Styers, Hannah  
Sussman, Carleigh  
Ta, Christina  
Tarrab, Stephanie  
Volpe, Christina

**Evaluation project:**

Students are to write a 1–2-page paper on how imaging can be used to answer a research question. These papers are to be emailed directly to the teaching fellow by Tuesday September 9, 2025.

## **Week 2: Genetics**

**9/8/2025 – 9/12/2025**

- Sessions each morning and afternoon (10am-12pm and 1-3)

Teaching Fellow: James Rodrigues

### **Monday 9/8**

#### **Morning session: Danwei Huangfu, lecture**

*CRISPR techniques and application*

1. Basic concepts of CRISPR technologies
2. Different applications of CRISPR technologies in genetic studies.
  - a. CRISPR/Cas-mediated genome editing
  - b. The expanding CRISPR toolbox
  - c. Diverse applications and beyond

#### **Afternoon session: Student small group presentations**

Using CRISPR technology to study and/or combat COVID-19: Prepare to discuss ideas using CRISPR technology to study and/or combat COVID-19. Your ideas can be creative and involve anything from the development of diagnostic tests, to foundational research or the development of treatments. You may search the literature, but you are also encouraged present your own original ideas. Please prepare a 10 minute presentation to discuss the technical and applied aspects of your idea(s). Consider both the potential benefits and also the limitations of your approaches.

#### **Working groups:**

##### **Group 1:**

Afroz, Jalwa  
Beattie, Kai  
Cherkas, Shelby  
Hanselman, Olivia

##### **Group 2:**

Illouz, Sylvia  
Lange, Matthew  
Magnus, Karina  
McIlhenny, Lauren

##### **Group 3:**

Levin, Bailey  
Mutaher, Mohammed  
Perea del Angel, Ana  
Pope, Eleanor

##### **Group 4:**

Prabakaran, Adithya  
Styers, Hannah  
Sussman, Carleigh  
Ta, Christina

##### **Group 5:**

Ahmed, Nibras  
Li, Ruofei  
Tarrab, Stephanie  
Volpe, Christina

## Tuesday 9/9

### **Morning Session:**

Advanced genetic approaches -1 Xiaolan Zhao

#### **Generate informative alleles**

##### **Conditional alleles**

- Temperature sensitive alleles
- Chemical induced degron
- Analog-sensitive alleles & small molecular inhibitors
- Transcription and translation turn off)

##### **Separation-of-functional alleles**

#### **Use suppressors to discover new factors, pathways, and mechanisms**

Dosage suppressors

Second site mutations

#### **Afternoon session: Paper discussion on synthetic viability screening**

##### **Synthetic viability screen**

- Puddu, F. et al. Chromatin determinants impart camptothecin sensitivity. *EMBO Rep* (2017).

**Student Presenter:** Afroz, Jalwa

## Wednesday 9/10

### **Morning Session:**

Advanced genetic approaches- 2 Xiaolan Zhao

- **Enrichment strategy**
- **Use synthetic lethality or sickness method to unravel new biology**
- **E-map**
- **Synthetic dosage suppression**
- **Biochemical readouts used in genetic screens**
- **Convert biochemical questions to genetic questions**
- **Overview of model organisms**
- **Emerging Genetic Approaches**

**Afternoon Session: Group Exercise.**

**Group 1:**

Afroz, Jalwa  
Beattie, Kai  
Cherkas, Shelby  
Lange, Matthew  
Levin, Bailey

**Group 3:**

Perea del Angel, Ana  
Styers, Hannah  
Ta, Christina  
Tarrab, Stephanie  
Volpe, Christina

**Group 2:**

Ahmed, Nibras  
Hanselman, Olivia  
Illouz, Sylvia  
McIlhenny, Lauren  
Mutaher, Mohammed

**Group 4:**

Li, Ruofei  
Magnus, Karina  
Pope, Eleanor  
Prabakaran, Adithya  
Sussman, Carleigh

**Thursday 9/11 – Morning Session**

**Morning session: Mary Baylies, lecture**  
*Genetics on the Fly: Drosophila Model Systems*

1. Analysis of mutations in fly
  - a. LOS
  - b. nulls
  - c. hypermorphs
  - d. hypomorphs
2. Genetic analyses in fly
  - a. complementation tests, pathway analysis (are genes in the same pathway for the specific function)
  - b. autonomous/nonautonomous functions of a gene (mosaic analysis);
  - c. epistasis
  - d. gene dosage
3. Genetic screens (using fly eye as an example):
  - a. recessive screens,
  - b. sensitized screens,
  - c. tissue specific screens RNAi/ Overexpression,
4. Usefulness of the fly
  - a. Conservation to human,
  - b. Conservation of processes, using to find new processes.

**Afternoon Session: Logic and Critical Analysis Session 1**  
**Dr. Lydia Finley**

**Discussion Paper Group A:**

Sullivan, et al. Supporting Aspartate Biosynthesis Is an Essential Function of Respiration in Proliferating Cells. *Cell.* 2015; 162, 552–563 July 30.

