Harvard Medical School
Biological and Biomedical Sciences
Cancer Biology Area of Concentration
CB211: Molecular and Systems Level Cancer Cell Biology

Course Syllabus

Course Code:	CB211
Course Dates:	January 27, 2020 – April 29, 2020
Meeting Days:	Mondays & Wednesdays
Meeting Time:	1:00-2:30 pm
Lecture location:	see course website

Discussion session locations: see course website

Course Directors:	Peter Sicinski (Peter_Sicinski@dfci.harvard.edu)
	Jarrod Marto (Jarrod_Marto@dfci.harvard.edu)
	Marc Vidal (Marc_Vidal@dfci.harvard.edu)
Curriculum Fellow:	Jelena Patrnogic, PhD (Jelena_Patrnogic@hms.harvard.edu)
Teaching Assistant:	Yan Geng, MD PhD (yan_geng@dfci.harvard.edu)
Course Website:	https://canvas.harvard.edu/courses/68166

Course Description: Examines the molecular basis of cancer formation including topics such as cancer epigenetic, tumor heterogeneity, cancer metabolism, system biology proteomic approaches to study cancer, immune therapy in cancer and therapeutic development.

Course Evaluation: 40% Presentation
40% Discussion
20% Participation & Attendance

Important Notes:

- Students are expected to attend all lectures and sessions. Please be on time.
- Ask questions – we want to make this a dynamic learning experience.
- Papers will be posted for each module under "Prep Readings" on the course Canvas website. Students are expected to have read these preparatory papers prior to the first lecture of each module.

- Assignments for session 3 of each module will be posted under "Paper Presentations" and should be prepared prior to session 3.

Participation/Attendance (20%): Attendance and participation at all course sessions is required and necessary for your success in the course. Excused absences are allowed only at the discretion of the course directors. Students are expected to contribute actively to each class meeting by asking and answering questions of the lecturers and during student presentations. In the event that the University cancels classes, such as for severe weather, students are expected to continue with readings as originally scheduled, unless other instructions are posted at the course website or communicated via email.

Presentation Guidelines (40%): Student presentations give you the opportunity to present an additional topic related to the lectures given by faculty. This will allow you to synthesize and implement the knowledge that you have gained while practicing your presentation skills. Each student presentation will explore a specific topic of cancer biology research in depth, as outlined in the schedule. Student presentations will occur during the third session of each module, when the class will be divided into sections of 6-8 students. Lecturers, postdocs from lecturers' labs, and/or course directors, will moderate sections. The presenting student will run the session, providing a presentation of their research paper and topic followed by a discussion session.

- Students will be expected to give a ~30-minute presentation (powerpoint) of the paper and topic and to lead a discussion of the paper with their classmates afterwards.
- The presentation should strive to be a clear, concise, and interesting.

The presentation should include:

1. Background Information on the topic
2. Hypothesis / Objectives / Aims of the authors of the assigned paper
3. Key Figures and Results (note: it is not necessary to present each figure)
4. Conclusion
5. Next Steps/Future Directions – i.e. if you were to continue these studies, what direction of research would you propose?
6. Discussion Questions (3-5) – these can be presented throughout or just at the end

Each student will receive written feedback on their presentation skills from the moderator that facilitated their session.

Discussion Guidelines (40%): Students are expected to come prepared to small group sessions, participate fully in the discussions, and to critically think through the posed discussion questions as a group. Ideally, all students will contribute equally to these sessions. When everyone contributes, regardless of background, some of the most interesting and dynamic discussion can arise.

