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Spring 2-1-2022

### BCH 600.01: Cell Organization & Mechanisms

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**Instructor: Mark Grimes**  
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Class Meeting Time and Place:  
9:30-11:00 MF Health Sciences 108

**G 600 Cell Organization and Mechanisms.** Offered every other spring. Prereq., BCH 480 or consent of instr. Same as BMED 600. Primary literature exploration of the regulation of structure, function, and dynamics of eukaryotic cells. Topics include membranes, cytoskeleton, transcription, translation, signal transduction, cell motility, cell proliferation, and programmed cell death.

### Overview

Cell Biology is vast and dense and encompasses biochemistry, biophysics, molecular biology, microscopy, genetics, physiology, bioinformatics, and developmental biology. We will explore the topics listed below by reading reviews and papers from the primary literature. Papers will be chosen, where possible, that are at the interface between two fields, so a large amount of background reading will be necessary to understand the paper and put it in context. The main learning goals are 1) to learn about a number of topics in cell biology; 2) understand a number of laboratory techniques, their purpose, and how to interpret and evaluate data derived from them; and 3) to gain the confidence and skills to attack any scientific paper even if it is in an unfamiliar area; in other words to learn how to learn new things. Alberts, et al., *Molecular Biology of the Cell*, 6<sup>th</sup> ed. (Garland Science; the 7<sup>th</sup> edition is coming out soon) is recommended as excellent textbook that frames the background as we explore the primary literature. (The 4<sup>th</sup> ed. is available online at <http://www.ncbi.nlm.nih.gov/books/NBK21054/>. Lodish et al., *Molecular Cell Biology*, 7<sup>th</sup> ed. may be substituted if you have already purchased this book. Lecture figures will come from Alberts, et al. and reviews.)

### Format

We recognize that students (and human beings in general) have diverse learning styles, personal styles, ethnicity, gender, nationality, and experience. Science is about learning new things, and communicating these things to other people, regardless of this diversity among people.

**Presentations** will be made by the instructor and graduate students. Instructor will optionally introduce a topic with a lecture, and a student presentation of a paper with data will follow in the next session. The weekly assignment is to read the primary paper(s) and review article(s) for the topic, and prepare to ask at least one question during class.

We intend a relaxed atmosphere where we all ask questions, and no questions are dumb questions. All students will be required to read all papers and ask questions of the presenter. It is expected that the student presenting the paper will be well informed on the topic, which will require extra work. While errors and misunderstandings are forgivable, we expect you to make an effort to understand the paper being presented, especially if you are the one presenting it!

When tackling any research paper in an unfamiliar area, the best way to start is by reading one or more textbooks (use the index and table of contents) and reviews, looking up unknown concepts mentioned in the paper's introduction (often reviews are cited there too). Then look at the data in the figures. If you don't understand the methods, look them up. Then read the results and discussion, and decide whether the author's interpretation of the data is the same or different than yours.

**Writing assignments** will be a one page summary of the primary paper due the day of the paper presentation, which includes a question to be asked during class, followed by a revision plus a one-half page new hypothesis, question, and experiment that arises from the presented paper.

## Presentations

The student's presentation should set the stage for the paper being presented with a brief introduction that draws on recent reviews or textbook figures. Keep in mind the following questions when presenting a paper. What is the hypothesis? What is the key question being addressed by the experiments? What are the key experiments that address the question? Do you believe their interpretation, and did they do the proper controls? Many of the methods used to study cell biology and biochemistry are evolving, and far from perfect, so it is important to look with a critical eye at the data, the methods used to obtain the data, and how the data are interpreted.

Students' presentation papers will be assigned in advance to allow time for preparation. Graduate students will be assigned one paper from the list below to present to the rest of the class. Before the student presentation to the class, the student will prepare a draft presentation and go over it with the instructor (Mark). The presenter should make sure that the all students understand the background, motivation, hypothesis, question, experimental techniques, data from key experiments, and conclusions in the paper. The expectations for the students in the audience are to ask questions - no questions are dumb questions - to make sure the presentation is clear; and ensure that you understand laboratory techniques used for the key experiments the paper. The presentation to the class should describe key experimental technique(s) and how to interpret the data when presenting the data.