**Discussion Paper Group B:**

Birsoy, et al. An Essential Role of the Mitochondrial Electron Transport Chain in Cell Proliferation Is to Enable Aspartate Synthesis. *Cell.* 2015; 162, 540–551 July 30.

**Group A:**

Afroz, Jalwa  
Ahmed, Nibras – **Student Presenter**  
Cherkas, Shelby  
Hanselman, Olivia  
Illouz, Sylvia  
Lange, Matthew  
Levin, Bailey  
Li, Ruofei  
Magnus, Karina  
McIlhenny, Lauren

**Group B:**

Beattie, Kai – **Student Presenter**  
Mutaher, Mohammed  
Perea del Angel, Ana  
Pope, Eleanor  
Prabakaran, Adithya  
Styers, Hannah  
Sussman, Carleigh  
Ta, Christina  
Tarrab, Stephanie  
Volpe, Christina

**Friday 9/12**

**Morning session: Kat Hadjantonakis, lecture**  
*Mouse genetics*

1. Overview of embryonic stem cells, mouse chimeras, and transgenic mouse models.
2. Generation and analysis of genetically engineered mouse models (GEMMs): nulls, hypermorphs, hypomorphs...
3. Genetic analyses in mice:
  - a. complementation tests
  - b. pathway analysis (are genes in the same pathway for the specific function)
  - c. autonomous/nonautonomous functions of a gene (chimera analysis);
4. Genetic screens: dominant and recessive screens
5. The International Mouse Phenotyping Consortium (IMPC)
  - a. unbiased comprehensive catalog of mammalian gene function
  - b. conservation to human

## **Afternoon session: Yas Furuta**

### *Development of Genetically Engineered Mouse (GEM) Models*

1. Practical considerations in choosing platforms for germ line genome modifications in the mouse
2. One size hardly fits all – complex realities in common approaches to targeted genome modifications
3. Cheating genetics to expedite complex *in vivo* genetic studies
4. Genome editing and germ line gene modifications today, tomorrow and beyond

### **Evaluation project:**

In class group projects will be used for evaluation.

## Week 3: Genomics

9/15/2025 – 9/19/2025

- Sessions each morning and afternoon (10am-12pm and 1-3pm)

Teaching Fellow: Manisha Srinivas Raghavan

### Monday 9/15

**Morning session: Iestyn Whitehouse, discussion leader**

1. Basic overview of genomes.
2. Intro to sequencing technologies.
3. What is a sequencing library, and how do you make one?

**Afternoon session:** Discussion and introduction to small group presentations. Dissecting a kit: commonly used “kits” from the research bench will be distributed to student groups as announced in class on Mon 9/15. Groups should then prepare to discuss on 9/16 how the individual components of their assigned kit actually work to achieve the desired technique.

### Tuesday 9/16

**Morning session: Iestyn Whitehouse**

Small group presentations: dissecting a kit.

**Afternoon session:**

Continuation of group presentations (if needed).

### Wednesday 9/17

**Morning session: Neeman Mohibullah, discussion leader**

1. Single cell DNA, Single cell RNA
2. Spatial transcriptomics
3. Single molecule transcriptomics

**Afternoon session:** IGO tour cohort 1/Tutorial on best practices for sample submission

**Tour group for 9/17:**

Afroz, Jalwa  
Beattie, Kai  
Cherkas, Shelby  
Lange, Matthew  
Li, Ruofei  
Magnus, Karina  
McIlhenny, Lauren  
Perea del Angel, Ana  
Styers, Hannah  
Volpe, Christina

**Thursday 9/18**

**Morning session: Cassidy Cobbs, Discussion leader:**

1. Sequencing Technologies

**Afternoon session:** IGO tour cohort II/Tutorial on best practices for sample submission

**Tour group for 9/18:**

Ahmed, Nibras  
Hanselman, Olivia  
Illouz, Sylvia  
Levin, Bailey  
Mutaher, Mohammed  
Pope, Eleanor  
Prabakaran, Adithya  
Sussman, Carleigh  
Ta, Christina  
Tarrab, Stephanie

## **Friday 9/19**

### **Morning session (10:00-12:00): Logic and Critical Analysis Session 2**

#### **Dr. Agnel Sfeir – Groups**

##### **Group A:**

Afroz, Jalwa  
Hanselman, Olivia  
Lange, Matthew  
Levin, Bailey  
Li, Ruofei  
McIlhenny, Lauren  
Mutaher, Mohammed  
Pope, Eleanor  
Ta, Christina  
Volpe, Christina

##### **Group B:**

Ahmed, Nibras  
Beattie, Kai  
Cherkas, Shelby  
Illouz, Sylvia  
Magnus, Karina  
Perea del Angel, Ana  
Prabakaran, Adithya  
Styers, Hannah  
Sussman, Carleigh  
Tarrab, Stephanie

#### **Discussion Papers Group A (Classic Papers - 3):**

Prusiner SB. Prions (Nobel Lecture). Proc. Natl. Acad. Sci. 1998; Nov (95)13363-13383.