Class schedule

CB211: Molecular and Systems Level Cancer Cell Biology

Date	Faculty	Topic/Lecture Title
Monday Jan 27	P. Sicinski	Course Introduction Cell Cycle Machinery
Wednesday Jan 29	K. Polyak	Module 1: Decoding Tumor Heterogeneity
Monday Feb 3		
Wednesday Feb 5		
Monday Feb 10	P. Puigserver	Module 2: Cancer Metabolism
Wednesday Feb 12		
Wednesday Feb 19		
Monday Feb 17	*President's Day – No Classes*	
Monday Feb 24	C. Kadoch	Module 3: Cancer Epigenetics
Wednesday Feb 26		
Monday Mar 2		
Wednesday Mar 4	J. Qi	Module 4: Using Chemistry to Conquer Cancer
Monday Mar 9		
Wednesday Mar 11		
Monday Mar 23	M. Vidal	Module 5: Cancer Cell Interactomes
Wednesday Mar 25		
Monday Mar 30		
Wednesday Apr 1	G. Shapiro	Module 6: Advances in Cancer Drug Development
Monday Apr 6		
Wednesday Apr 8		
Monday Apr 13	K. Wucherpfennig	Module 7: Immune Therapy in Cancer
Wednesday Apr 15		
Wednesday Apr 22		
Monday April 20		*Patriots Day – No Class*
Monday Apr 27	J. Marto	Module 8: Functional Proteomics
Wednesday Apr 29		

Module Descriptions

Module 1: Decoding Tumor Heterogeneity — K. Polyak

Cancer cells even within the same tumor can display startling differences for many features including migratory/invasive potential and sensitivity to therapeutic agents. This intratumor heterogeneity is a major obstacle toward understanding and treatment of cancers. Dr. Polyak will review the various types of intratumor heterogeneity (e.g., genetic, phenotypic), methods to assess them, and their functional and clinical relevance.

Module 2: Cancer Metabolism — P. Puigserver

Cancer cells reprogram metabolism to drive tumor initiation, progression and metastasis. In some cases, specific mutations in metabolic genes are sufficient to cause cancer. The metabolic and energetic reprogramming of cancer cells depends on the specific type of tumor as well as the stage. Dr. Puigserver will review the different metabolic adaptations in cancer cells and how they support different aspects of tumor biology. In addition, he will focus on how cancer metabolism can be exploited to define tumor vulnerabilities and potential therapeutic interventions in cancer patients.

Module 3: Cancer Epigenetics — C. Kadoch

Recent whole-exome and whole-genome sequencing efforts have unmasked the major contributions of chromatin regulatory processes to human disease. Mutations in genes encoding chromatin-associated proteins and protein complexes are present in over 50% of human cancers, as well as several rare cancer types in which such perturbations represent the hallmark and driving features of disease. In addition, genes encoding chromatin regulatory machinery are frequently mutated in neurodevelopmental and intellectual disability syndromes, including autism. Taken together, these human genetic studies underscore the important role for epigenetic processes in regulating timely and appropriate gene expression. In this module, we will review the various mechanisms by which chromatin architecture and gene expression is established and maintained, and will highlight emerging therapeutic opportunities that have arisen from both human genetic and mechanistic studies. We will highlight experimental approaches ranging from protein biochemistry and structural biology to functional genomics and systems biology as strategies to mechanistically interrogate chromatin-associated protein and protein complex activity and genomic targeting in normal and disease states.

Module 4: Using Chemistry to Conquer Cancer — J. Qi

The robust epigenetic landscape plays a vital role in gene expression via its ability to promote or repress transcription. Reprogramming of these processes can lead to genomic instability, which may propagate a cancerous state. Small molecule inhitors provide an excellent opportunity to combat this reprogramming; targeting epigenetic proteins involved in these gene regulatory pathways. The small moelcule probes also offerred unitque opportunity to both understand the biological rationale for potential cancer therapuetics and develop drug/therapeutic strategies. Dr. Qi will review the small molecule probe design and development and their use for understanding the biological function of targetted proteins in cancer as well as the drug development.

Module 5: Cancer Cell Interactomes **M. Vidal**

Complex networks or systems of dynamically interacting macromolecules mediate most, if not all, cellular functions. Cellular systems exhibit global and emergent properties that are not necessarily obvious from observing one or a few genes or gene products at-a-time. This module will cover how the properties of cellular systems might be perturbed in cancer.