## Writing Assignments

**Paper summaries.** For all students except for the presenters: one for each paper from the primary literature. Due on the day of the paper presentation as a pdf file uploaded to moodle before the presentation. Put your name and assignment name in the header, and name your file: "YourNameAssignmentName.pdf." One page maximum, 11 point font minimum. In your own words (do *not* cut and paste from the paper), in a cohesive summary paragraph, write one-two sentence(s) to answer each question:

1. What is the research topic/question and why is it important/interesting? Include at least one statement of hypothesis, as in, "The authors hypothesize that cortactin binds to a protein at the plasma membrane."
2. What method/approaches are used? When describing experiments, motivate them as a question. For example, "The investigators asked whether cortactin and protein X were co-localized at the plasma membrane using two experimental approaches..."
3. What are the main results of the paper? (This may take three-four sentences, but should not include experimental details.)
4. What are the conclusions from the experiments, and the significance?
5. What would you like to know more about/understand better? Write down at least one question that you plan to ask the presenter.

**Revisions:** After the presentation the instructor will hand back your assignment with comments. Please revise the summary according to your (hopefully) better understanding of the paper after the presentation and address any requested revisions or clarifications. The intent for the rewrite is 1) to clear up your thinking and writing after we discuss the paper in class and 2) to come up with a new hypothesis, question, and experiment in the topic. In the revision, use an additional one-half page maximum to identify a question that emerges from the paper that represents a next step towards understanding the biological mechanism under study. What technique(s) would you use to answer the question with an experiment? Keep this brief, but think about it carefully. Use the review article(s) to help frame the hypothesis and question. Think of this as a rough draft of a proposal.

The typical timing is expected to be: student presentations on Fridays; summaries handed back the next Monday; revisions due Wednesday.

## Bioinformatics assignment

1. See <http://www.ncbi.nlm.nih.gov/guide/> and <http://www.genenames.org/>. Pick a gene, preferably a gene from the paper you will be presenting (you may find this exercise useful as background information for your presentation), and find its HUGO gene name, nucleic acid and protein sequence, and domain structure. If there is a structure for the protein, find the structure. Use <http://stitch.embl.de> to ask if any drugs bind to the protein; <http://www.hprd.org> and <http://www.phosphosite.org> to find the domain structure and post-translational modifications of the protein.

2. Use two different Protein-Protein Interaction (PPI) resources [see PSICQUIC (<http://www.ebi.ac.uk/Tools/webservices/psicquic/view/main.xhtml>); I recommend GeneMANIA ([genemania.org](http://genemania.org)) and String ([string-db.org](http://string-db.org))] to retrieve interacting partners based only on physical interactions, pathways (knowledge), genetic interactions, and predictions from interactions known to occur in other species or due to the domain structure (*not* text-mining and co-expression). (If there are no known interacting partners, pick another gene.) Use PubMed (<https://www.ncbi.nlm.nih.gov/pubmed>) to find evidence (published papers) showing that your gene and one of the interacting partners retrieved by PPI resources actually interact with each other.
3. Report the gene name, synonyms, sequences, structure(s), modifications, network graphs, and one or two references for an interaction. Optional: use Cytoscape (<http://www.cytoscape.org>) to graph the networks, otherwise copying and pasting diagrams and graphs from the websites is sufficient. Write a short paragraph summarizing the results and conclusions. Save the report as a pdf file and email it to the instructor.

Each student must pick their own gene and submit their own report. Due by the 5<sup>th</sup> week of class (February 17 or sooner).

### **Science is useful proposal**

Imagine that a new Scientific Special Forces Creative Reserve (SSFCR) was established by the Rational Approach to Government Act (RAGA). The RAGA was passed by unanimous vote by both houses of Congress and signed into law by President Stacy Abrams. Its budget is equal to the Apollo program at its height, 5% of GDP. All graduate students in scientific fields are paid a generous stipend if they join the SSFCR, and 99% of graduate students (including you) enrolled within six months of passage of RAGA.

**In 2020 we did this:** The COVID-19 pandemic necessitates that we declare war on a coronavirus named SARS-CoV-2. The SSFCR has been called up to fight. Your mission is to come up with a novel idea to combat this COVID-19 coronavirus at the molecular/cellular level. In 2022 we could open up the range of topics, which will be discussed in class.

