7.344 Mortal Beings, Immortal Cells: Cellular Immortality in Normal Biology and Human Disease

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Course Description

All life relies on cellular immortality: although living individuals are mortal, genomes have been passed down with remarkable fidelity through immortal cell lines for as long as life has existed. Every cell in every human body arose from two germ cells, and each of these germ cells was produced from a body that itself arose from two germ cells, and so on since the origin of cellular life. Cellular immortality, though, has a dark side: uncontrolled cell survival is a driving force of cancer. In this class, we will examine cutting-edge data concerning the features of cellular immortality, how cellular immortality functions in normal biological systems, how cellular immortality can be induced in otherwise mortal cells, and what happens when cellular immortality goes awry. First, we will discuss how cellular immortality requires (1) strict genomic protection against damaging agents; (2) cellular competition and selection for the most intact genomes and organelles; and (3) regeneration of lost components. Next, we will examine how germline immortality is inherited from generation to generation, with a special focus on the nature and necessity of intracellular phase-separated bodies known as "germ granules." We will discuss the frequent use of inductive signals to determine the germline, including for mammalian immortal cells, as well as the molecular networks required to induce the germline fate *in vivo*. One active area of current research concerning inductive germline signaling involves methods for inducing the germline fate *in vitro*, and we will discuss how to engineer immortality in a dish. Finally, we will examine cellular immortality in a pathogenic context and discuss how cancer cells co-opt natural developmental inducers of immortality with consequences that are detrimental to the organism. This course will include a Q+A session with the CEO of Conception Bio, a startup focused on generating *in vitro* oocytes with the features of natural cellular immortality, and an in-person field trip to the laboratory of Professor Ya-Chieh Hsu of the Harvard Stem Cell Institute to learn about approaches to studying stem cell aging and the patent process for related therapies. During this course, students will learn how to (1) read and critically evaluate the primary research literature, (2) determine key mechanistic components of cellular immortality, (3) use experimental methods (including cell-lineage tracing, histology, protein biochemistry, and multiple Next Generation Sequencing technologies) to evaluate cell state and identity, (4) share their findings and opinions with peers, and (5) design experiments to test their own hypotheses.

Course Format and Expectations

This course will meet once per week for two hours. Class meeting day and time is flexible and will be determined by classroom availability and the schedules of the students and instructors. Each week we will discuss two primary research articles focusing on a different aspect of cellular immortality. Students should carefully read the assigned papers before coming to class and post answers to the weekly discussion questions to Canvas. To facilitate an informed discussion, the last 15 minutes of each class will be devoted to an introduction of the topic for the following week. Assigned papers will be posted to the course website in advance. Students should bring a copy (paper or electronic) of the papers to each class for reference and be ready to discuss. During class, students will drive the discussion of the papers.

Course Objectives and Learning Outcomes

The major goals of this course are to help students develop a strong ability to critically read and discuss research articles and to learn about the biology of cellular immortality. By the end of this course, students should be able to:

- Read and critique primary research literature.
- Interpret experimental and control data presented in text, tables and figures.
- Describe the mechanisms that protect, select, and restore immortal cell fate in naturally immortal

cells and how these processes can be dysregulated in cancer progression.
- Explain commonly used methods in genetics, developmental biology, cell biology, and molecular biology, related to the study of cellular immortality.
- Formulate well-controlled experiments with appropriate controls to answer biological questions.

Course Communication

The course will have a Canvas site. It is the students' responsibility to ensure they are checking Canvas to access the papers and discussion questions. To contact the instructor, please e-mail **araz@wi.mit.edu.**

Assignments

(1) Weekly assignments: critically read two posted research articles and answer short discussion questions on Canvas. Each week, two papers about a specific topic will be discussed in class, except for the first week, the week of the field trip, the week of Thanksgiving, and the last week. Students are required to critically evaluate both papers, including understanding the necessary background, the key research question, the methodological approach(es), the results, and the interpretation. We will then discuss these takeaways in class, focused on experimental design and interpretation. To promote energetic classroom conversation, weekly short discussion questions will be posted on Canvas. These questions will not have one "right or wrong" answer; rather, the intent is to encourage students to think critically about the many potential research paths. Students will post answers to these questions no later than 24 hours before class begins.