Sparrer et al., Evidence for the prion hypothesis: induction of the yeast [PSI+] factor by in vitro-converted Sup35 protein. Science. 2000 Jul 28;289(5479):595-9.

Prusiner SB. Novel proteinaceous infectious particles cause scrapie. Science. 1982; Apr 9;216(4542):136-44.

#### **Discussion Paper Group B (Contemporary Paper):**

EN Neumann et al. Science 2024 Jun 28;384(6703). Brainwide silencing of prion protein by AAV-mediated delivery of an engineered compact epigenetic editor. PMID: 38935715

#### **Afternoon session (1:00-4:00pm): Tobias Walther, lecture**

*Essential concepts in Lipid and Membrane Biology/Mass spectrometry analysis for biochemistry*

#### **Discussion Paper:**

Abrams ME, Johnson KA, Perelman SS, Zhang LS, Endapally S, Mar KB, Thompson BM, McDonald JG, Schoggins JW, Radhakrishnan A, Alto NM. Oxysterols provide innate immunity to bacterial infection by mobilizing cell surface accessible cholesterol. Nat Microbiol. 2020 Jul;5(7):929-942. doi: 10.1038/s41564-020-0701-5. Epub 2020 Apr 13. PMID: 32284563; PMCID: PMC7442315.

**Student presenter: Cherkas, Shelby**

#### **Evaluation project:**

Students will be emailed a 2-question problem set for completion in one week. Completed problem sets will be emailed to the Registrar.

## Week 4: Biochemistry

**9/22/2025-9/26/2025**

- Sessions in mornings and afternoons (10am-12pm, and 1-3pm)

Teaching Fellow: Lucia Wang

### Monday 9/22

**Morning session (10am-12pm): Dirk Remus, lecture**

*Molecular techniques for the analysis of DNA*

**Afternoon session (1-3pm): Dirk Remus, Discussion**

### Tuesday 9/23

**Morning session (10am-12pm): Chris Lima, lecture**

*Molecular techniques for the analysis of RNA*

**Afternoon session (1-3pm): Joshua Peter, paper discussion leader**

Paper: Linder B, Grozhik AV, Olarerin-George AO, Meydan C, Mason CE, Jaffrey SR. Single-nucleotide-resolution mapping of m6A and m6Am throughout the transcriptome. *Nat Methods*. 2015 Aug;12(8):767-72. doi: 10.1038/nmeth.3453. Epub 2015 Jun 29. PMID: 26121403; PMCID: PMC4487409.

**Student Presenter:** Hanselman, Olivia

### Wednesday 9/24

**Morning session (10am-12pm): Stewart Shuman, lecture and group discussion**

*Molecular techniques for the analysis of Protein*

Please read in advance: Protein production and purification. *Nature Methods*. Volume 5, Pages135–146 (2008).

**Afternoon session (1-3pm): Stewart Shuman, Group Discussion**

### Thursday 9/25

**Morning session (10am-12pm): Richard Hite, lecture**

*Alpha-fold and modern Protein structure determination.*

#### **Paper discussion**

Jumper J, Evans R, Pritzel A, Green T, Figurnov M, Ronneberger O, Tunyasuvunakool K, Bates R, Žídek A, Potapenko A, Bridgland A, Meyer C, Kohl SAA, Ballard AJ, Cowie A, Romera-Paredes B, Nikolov S, Jain R, Adler J, Back T, Petersen S, Reiman D, Clancy E, Zielinski M, Steinegger M, Pacholska M, Berghammer T, Bodenstein S, Silver D, Vinyals O, Senior AW, Kavukcuoglu K, Kohli P, Hassabis D. Highly accurate protein structure prediction

with AlphaFold. *Nature*. 2021 Aug;596(7873):583-589. doi: 10.1038/s41586-021-03819-2. Epub 2021 Jul 15. PMID: 34265844; PMCID: PMC8371605.

**Student Presenter: Illouz, Sylvia**

**Afternoon session (1-3pm):**

**Paper discussion**

Abramson J, Adler J, Dunger J, Evans R, Green T, Pritzel A, Ronneberger O, Willmore L, Ballard AJ, Bambrick J, Bodenstein SW, Evans DA, Hung CC, O'Neill M, Reiman D, Tunyasuvunakool K, Wu Z, Žemgulyté A, Arvaniti E, Beattie C, Bertolli O, Bridgland A, Cherepanov A, Congreve M, Cowen-Rivers AI, Cowie A, Figurnov M, Fuchs FB, Gladman H, Jain R, Khan YA, Low CMR, Perlin K, Potapenko A, Savy P, Singh S, Stecula A, Thillaisundaram A, Tong C, Yakneen S, Zhong ED, Zielinski M, Žídek A, Bapst V, Kohli P, Jaderberg M, Hassabis D, Jumper JM. Accurate structure prediction of biomolecular interactions with AlphaFold 3. *Nature*. 2024 Jun;630(8016):493-500. doi: 10.1038/s41586-024-07487-w. Epub 2024 May 8. PMID: 38718835; PMCID: PMC11168924.

**Student Presenter: Levin, Bailey**

**Evaluation project:**

In class group projects will be used for evaluation.