The format of the proposal is as follows.

A 5 minute “elevator pitch” oral presentation. Imagine you find yourself in an elevator with a Senator and have five minutes to pitch your idea.

A 100-word summary in language understandable to politicians and the lay public.

A one-page Specific Aims document that may include figures (single spaced, 11 point Arial or Helvetica font; 0.5 inch margins all around). The hypothesis must be clearly stated. One to three Aims will outline key experiments to test the hypothesis.

References to support the proposal, separate from the Specific Aims page.

The level of funding (graded A-C) will be determined by the effort put into coming up with a scientifically valid, technically achievable, well-written, and well-researched proposal.

### **Assessment**

The course grade will be assigned based on oral presentations, written assignments, and exams. There will be two exams in which interpretation of data will be emphasized. The instructor will identify key figures to focus on from papers that have been presented. Expect broad questions about the motivation for the experiments (*e.g.*, “What signaling pathway is under investigation?”), and specific questions about the data (*e.g.*, “Which lane in Figure 4 shows that cortactin is bound to a plasma membrane protein?”). Written questions from all students (except presenting students) will be required for student presentations, and students will be expected to ask those questions (and other questions) during class. There is no such thing as a dumb question!

#### Point values:

Bioinformatics assignment: 20 points.

Paper review summaries: 10 points each (split between first drafts and revisions). One lowest score will be dropped.

Exam: 100 points.

Presentation: 100 points each.

Proposal and elevator pitch: 100 points

## **The Provost's Official Fine Print**

All students must practice academic honesty. Academic misconduct is subject to an academic penalty by the course instructor and/or a disciplinary sanction by the University.

All students need to be familiar with the Student Conduct Code. The Code is available for review online at <http://www.umt.edu/safety/policies/>. Treat each other with respect!

### **COVID-19 - From the Provost's Office:**

Mask use is required within the classroom or laboratory.

If you feel sick and/or are exhibiting COVID symptoms, please don't come to class and contact the Curry Health Center at (406) 243-4330.

If you are required to isolate or quarantine, you will receive support in the class to ensure continued academic progress. We will provide zoom access if necessary.

UM (and the scientific community) recommends students get the COVID vaccine and booster. Please direct your questions or concerns about vaccines to the Curry Health Center.

## Topics

### **Review and Overview of Cells and Biochemistry (Alberts, Chapters 1 and 2)**

Oral questions will be used to assess how well students are prepared for this class.

### **Review and Overview of Methods (Alberts, Chapters 8 and 9)**

Students will be asked in class to explain different methods used to manipulate nucleic acids and proteins, and to visualize cells. These chapters are a good first review or source for methods.

### **Cell structure, lipids and membrane traffic (Alberts, Chapters 10-13)**

#### **Reviews**

Vietri M, Radulovic M, Stenmark H. The many functions of ESCRTs. *Nat Rev Mol Cell Biol*. Nature Publishing Group; 2020 Jan;21(1):25–42.

Schöneberg, J., Lee, I.-H., Iwasa, J. H., & Hurley, J. H. (2017). Reverse-topology membrane scission by the ESCRT proteins. *Nature Reviews Molecular Cell Biology*, 18(1), 5–17. <http://doi.org/10.1038/nrm.2016.121>

van Niel, G., D'Angelo, G., & Raposo, G. (2018). Shedding light on the cell biology of extracellular vesicles. *Nature Reviews Molecular Cell Biology*, 1–16. <http://doi.org/10.1038/nrm.2017.125>

#### **Primary papers**

**Instructor presentation:** Matsuo, H., Chevallier, J., Mayran, N., Le Blanc, I., Ferguson, C., Faure, J., Blanc, N.S., Matile, S., Dubochet, J., Sadoul, R., Parton, R.G., Vilbois, F., and Gruenberg, J. (2004). Role of LBPA and Alix in multivesicular liposome formation and endosome organization. *Science* 303, 531-534.

#### **Two related papers together:**

\*\*Wollert, T., and J. H. Hurley. 2010. Molecular mechanism of multivesicular body biogenesis by ESCRT complexes. *Nature* 464:864-869.