A satisfactory answer will be 2-4 sentences in length and will demonstrate:
- Understanding of the weekly paper
- Critical thinking beyond the what is directly presented in the paper

Please briefly review your classmates' answers before coming to class.

(2) Written research proposal about an area of cellular immortality (due October 25th before class). Students will prepare a short (2 pages, double spaced, 12 point font) research proposal about a question focused on the topic of cellular immortality that has not yet been addressed in the class. Students can and should draw inspiration from papers discussed in class and/or outside knowledge. The proposal should be in the following format:
- *Question and rationale*: What is the question, and why is it important? This section should be one paragraph long.
- *Hypothesis*: A testable statement related to the question. This section should be one or two sentences long.
- *Experiment*: Describe the approach that will be used to support or falsify your hypothesis. Be explicit about key experiment(s), including what positive and negative controls you will use and for what purpose. What result(s) would support your hypothesis, and what result(s) would refute it? Are there any results that would be ambiguous with respect to your hypothesis? What are the limitations of this experiment? This section should be two to four paragraphs long. This is the most important section of your proposal.
- *Significance*: How would the results of your proposed experiments add to our knowledge of cellular immortality? This section should be one to three sentences long.

(3) Oral presentation (on December 13th, in class).
Immortality is a topic of great public interest, but reporting about the current state of the field of cellular immortality is not always accurate. For final oral presentations, each student will identify a research paper about cellular immortality that has been reported by popular media. Potential subtopics for this literature search include germ cell biology, regeneration, aging, and cancer. This paper should not be

one discussed in the course.

Students will first critically evaluate the primary research paper, discussing if the key conclusion is compelling. Next, students will describe how the result was reported in the popular press and the significance assigned to this result. How do the primary and popular-press reports agree, and how do they differ? In what ways did the popular press report accurately represent the data, and in what ways could this report have been improved? These presentations should be 15 minutes long and should be supported by correspondent PowerPoint/Keynote slides. The presentation should include the following sections: identifying the main question of the primary research paper (one slide), explaining the key experiment and its controls (one slide), presenting and critiquing the results (one to three slides), presenting and critiquing the conclusions of the primary research paper (one to three slides), and presenting and critiquing the conclusions of the popular press article (one to three slides). Students will search for and select their own popular press and primary research articles to critique, but must submit these articles for approval by the instructor at least four weeks before the presentation date.

Virtual Q+A with CEO of Conception Bio (Optional)

To complement our classroom discussions about cellular immortality, the CEO of Conception Bio will be hosting a Q+A for our class. Conception is a biotechnology start-up in the field of *in vitro* gametogenesis, a topic we will be discussing in depth in Week 10, prior to this discussion. This field aims to develop technology that will allow mortal somatic stem cells to be reprogrammed *in vitro* to express an immortal germline fate – for example, to allow the generation of oocytes from somatic cells of XY karyotype individuals. The inducible nature of cellular immortality has considerable scientific, clinical and societal potential impacts. While *in vitro* gametogenesis could solve social and biological infertility, transmissible genome editing, which is currently required for this technology, is banned in the US. During this session, students will have the opportunity to learn about careers related to the topics discussed in class as well as about cutting-edge technologies that can be used to induce cellular immortality. This session will take place outside of our normal class time and will be optional.

In-person field trip to the Harvard Stem Cell Institute

We will also be going on an in-person field trip to the Harvard Stem Cell Institute, hosted by the laboratory of Professor Ya-Chieh Hsu. The Hsu laboratory uses cutting-edge high-resolution imaging and tracing techniques coupled with functional assays of mammalian cells to analyze and manipulate adult stem cell aging and behavior. Professor Hsu's laboratory has several recent patents to treat aging hair follicle stem cells, the scientific specifics of which we will discuss in Week 11. During our visit, we will see newly developed imaging setups and discuss the bridge between academic research and industrial Research and Development (R&D).

Grading and Attendance Policies

The course will be graded on a "pass/fail" basis. To earn a passing grade, students must attend the course, participate in discussions, and satisfactorily complete the assignments. Because active participation is integral to this course, students are expected to attend all class sessions. Students are responsible for notifying the instructor should extenuating circumstances arise and class be missed. Additional assignments will be given to make up for absences at the instructor's discretion.

Prerequisites

There are no set prerequisites for the course, but some knowledge of genetics, biochemistry and cell biology is expected. Ideally, students will have taken at least one of the following classes: 7.03 Genetics, 7.06 Cell Biology, or 7.28 Molecular Biology. Students not meeting these prerequisites but still interested in enrolling for the class should contact the instructors.

