

## Mol Biol 254C: Genetic approaches to the study of metabolism

### Instructors

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### Time and Zoom links

Faculty/student sessions.

Zoom links for all sessions will be provided.

Tuesdays 10am-12pm, Fridays 10am-12pm

*First session – Tuesday, January 12*

Student-only sessions

Zoom links for all sessions will be provided.

Mondays/Thursdays 10am-12pm

*First session - Thursday, January 14*

### Objective

This section is designed to introduce students to genetic concepts and approaches used to address cell metabolism in yeast, mice, and humans

- read and understand primary research articles in the area of genetics
- analyze experimental design, results and conclusions critically
- discuss how to solve biological problems creatively

### General Format

The course is composed of nine 2 hr class meetings with faculty instructors and eight student discussion meetings in the day preceding each class. The first meeting will consist of assignment of student discussion leaders and an introductory lecture on yeast genetics. Following this session, each pair of student discussion and faculty-student class meetings will center around one research article.

### Specific Format

Students are expected to have read the paper and have carefully considered the important advances in the paper, the approaches and data in **all** figures (including supplemental figures). During the faculty-student classes, all students are expected to be prepared to address any of the figures.

For each paper, 2 student discussion leaders will be assigned in the first meeting. Each student will be asked to volunteer as a discussion leader for at least two papers (preferably one paper on yeast and one on a mammalian system).

The leaders will direct the discussions at both the student-only and the faculty-student meetings.

*Student meetings* should be an initial group consideration of the paper, students should work together to understand necessary background material, experimental design and approaches, results, conclusions, significance and next steps.

*Faculty-student meetings:* the discussion leaders are expected to present the necessary background material and to prepare a powerpoint with slides for the background presentation and for each figure (and any supplemental figures selected at the student-only meeting as worth discussing). Discussion leaders are also expected to lead a discussion of the significance of the work and what follow-up lines of investigation would be worth pursuing.

At the faculty-student class, the discussion leaders will present the background material. Students will then be chosen at random by the instructors to present each figure. Key to figure presentation will be: (1) to articulate the question the authors are addressing and why it is important, (2) to provide the appropriate background and context to the experiment, (3) to discuss the experimental approaches and critically evaluate results obtained, and (4) to summarize the main findings and conclusions. The final 15 minutes of each class will be reserved for the discussion leaders to engage the group in consideration of the overall significance of the work and what follow-up experiments should be pursued.

### **Class attendance**

Mol Biol 254 should be considered a priority; attendance at all meetings is required.

### **Grades**

Grades will be assigned based on class participation (50%) and a written exam (50%) to be given at the end of the class.

An open-book exam will be given on Feb. 12, the last day of class. The exam will consist of questions that ask you to interpret data or design experiments based on the studies presented in the class. The exam will be divided into two sections (50 points each), one addressing the papers on yeast and the other addressing papers on mammals.

Participation will be assessed based on the following criteria:

- On-time attendance
- Active participation in discussion of all figures, significance and next steps (not just assigned presentations).
- Ability to succinctly and accurately describe experiments and explain figures
- Ability to provide critical insight into the methodological soundness and significance of the experiments
- Ability to provide original insight into experimental implications and unanswered questions and point out issues/problems with the study.

### *Midcourse feedback*

In the third week of the course the faculty instructors will meet with each student individually to provide feedback on the participation criteria.

## PAPERS

All papers posted in CCLE according to session number.

### Session 1

Tuesday, January 12

Course logistics; introductory lecture on yeast genetics

Reading

[Yeast: an experimental organism for 21st Century biology.](#)

Botstein D, Fink GR.

Genetics. 2011 Nov;189(3):695-704. doi: 10.1534/genetics.111.130765. Review.

### Session 2

Students only: Thursday, January 14

Faculty/students: Friday, January 15

Discussion paper

[Engineering complex synthetic transcriptional programs with CRISPR RNA scaffolds.](#)

Zalatan JG, Lee ME, Almeida R, Gilbert LA, Whitehead EH, La Russa M, Tsai JC, Weissman JS, Dueber JE, Qi LS, Lim WA.

Cell. 2015 Jan 15;160(1-2):339-50. doi: 10.1016/j.cell.2014.11.052.

Review

[Engineering Cellular Metabolism.](#)

Nielsen J, Keasling JD.

Cell. 2016 Mar 10;164(6):1185-1197. doi: 10.1016/j.cell.2016.02.004.

Review

### Session 3

Students only: Monday, January 18

Faculty/students: Tuesday, January 19

Discussion paper

[Natural Diversity in Pentose Fermentation Is Explained by Variations in Histone Deacetylases.](#)

Tamari Z, Barkai N.

Cell Rep. 2016 Jan 26;14(3):458-463. doi: 10.1016/j.celrep.2015.12.048.

Review

[Glucose repression in \*Saccharomyces cerevisiae\*.](#)

Kayikci Ö, Nielsen J. FEMS Yeast Res. 2015 Sep;15(6):fov068. doi: 10.1093/femsyr/fov068.