\*\*Wollert, T., C. Wunder, J. Lippincott-Schwartz, and J. H. Hurley. 2009. Membrane scission by the ESCRT-III complex. *Nature* 458:172-177.

Single paper:

\*Larios J, Mercier V, Roux A, Gruenberg J. ALIX- and ESCRT-III-dependent sorting of tetraspanins to exosomes. *The Journal of Cell Biology*. 2020 Mar 2;219(3).

### **Signal transduction and intracellular localization (Alberts, Chapters 15 as well as 12, 13, and 16)**

#### **Reviews**

Sigismund, S., Lanzetti, L., Scita, G., and Di Fiore, P.P. (2021). Endocytosis in the context-dependent regulation of individual and collective cell properties. *Nat Rev Mol Cell Biol* 22, 625-643. 10.1038/s41580-021-00375-5.

Bilanges B, Posor Y, Vanhaesebroeck B. PI3K isoforms in cell signalling and vesicle trafficking. *Nat Rev Mol Cell Biol*. Springer US; 2019 Aug 9;20(9):1–20.

McCrea, P. D., and Gottardi, C. J. (2015). Beyond  $\beta$ -catenin: prospects for a larger catenin network in the nucleus. *Nat Rev Mol Cell Biol* 17, 55–64. Tomas, A., Futter, C. E., & Eden, E. R. (2014).

Manning, B. D., & Toker, A. (2017). AKT/PKB Signaling: Navigating the Network. *Cell*, 169(3), 381–405. <http://doi.org/10.1016/j.cell.2017.04.001>

Mayer, B. J. (2015). The discovery of modular binding domains: building blocks of cell signalling. *Nat Rev Mol Cell Biol* 16, 691–698.

#### **Primary papers**

\*Taelman, V. F., R. Dobrowolski, J. L. Plouhinec, L. C. Fuentealba, P. P. Vorwald, I. Gumper, D. D. Sabatini, and E. M. De Robertis. 2010. Wnt signaling requires sequestration of glycogen synthase kinase 3 inside multivesicular endosomes. *Cell* 143:1136-1148.

Gulluni F, Martini M, De Santis MC, Campa CC, Ghigo A, Margaria JP, et al. Mitotic Spindle Assembly and Genomic Stability in Breast Cancer Require PI3K-C2 $\alpha$  Scaffolding Function. *Cancer Cell*. 2017 Oct 9;32(4):444–7.

\*Vasudevan, K. M., D. A. Barbie, M. A. Davies, R. Rabinovsky, C. J. McNear, J. J. Kim, B. T. Hennessy, H. Tseng, P. Pochanard, S. Y. Kim, I. F. Dunn, A. C. Schinzel, P. Sandy, S. Hoersch, Q. Sheng, P. B. Gupta, J. S. Boehm, J. H. Reiling, S. Silver, Y. Lu, K. Stemke-Hale, B. Dutta, C. Joy, A. A. Sahin, A. M. Gonzalez-Angulo, A. Lluch, L. E. Rameh, T. Jacks, D. E. Root, E. S. Lander, G. B. Mills, W. C. Hahn, W. R. Sellers, and L. A. Garraway. 2009. AKT-independent signaling downstream of oncogenic PIK3CA mutations in human cancer. *Cancer Cell* 16:21-32.

Tassew, N. G., Charish, J., Shabanzadeh, A. P., Luga, V., Harada, H., Farhani, N., et al. (2017). Exosomes Mediate Mobilization of Autocrine Wnt10b to Promote Axonal Regeneration in the Injured CNS. *Cell Reports*, 20(1), 99–111. <http://doi.org/10.1016/j.celrep.2017.06.009>

**Instructor presentation:** Zheng, Y. et al. (2013). Temporal regulation of EGF signalling networks by the scaffold protein Shc1. *Nature* 499, 166–171.

### **The cytoskeleton and membranes (Alberts, Chapters 16 and 19)**

#### **Reviews**

Gudimchuk, N.B., and McIntosh, J.R. (2021). Regulation of microtubule dynamics, mechanics and function through the growing tip. *Nat Rev Mol Cell Biol* 22, 777-795. 10.1038/s41580-021-00399-x.