COURSE SCHEDULE

Week 1 – Week of September 11th (Wednesday, September 13th)
Introduction
Getting to know each other
Introduction to finding, reading, and understanding the primary biological and biomedical research literature
What is cellular immortality, and when is it used by cells as a normal aspect of biology, in disease, and in industry?
What methods do people use to study cellular immortality?
Introduction to next week's topic: genomic protection

Week 2 – Week of September 18th (Wednesday, September 20th)
Cellular immortality requires protection from damaging agents, e.g., transposons
Several key features must accompany cellular immortality. First, immortal cells must be under protection from injury to continue to give rise to new individuals indefinitely. All cycling cells face threats to genomic integrity from unstable regions, including shortening telomeres, mobile transposons, and repetitive regions prone to recombination-based gain and loss. Mechanisms that protect against these threats include the piRNA pathway, a conserved small-RNA-based silencing pathway that protects against selfish, repetitive genomic elements. The pathway suppresses both transcription and translation of transposons. Biogenesis of piRNAs depends on the transposons themselves, which are used to template new piRNA sequences. The first paper presents evidence that piRNAs establish a silent chromatin state at transposon loci in germ cells. The second paper describes the consequences to an immortal stem cell lineage when transposon silencing is lost. We will focus on sequencing methods that allow analysis of chromatin state and/or RNA expression levels.

Le Thomas A, Rogers AK, Webster A, Marinov GK, Liao SE, Perkins EM, Hur JK, Aravin AA, Tóth KF. Piwi induces piRNA-guided transcriptional silencing and establishment of a repressive chromatin state. Genes Dev. 2013 Feb 15;27(4):390-9. doi: 10.1101/gad.209841.112.

Li D, Taylor DH, van Wolfswinkel JC. PIWI-mediated control of tissue-specific transposons is essential for somatic cell differentiation. Cell Rep. 2021 Oct 5;37(1):109776. doi: 10.1016/j.celrep.2021.109776.

Week 3 – Week of September 25th (Wednesday, September 27st)
Cellular selection for the least damaged cells and cellular components facilitates the maintenance of immortal cells
As discussed last week, cellular protection is imperfect. There must also be mechanisms for selection of the least damaged genomes and cells. Although the existence of immortal cells is not essential for organismal viability, elimination of subpar cells or cellular components – thus enriching for the least damaged cells – need not sacrifice individual fitness. This selection of the "best" genomes requires both surveillance of genome stability and a mechanism to eliminate imperfect cells or components. The first paper discusses how stringent internal cellular controls called checkpoints keep germline cells highly sensitive to DNA damage; germline cells with DNA damage frequently die rather than continue cycling with deleterious mutations. The second paper describes how damaged mitochondrial genomes are likewise selected against in the germline through mitochondrial fragmentation, followed by removal of individual mitochondria with deleterious mitochondrial DNA (mtDNA). Both papers use primarily histological readouts of cell state after genetic perturbation.

Lu KL, Yamashita YM. Germ cell connectivity enhances cell death in response to DNA damage in the *Drosophila* testis. Elife. 2017 Aug 15;6:e27960. doi: 10.7554/eLife.27960. *supplement online

Lieber T, Jeedigunta SP, Palozzi JM, Lehmann R, Hurd TR. Mitochondrial fragmentation drives selective

removal of deleterious mtDNA in the germline. Nature. 2019 Jun;570(7761):380-384. doi: 10.1038/s41586-019-1213-4.

Week 4 – Week of October 2nd (Wednesday, October 4th)

Pre-class assignment: Students should e-mail their research proposal paper topics to the instructor for approval.

When protection and selection are insufficient: how lost cellular components are restored

Selection and protection, even in combination, are insufficient to overcome inevitable injury or loss of immortal cells. Immortal cells also must be capable of repair and restoration. Repair frequently occurs by replacing lost elements. All eukaryotic cycling cells, including immortal cells, face the "end replication problem" in which the ends of linear DNA cannot be replicated completely during lagging DNA strand synthesis. During replication, one strand of DNA is synthesized through sequential extension off of a short RNA primer to form Okazaki fragments. When the primers are removed, there is no way to synthesize lagging-strand sequence that is complementary to the end of the chromosome, leaving a gap approximately the size of a single primer. DNA at the termini of chromosomes are called telomeres and consist of simple sequence repeats, allowing a longer repeat copy number to be restored through a process of "telomere lengthening" that requires a specialized ribonucleoprotein complex known as telomerase. The seminal first paper describes the identification of a cell extract that can drive telomere elongation; the key factors in this extract were later determined to include telomerase. The second discusses how immortal cells require telomerase and without telomerase become mortal.