### Session 4

Students only: Thursday, January 21

Faculty/students: Friday, January 22

Discussion paper

[Genetic control of obesity and gut microbiota composition in response to high-fat, high-sucrose diet in mice.](#)

Parks BW, Nam E, Org E, Kostem E, Norheim F, Hui ST, Pan C, Civelek M, Rau CD, Bennett BJ, Mehrabian M, Ursell LK, He A, Castellani LW, Zinker B, Kirby M, Drake TA, Drevon CA, Knight R, Gargalovic P, Kirchgessner T, Eskin E, Lusk AJ.  
Cell Metab. 2013 Jan 8;17(1):141-52. doi: 10.1016/j.cmet.2012.12.007.

### **Session 5**

Students only: Monday, January 25

Faculty/students: Tuesday, January 26

Discussion paper

[From noncoding variant to phenotype via SORT1 at the 1p13 cholesterol locus.](#)

Musunuru K, Strong A, Frank-Kamenetsky M, Lee NE, Ahfeldt T, Sachs KV, Li X, Li H, Kuperwasser N, Ruda VM, Pirruccello JP, Muchmore B, Prokunina-Olsson L, Hall JL, Schadt EE, Morales CR, Lund-Katz S, Phillips MC, Wong J, Cantley W, Racie T, Ejebe KG, Orholm Melander M, Melander O, Kotliansky V, Fitzgerald K, Krauss RM, Cowan CA, Kathiresan S, Rader DJ.

Nature. 2010 Aug 5;466(7307):714-9. doi: 10.1038/nature09266.

### **Session 6**

Students only: Thursday, January 28

Faculty/students: Friday, January 29

Discussion paper

[Changes of Cell Biochemical States Are Revealed in Protein Homomeric Complex Dynamics.](#)

Stylen B, Abd-Rabbo D, Kowarzyk J, Miller-Fleming L, Aulakh SK, Garneau P, Ralser M, Michnick SW.

Cell. 2018 Nov 15;175(5):1418-1429.e9. doi: 10.1016/j.cell.2018.09.050. Epub 2018 Oct 25.

Review

[Metformin: from mechanisms of action to therapies.](#)

Foretz M, Guigas B, Bertrand L, Pollak M, Viollet B.

Cell Metab. 2014 Dec 2;20(6):953-66. doi: 10.1016/j.cmet.2014.09.018. Epub 2014 Oct 30.

### **Session 7**

Students only: Monday, February 1

Faculty/students: Tuesday, February 2

Discussion paper

[Exploring genetic suppression interactions on a global scale.](#)

van Leeuwen J, Pons C, Mellor JC, Yamaguchi TN, Friesen H, Koschwanez J, Ušaj MM, Pechlaner M, Takar M, Ušaj M, VanderSluis B, Andrusiak K, Bansal P, Baryshnikova A, Boone CE, Cao J, Cote A, Gebbia M, Horecka G, Horecka I, Kuzmin E, Legro N, Liang W, van Lieshout N, McNee M, San Luis BJ, Shaeri F, Shuteriqi E, Sun S, Yang L, Youn JY, Yuen

M, Costanzo M, Gingras AC, Aloy P, Oostenbrink C, Murray A, Graham TR, Myers CL, Andrews BJ, Roth FP, Boone C.  
Science. 2016 Nov 4;354(6312). pii: aag0839.

Review

[Mechanisms of suppression: The wiring of genetic resilience.](#)

van Leeuwen J, Pons C, **Boone C**, **Andrews BJ**.

Bioessays. 2017 Jul;39(7). doi: 10.1002/bies.201700042. Epub 2017 Jun 5.

### **Session 8**

Students only: Thursday, February 4

Faculty/students: Friday, February 5

Discussion paper

**A proteome- and lipidome-wide systems genetic analysis of hepatic lipid metabolism**

Parker BL, Calkin AC, Seldin MM, Keating MF, Tarling EJ, Yang P, Moody SC, Liu Y, Zerenturk EJ, Needham EJ, Jayawardana K, Pan C, Mellett NA, Weir JM, Lazarus R, Lusic AJ, Meikle PJ, James DE, de Aguiar Vallim TQ, Drew BG.

Submitted to Nature

### **Session 9**

Students only: Monday, February 8

Faculty/students: Tuesday, February 9

Discussion paper

[An integrative systems genetic analysis of mammalian lipid metabolism.](#)

Parker BL, Calkin AC, Seldin MM, Keating MF, Tarling EJ, Yang P, Moody SC, Liu Y, Zerenturk EJ, Needham EJ, Miller ML, Clifford BL, Morand P, Watt MJ, Meex RCR, Peng KY, Lee R, Jayawardana K, Pan C, Mellett NA, Weir JM, Lazarus R, Lusic AJ, Meikle PJ, James DE, de Aguiar Vallim TQ, Drew BG.

Nature. 2019 Mar;567(7747):187-193. doi: 10.1038/s41586-019-0984-y.

### **Session 10**

Friday, February 12

Final Exam