Dogterom M, Koenderink GH. Actin–microtubule crosstalk in cell biology. *Nat Rev Mol Cell Biol*. Springer US; 2018 Dec 11;20(1):1–17.

Leterrier, C., Dubey, P., & Roy, S. (2017). The nano-architecture of the axonal cytoskeleton. *Nature Reviews Neuroscience*, 18(12), 713–726. <http://doi.org/10.1038/nrn.2017.129>

#### **Primary papers**

\*Rodriguez-Garcia, R., Volkov, V.A., Chen, C.Y., Katrukha, E.A., Olieric, N., Aher, A., Grigoriev, I., Lopez, M.P., Steinmetz, M.O., Kapitein, L.C., et al. (2020). Mechanisms of Motor-Independent Membrane Remodeling Driven by Dynamic Microtubules. *Curr Biol* 30, 972-987 e912. 10.1016/j.cub.2020.01.036.

Henty-Ridilla JL, Rankova A, Eskin JA, Kenny K, Goode BL. Accelerated actin filament polymerization from microtubule plus ends. *Science*. American Association for the Advancement of Science; 2016 May 20;352(6288):1004–9.

Xu, Z., Schaedel, L., Portran, D., Aguilar, A., Gaillard, J., Marinkovich, M. P., et al. (2017). Microtubules acquire resistance from mechanical breakage through intraluminal acetylation. *Science (New York, NY)*, 356(6335), 328–332. [http://doi.org/10.1126/science.aai8764`](http://doi.org/10.1126/science.aai8764)

### **The Cell Cycle (Alberts Chapters 17 and 20)**

#### **Reviews**

Craney, A., & Rape, M. (2013). Dynamic regulation of ubiquitin-dependent cell cycle control. *Current Opinion in Cell Biology*, 25(6), 704–710. doi:10.1016/j.ceb.2013.07.004

Teixeira LK, Reed SI. Ubiquitin ligases and cell cycle control. *Annu Rev Biochem*. 2013;82(1):387–414.

#### **Primary papers**

#### **Two related papers together:**

\*\*Bashir, T., Dorrello, N.V., Amador, V., Guardavaccaro, D., and Pagano, M. (2004). Control of the SCF(Skp2-Cks1) ubiquitin ligase by the APC/C(Cdh1) ubiquitin ligase. *Nature* 428, 190-193.

\*\*Wei, W., Ayad, N.G., Wan, Y., Zhang, G.J., Kirschner, M.W., and Kaelin, W.G., Jr. (2004). Degradation of the SCF component Skp2 in cell-cycle phase G1 by the anaphase-promoting complex. *Nature* 428, 194-198.

## **Programmed cell death (Alberts Chapter 18)**

### **Reviews**

Bonora, M., Giorgi, C., and Pinton, P. (2021). Molecular mechanisms and consequences of mitochondrial permeability transition. *Nat Rev Mol Cell Biol.* 10.1038/s41580-021-00433-y.

Singh R, Letai A, Sarosiek K. Regulation of apoptosis in health and disease: the balancing act of BCL-2 family proteins. *Nat Rev Mol Cell Biol.* Springer US; 2019 Feb 15;:1–19.

Fuchs, Y., & Steller, H. (2011). Programmed cell death in animal development and disease. *Cell*, 147(4), 742–758. <http://doi.org/10.1016/j.cell.2011.10.033>

### **Primary papers**

\*Pinke, G., Zhou, L., and Sazanov, L.A. (2020). Cryo-EM structure of the entire mammalian F-type ATP synthase. *Nat Struct Mol Biol* 27, 1077-1085. 10.1038/s41594-020-0503-8.

\*Ke FFS, Vanyai HK, Cowan AD, Delbridge ARD, Whitehead L, Grabow S, et al. Embryogenesis and Adult Life in the Absence of Intrinsic Apoptosis Effectors BAX, BAK, and BOK. *Cell.* Cell Press; 2018 May 17;173(5):1217–7.

(Historical) Liu, X., Kim, C. N., Yang, J., Jemmerson, R., & Wang, X. (1996). Induction of apoptotic program in cell-free extracts: requirement for dATP and cytochrome c. *Cell*, 86(1), 147–157.