Greider CW, Blackburn EH. Identification of a specific telomere terminal transferase activity in Tetrahymena extracts. Cell. 1985 Dec;43:405-13. doi: 10.1016/0092-8674(85)90170-9.

Lee HW, Blasco MA, Gottlieb GJ, Horner JW 2nd, Greider CW, DePinho RA. Essential role of mouse telomerase in highly proliferative organs. Nature. 1998 Apr 9;392(6676):569-74. doi: 10.1038/33345.

Week 5 – Week of October 9th (Wednesday, October 11th)

Phase-separated bodies and the inheritance of immortal fate

It has been hypothesized that in many species germline specification involves a perfect cellular continuity of immortality, passed from oocyte to primordial germ cells (PGCs) immediately after fertilization to protect the germline from mutations occurring in extensive "exposed" or genomically unstable cell lineages. Indeed, in many classically studied experimental organisms, including the nematode *C. elegans*, fruit fly *Drosophila*, zebrafish, and frog, the germline and germline determinants are segregated in the first cell divisions of development. What are these inherited determinants? For 200 years, scientists have studied dense, membrane-free organelles called germ granules that are specifically found in germ cells. These germ granules are phase-separated ribonucleoproteins (RNPs) that condense from the surrounding cytoplasm. This week's papers describe the formation (Folkmann et al.) and function (Updike et al.) of germ granules in *C. elegans*. The first paper creatively uses biophysical principles to understand surprising genetic phenotypes: factors that were known from genetic experiments to be required for specific germ granule presence in the germline act by absorbing to the surface of the condensates, thus preventing condensate fusion and maintaining a large number of smaller condensates. The second paper uses direct lineage tracing to assay cell fate: after loss of germ granules, germ cells will adopt specific somatic fates, suggesting that germ granules are required for the maintenance of germline totipotency.

Folkmann AW, Putnam A, Lee CF, Seydoux G. Regulation of biomolecular condensates by interfacial protein clusters. Science. 2021 Sep 10;373(6560):1218-1224. doi: 10.1126/science.abg7071.

Updike DL, Knutson AK, Egelhofer TA, Campbell AC, Strome S. Germ-granule components prevent somatic development in the *C. elegans* germline. Curr Biol. 2014 May 5;24(9):970-5. doi: 10.1016/j.cub.2014.03.015.

Week 6 – Week of October 16th (Wednesday, October 18th)

Epigenesis: natural induction of immortal fate in development

Immortal germline fate is not always strictly inherited. Recent data suggest that inductive specification of the germline, as found in cricket, mouse, salamander, (notably) humans, and many other species, is the ancestral and dominant developmental strategy. In inductive specification, also called "epigenesis," the reception of intercellular signals allows PGCs to arise from a more homogenous cell population at a surprisingly late developmental stage, after fate commitment of most somatic cell types. The widespread prevalence of mechanisms of inductive specification among the Metazoa indicated that immortal cell identity is not simply an inherited fate through a direct cellular lineage, but rather an inducible cell state that can arise from cells of multiple lineages. The first paper discusses the evidence that some insects, like the cricket, lack direct inheritance. The second paper reveals what occurs downstream of mechanisms of inductive specification in mice.

Ewen-Campen B, Donoughe S, Clarke DN, Extavour CG. Germ cell specification requires zygotic mechanisms rather than germ plasm in a basally branching insect. Curr Biol. 2013 May 20;23(10):835-42. doi: 10.1016/j.cub.2013.03.063.