Module 6: Advances in Cancer Drug Development **G. Shapiro**

Cancer drug development is currently proceeding at a rapid pace, aided by tumor profiling allowing biomarker-driven patient selection strategies. Dr. Shapiro will review broad principles of targeted therapies, including inhibitors of signal transduction, the cell cycle and DNA repair, highlighting results from recent clinical trials that have led to transformative FDA approvals. Additionally, he will discuss approaches to overcome mechanisms of resistance to these agents, as well as insights into their interactions with the immune microenvironment, both of which are leading to novel combination therapies.

Module 7: Immune Therapy in Cancer **K. Wucherpfennig**

The immune system has the ability to specifically detect and eliminate transformed cells, but this protective mechanism is frequently undermined by a number of immunosuppressive factors in the tumor microenvironment. Dr. Wucherpfennig will review the different cellular and molecular mechanisms through which immune cells can eliminate transformed cells. Furthermore, he will discuss exciting results from recent clinical trials, which have shown that immunotherapies can induce durable responses in patients with metastatic disease.

Module 8: Functional Proteomics **J. Marto**

While our knowledge of the genomic landscape associated with human cancer continues to grow at a rapid rate, it remains difficult to understand how genetic alterations manifest *en masse* across the proteome to drive cellular, clinical, or other phenotypes. These hurdles also impede our ability to prioritize specific molecules or biological pathways for therapeutic benefit. In this module Dr. Marto will discuss approaches to interrogate the functional proteome, and how these data allow us to decipher the impact of cancer genomes on individual proteins, biochemical complexes, or signaling networks.

The schedule, policies, and assignments in this course are subject to change in the event of extenuating circumstances, by mutual agreement, and/or to ensure better student learning.

Academic Integrity

All work in this course is governed by the academic integrity policies of GSAS Academic Integrity and HMS Academic Dishonesty and Plagiarism.It is the students' responsibility to be aware of these policies and to ensure that their work adheres to them both in detail and in spirit. Unless otherwise specified by the instructor, the assumption is that all work submitted must reflect the student's own effort and understanding. Students are expected to clearly distinguish their own ideas and knowledge from information derived from other sources, including from collaboration with other people. If you have a question about how best to complete an assignment in light of these policies, ask the instructor for clarification.

Reasonable Accommodations

As an institution that values diversity and inclusion, our goal is to create learning environments that are usable, equitable, inclusive and welcoming. Harvard University complies with federal legislation for individuals with disabilities and offers reasonable accommodations to qualified students with documented disabilities and temporary impairments. To make a request for reasonable accommodations in a course, students must first connect with their local disability office. The primary point of contact for GSAS students is Accessible Education Office. The HMS Director of Disability Services, Timothy Rogers (timothy_rogers@hms.harvard.edu) is another potential source of accommodation information for PhD students and is the primary contact for MD and master's students. Accommodations are determined through an interactive process and are not retroactive. Therefore, students should contact their local disability office as soon as possible, preferably at least two weeks before accommodations are needed in a course. Students are strongly encouraged to discuss their access needs with their instructors; however, instructors cannot independently institute individual accommodations without prior approval from the disability office. Student privacy surrounding disability status is recognized under FERPA. Information about accommodations is shared on a need-to-know basis, and with only those individuals involved in instituting the accommodation.

Academic and other Support Services

We value your well-being and recognize that as a graduate student you are asked to balance a variety of responsibilities and potential stressors: in class, in lab, and in life. If you are struggling with experiences either in- or outside of class, there are resources available to help. Jackie Yun, the GSAS Director of Student Services (617-495-5005) is available to assist students navigating academic or personal difficulties and to connect students to university resources. HILS PhD students have access to free academic tutoring which can be arranged through the DMS office. A variety of academic support services are also available to GSAS students through the Bureau of Study Counsel and the Center for Writing and Communicating Ideas .

All students have access to Counseling and Mental Health Services (CAMHS) available in Longwood, Cambridge or remotely via webcam or phone. The use of CAMHS is included in the student health fee, regardless of insurance, at no additional cost. More information is available CAMHS or by calling the main office at 617-495-2042. Urgent care can be reached 24/7 at 617-495-5711.