## **Asymmetric Cell Division and Cell Fate (Alberts Chapters 17 and 21)**

### **Reviews**

Hafner A, Bulyk ML, Jambhekar A, Lahav G. The multiple mechanisms that regulate p53 activity and cell fate. *Nat Rev Mol Cell Biol.* Springer US; 2019 Mar 14;:1–12.

Knoblich, J. A. 2010. Asymmetric cell division: recent developments and their implications for tumour biology. *Nat Rev Mol Cell Biol* 11:849-860.

### **Primary papers**

Contadini C, Monteonofrio L, Virdia I, Prodosmo A, Valente D, Chessa L, et al. p53 mitotic centrosome localization preserves centrosome integrity and works as sensor for the mitotic surveillance pathway. *Cell Death Dis.* Nature Publishing Group; 2019 Nov 7;10(11):850–16.

Cicalese, A., G. Bonizzi, C. E. Pasi, M. Faretta, S. Ronzoni, B. Giulini, C. Brisken, S. Minucci, P. P. Di Fiore, and P. G. Pelicci. 2009. The tumor suppressor p53 regulates polarity of self-renewing divisions in mammary stem cells. *Cell* 138:1083-1095.

## **RNA and Regulation of gene expression (Alberts Chapters 4, 6 and 7)**

### **Reviews**

Statello, L., Guo, C.J., Chen, L.L., and Huarte, M. (2021). Gene regulation by long non-coding RNAs and its biological functions. *Nat Rev Mol Cell Biol* 22, 96-118. 10.1038/s41580-020-00315-9.

Zhu H, Xing Z, Zhao Y, Hao Z, Li M. The Role of Circular RNAs in Brain Injury. *Neuroscience.* 2020 Jan 7.

Alessio E, Bonadio RS, Buson L, Chemello F, Cagnin S. A Single Cell but Many Different Transcripts: A Journey into the World of Long Non-Coding RNAs. *Int J Mol Sci.* Multidisciplinary Digital Publishing Institute; 2020 Jan 1;21(1):302.

Cech, T. R., & Steitz, J. A. (2014). The noncoding RNA revolution-trashing old rules to forge new ones. *Cell*, 157(1), 77–94. <http://doi.org/10.1016/j.cell.2014.03.008>

Bergmann, J. H., & Spector, D. L. (2014). Long non-coding RNAs: modulators of nuclear structure and function. *Current Opinion in Cell Biology*, 26, 10–18. doi:10.1016/j.ceb.2013.08.005



Scadden, D. 2009. A NEAT Way of Regulating Nuclear Export of mRNAs. *Mol Cell* 35:395.

### **Primary papers**

\*Yamazaki, T., Souquere, S., Chujo, T., Kobelke, S., Chong, Y.S., Fox, A.H., Bond, C.S., Nakagawa, S., Pierron, G., and Hirose, T. (2018). Functional Domains of NEAT1 Architectural lncRNA Induce Paraspeckle Assembly through Phase Separation. *Mol Cell* 70, 1038-1053 e1037. 10.1016/j.molcel.2018.05.019.

\*Chen, L. L., and G. G. Carmichael. 2009. Altered nuclear retention of mRNAs containing inverted repeats in human embryonic stem cells: functional role of a nuclear noncoding RNA. *Molecular cell* 35:467-478.

## **Stem cells and chromatin modifications (Alberts Chapters 7 and 22)**

### **Reviews**

Dang-Nguyen, T. Q., and Torres-Padilla, M.-E. (2015). How cells build totipotency and pluripotency: nuclear, chromatin and transcriptional architecture. *Current Opinion in Cell Biology* 34, 9–15.

Hajkova, P. 2010. Epigenetic reprogramming--taking a lesson from the embryo. *Current Opinion in Cell Biology* 22:342-350.

### **Primary paper**

Hajkova, P., S. J. Jeffries, C. Lee, N. Miller, S. P. Jackson, and M. A. Surani. 2010. Genome-wide reprogramming in the mouse germ line entails the base excision repair pathway. *Science* 329:78-82.

## **Stem Cells and Organoids (Alberts Chapter 22)**

### **Reviews**

Tsuboi M, Gotoh Y. Endfoot regrowth for neural stem cell renewal. *Nat Cell Biol.* Nature Publishing Group; 2020 Jan;22(1):3–5.