Ohinata Y, Payer B, O'Carroll D, Ancelin K, Ono Y, Sano M, Barton SC, Obukhanych T, Nussenzweig M, Tarakhovsky A, Saitou M, Surani MA. Blimp1 is a critical determinant of the germ cell lineage in mice. Nature. 2005 Jul 14;436(7048):207-13. doi: 10.1038/nature03813. *supplement online

Week 7 – Week of October 23rd (Wednesday, October 25th)

Pre-class assignment: Research proposal due

Regeneration of the immortal germline through cell type conversions

Studies of diverse organisms, including species of annelids, flatworms, cnidarians, and echinoderms, have demonstrated similar inductive capabilities for the generation of germline cells from somatic cells in adults. These transitions largely require an inductive mechanism to initiate conversion and utilize the same germline specification program as used in embryonic development. Such induction demonstrates that – like germline epigenesis in the embryo, discussed last week – cells in adults can be transformed into germ cells. As described in the first paper, extrinsic signals from somatic cells form a "niche" for the formation and specification of germline cells in the adult. The second paper discusses how a cell-intrinsic transcription factor plays a role in both embryonic and adult specification of germ cells in a cnidarian model.

Chong T, Collins JJ 3rd, Brubacher JL, Zarkower D, Newmark PA. A sex-specific transcription factor controls male identity in a simultaneous hermaphrodite. Nat Commun. 2013;4:1814. doi: 10.1038/ncomms2811.

DuBuc TQ, Schnitzler CE, Chrysostomou E, McMahon ET, Febrimarsa, Gahan JM, Buggie T, Gornik SG, Hanley S, Barreira SN, Gonzalez P, Baxevanis AD, Frank U. Transcription factor AP2 controls cnidarian germ cell induction. Science. 2020 Feb 14;367(6479):757-762. doi: 10.1126/science.aay6782.

Week 8 – Week of October 30th (Wednesday, November 1st)

Germ cell identity requires epigenetic suppression of somatic fates

The germline fate not only must be established but also once established must be actively maintained. Rather than activation of a specific germline factor, the maintenance of the germline state typically occurs by *repression* of somatic [non-germline] factors. Much transcriptomic repression occurs through epigenetic modifications that transiently alter broad patterns of gene expression. This week we will discuss how the Polycomb repressive complex, which promotes epigenetic silencing at specific target genes, is required to maintain germline fate. As discussed in the first paper, a genetic screen revealed that in *C. elegans* inhibition of this complex allows the targeted reprogramming of germ cells into specific somatic cell types, including

neurons and muscle. In *Drosophila*, the Polycomb complex acts in somatic cells to repress a signal that otherwise promotes loss of germ cell identity in neighboring germline cells. Both papers use elegant genetic tools and lineage tracing to follow germline cells that have undergone changes in cell fate.

Patel T, Tursun B, Rahe DP, Hobert O. Removal of Polycomb repressive complex 2 makes *C. elegans* germ cells susceptible to direct conversion into specific somatic cell types. Cell Rep. 2012 Nov 29;2(5):1178-86. doi: 10.1016/j.celrep.2012.09.020.

Eun SH, Shi Z, Cui K, Zhao K, Chen X. A non-cell autonomous role of E(z) to prevent germ cells from turning on a somatic cell marker. Science. 2014 Mar 28;343(6178):1513-6. doi: 10.1126/science.1246514.

Week 9 – Week of November 6th (Wednesday, November 8th)
Pre-class assignment: Students should e-mail the paper they have selected for their oral presentation to the instructor for approval.
Field trip to Harvard Stem Cell Institute (see above for details)

Week 10 – Week of November 13th (Wednesday, November 15th)
Pre-class assignment: Students should e-mail questions for the CEO of Conception Bio to the instructor for approval and sharing.
in vitro *establishment of the germline cell fate: immortalization in a dish*
An understanding of the natural inducers of an immortal cell fate, as discussed so far in this class, can allow scientists to *engineer* the germline fate outside of an organism. Such experiments can conclusively identify components sufficient for the formation of an immortal germline fate rather than for differentiation and maturation into somatic cell types. Such studies indicate the possibility *in vitro* generating human gametes, e.g., taking a small sample of somatic tissue from a person and using it to generate gametes with that person's genome. This topic has ignited a great deal of public interest, but the reporting is not always accurate. The first paper describes the first successful transformation of mouse embryonic stem cells and induced pluripotent stem cells into viable gametes. This study evaluated engineered cells using histological, transcriptomic, epigenomic, and functional tools. The second paper zooms in on the problems of meiosis in the development of mature sperm *in vitro*, using cell biological histological analyses.

Hayashi K, Ohta H, Kurimoto K, Aramaki S, Saitou M. Reconstitution of the mouse germ cell specification pathway in culture by pluripotent stem cells. Cell. 2011 Aug 19;146(4):519-32. doi: 10.1016/j.cell.2011.06.052.

Lei Q, Lai X, Eliveld J, Chuva de Sousa Lopes SM, van Pelt AMM, Hamer G. *In Vitro* meiosis of male germline stem cells. Stem Cell Reports 2020 Nov 10;15(5):1140-1153. doi: 10.1016/j.stemcr.2020.10.006.

NO CLASS NOVEMBER 22nd

Week 11 – Week of November 27th (Wednesday, November 29th)
Pre-class assignment: Students should e-mail an outline of their oral presentations to the instructor, including the identification of the question, the hypothesis, the key results, and the major conclusion of the primary research paper.
Causes and consequences of mortality: aging and stem cell depletion
Of course, unlike germ cells, all vertebrates are mortal – on an organismal level. Without germline-level protection, selection, and repair, as we discussed earlier in the semester, somatic cells accumulate damage and eventually succumb to aging. What does mortality look like on a cellular level? The first paper describes how whole-organism single-cell RNA sequencing allows can reveal changes in cell-type composition (including an increase in fat cells and a decrease in muscle cells) during the aging process. The second paper reveals a mechanism for a commonly understood connection: stress can cause an acceleration of aging, including hair greying. In this paper researchers show that the nervous system can transmit a stress

response to the stem cells responsible for producing hair color, causing those cells to proliferate faster and eventually exhaust.

Lu TC, Brbić M, Park YJ, Jackson T, Chen J, Kolluru SS, Qi Y, Katheder NS, Cai XT, Lee S, Chen YC, Auld N, Liang CY, Ding SH, Welsch D, D'Souza S, Pisco AO, Jones RC, Leskovec J, Lai EC, Bellen HJ, Luo L, Jasper H, Quake SR, Li H. Aging Fly Cell Atlas identifies exhaustive aging features at cellular resolution. Science. 2023 Jun 16;380(6650):eadg0934. doi: 10.1126/science.adg0934.

Zhang B, Ma S, Rachmin I, He M, Baral P, Choi S, Gonçalves WA, Shwartz Y, Fast EM, Su Y, Zon LI, Regev A, Buenrostro JD, Cunha TM, Chiu IM, Fisher DE, Hsu YC. Hyperactivation of sympathetic nerves drives depletion of melanocyte stem cells. Nature. 2020 Jan;577(7792):676-681. doi: 10.1038/s41586-020-1935-3.

Week 12 – Week of December 4th (Wednesday, December 6th)
Acquisition of immortality in cancer progression
Cancer is a disease of cellular immortality – limitless replicative potential is essential for the development of malignant growth. To divide endlessly, tumor cells co-opt immortality mechanisms used by the germline. Our last two papers of the semester will help us explore both broad and specific germline immortality targets for cancer treatment. In the first paper, based on preexisting RNA sequencing data, the authors propose that many genes typically expressed only in germ cells are upregulated broadly in many different cancer types. Note that this paper lacks validation for many of its hypotheses. Recalling our session focused on genomic rejuvenation, the second paper discusses the discovery of a telomerase inhibitor that can "mortalize" cancer cells. Interestingly, the inhibitor is an oligonucleotide that serves as a sink for telomerase activity such that it outcompetes telomeres themselves for telomerase binding. As of 2023, this inhibitor, under the name Imetelstat, is in Phase 3 clinical trials for treatment of several specific cancers.

Bruggeman JW, Koster J, Lodder P, Repping S, Hamer G. Massive expression of germ cell-specific genes is a hallmark of cancer and a potential target for novel treatment development. Oncogene. 2018 Oct;37(42):5694-5700. doi: 10.1038/s41388-018-0357-2. *supplement online

Dikmen ZG, Gellert GC, Jackson S, Gryaznov S, Tressler R, Dogan P, Wright WE, Shay JW. *In vivo* inhibition of lung cancer by GRN163L: a novel human telomerase inhibitor. Cancer Res. 2005 Sep 1;65(17):7866-73. doi: 10.1158/0008-5472.CAN-05-1215.

Week 13 – Week of December 11th (Wednesday, December 13th)
Final Oral Presentations (see details above)
We will also discuss the course – what worked and what didn't – and complete course evaluations.