Giandomenico, S. L., & Lancaster, M. A. (2017). Probing human brain evolution and development in organoids. *Current Opinion in Cell Biology*, 44, 36–43. <http://doi.org/10.1016/j.ceb.2017.01.001>

Quadrato, G., & Arlotta, P. (2017). Present and future of modeling human brain development in 3D organoids. *Current Opinion in Cell Biology*, 49, 47–52. <http://doi.org/10.1016/j.ceb.2017.11.010>

Johnson, J. Z., and Hockemeyer, D. (2015). Human stem cell-based disease modeling: prospects and challenges. *Current Opinion in Cell Biology* 37, 84–90.

Zeltner, N., and Studer, L. (2015). Pluripotent stem cell-based disease modeling: current hurdles and future promise. *Current Opinion in Cell Biology* 37, 102–110.

### **Primary Paper**

\*Bershteyn M, Nowakowski TJ, Pollen AA, Di Lullo E, Nene A, Wynshaw-Boris A, Kriegstein AR: Human iPSC-derived cerebral organoids model cellular features of lissencephaly and reveal prolonged mitosis of outer radial glia. *Cell Stem Cell* 2017, 20:435-449 e434.

## **CRISPR and Gene Drive**

### **Reviews**

Champer J, Buchman A, Akbari OS. Cheating evolution: engineering gene drives to manipulate the fate of wild populations. *Nat Rev Genet.* Nature Publishing Group; 2016 Mar;17(3):146–59.

McFarlane GR, Whitelaw CBA, Lillico SG. CRISPR-Based Gene Drives for Pest Control. *Trends in Biotechnology.* 2018 Feb;36(2):130–3.

Esvelt KM, Smidler AL, Catteruccia F, Church GM. Concerning RNA-guided gene drives for the alteration of wild populations. *Elife.* 2014 Jul 17;3:20131071.

Pickar-Oliver A, Gersbach CA. The next generation of CRISPR–Cas technologies and applications. *Nat Rev Mol Cell Biol*. Springer US; 2019 Jul 16;20(8):1–18.

Dominguez, A. A., Lim, W. A., and Qi, L. S. (2016). Beyond editing: repurposing CRISPR-Cas9 for precision genome regulation and interrogation. *Nat Rev Mol Cell Biol* 17, 5–15.

Doudna JA, Charpentier E. Genome editing. The new frontier of genome engineering with CRISPR-Cas9. *Science*. American Association for the Advancement of Science; 2014 Nov 28;346(6213):1258096–6.

### **Primary Papers**

Grunwald HA, Gantz VM, Poplawski G, Xu X-RS, Bier E, Cooper KL. Super-Mendelian inheritance mediated by CRISPR-Cas9 in the female mouse germline. *Nature*. Nature Publishing Group; 2019 Feb;566(7742):105–9.

Gantz VM, Science EB, 2015. The mutagenic chain reaction: a method for converting heterozygous to homozygous mutations. *sciencescience*magorg. 2015 Apr 24;348(6233):439–42.

Kleinstiver, B. P., Pattanayak, V., Prew, M. S., Tsai, S. Q., Nguyen, N. T., Zheng, Z., and Joung, J. K. (2016). High-fidelity CRISPR–Cas9 nucleases with no detectable genome-wide off-target effects. *Nature*, 1–17.

\*H. Ma et al., Correction of a pathogenic gene mutation in human embryos. *Nature*. 548, 1–24 (2017).

## **Endoplasmic Reticulum: The Unfolded Protein Response (Alberts Chapter 12)**

### **Reviews**

Wang, M., and Kaufman, R. J. (2016). Protein misfolding in the endoplasmic reticulum as a conduit to human disease. *Nature* 529, 326–335.

Volmer, R., and Ron, D. (2015). Lipid-dependent regulation of the unfolded protein response. *Current Opinion in Cell Biology* 33, 67–73.

Hetz, C. (2012) The unfolded protein response: controlling cell fate decisions under ER stress and beyond. *Nature Reviews Molecular Cell Biology*, 13(2), 89–102. . <http://doi.org/10.1038/nrm3270>

### **Primary paper**

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