COURSE DESCRIPTION

This semester long course will explore molecular basis of cancer formation through introduction of a wide range of topics that highlight foundational research and concepts, current major findings, and future directions. You will learn how cancer cells reprogram metabolism to feed their own needs, and that in over 50% of human cancers mutations are present in genes encoding chromatin-associated proteins and protein complexes. To understand the impact of cancer genomes on individual proteins, biochemical complexes, or signaling networks, you'll interrogate the functional proteome, and you'll take a step back to understand how the properties of cellular systems might be perturbed in cancer. Deep dive into cancer cells will reveal that even within the same tumor, cells can display startling differences for many features making intratumor heterogeneity a major obstacle toward understanding and treatment of cancers. You will learn about small molecule probes and how they offer a unique opportunity to understand the biological rationale for potential cancer therapeutics, how immune cells employ different cellular and molecular mechanisms to eliminate transformed cells, and you will learn about the rapid pace of cancer drug development highlighting results from recent clinical trials that have led to transformative FDA approvals. The topics are organized into eight modules and led by one faculty member. Faculty joining us this Spring are experts in the various fields and will provide you with an integrated perspective on past, current, and future approaches in cancer biology research. Modules consist of three sessions – an introductory lecture that provides an overview of the topic, a keynote lecture that talks about recent discoveries in the field, and, a group discussion that gives you the opportunity to synthesize the knowledge and think critically about the scientific questions in the field, while focusing on building and improving scientific communication skills through the practice of presentation, discussion, and peer evaluation & feedback.

COURSE DETAILS & GENERAL INFORMATION

Course Code	CellBio 211
Course Dates:	January 22, 2024 – April 24, 2024
Meeting Days	Mondays & Wednesdays
Meeting Time	1:00-2:30 pm
Lecture Location	Longwood Campus, *see below & Canvas for details*
Discussion Session Location	*See Canvas page for details on discussion sessions and assigned groups*
Course Directors	Peter Sicinski, MD, PhD (Peter_Sicinski@dfci.harvard.edu) Jarrod Marto, PhD (Jarrod_Marto@dfci.harvard.edu) Marc Vidal, PhD (Marc_Vidal@dfci.harvard.edu)
Curriculum Advisor	Jelena Patrnogić, PhD (Jelena_Patrnogic@hms.harvard.edu)
Course Associate Director	Yan Geng, MD, PhD (yan_geng@dfci.harvard.edu)
Course Website	https://canvas.harvard.edu/courses/131682
Course Prerequisites	General knowledge of biochemistry, molecular genetics, and cell biology

COURSE OBJECTIVES

- Understand foundational discoveries that led to major concepts in the field
- Describe the molecular basis of cancer formation
- Identify big open questions in the research areas around the course topics
- Synthesize and implement content knowledge while practicing your presentation skills
- Practice providing evaluation and feedback to your peers

COURSE ASSESSMENT & GRADING

Small Group Discussion – 18 pts total

- Participation during group discussions
- 3 pts per Module – graded for completion (*3 pts participation/0 pts no participation*)

Scientific presentation – 24 pts total

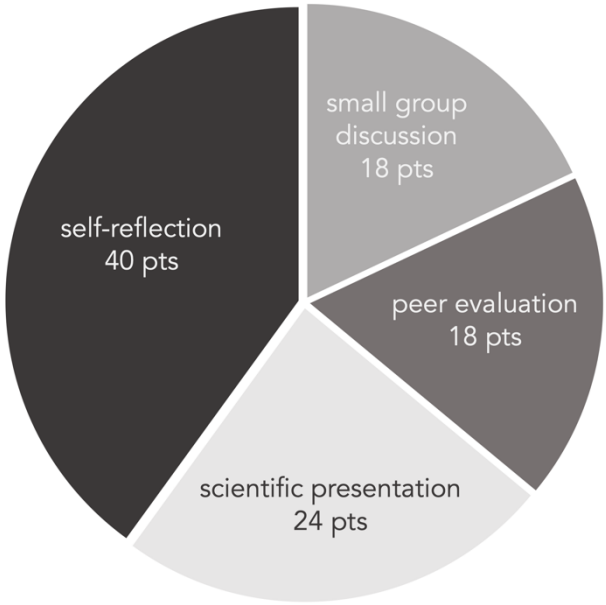
- Presentation during session three

Peer evaluation & critique – 18 pts total

- Providing peer evaluation and critique to the presenter
- 3 pts per Module – graded for completion (*3 pts participation/0 pts no participation*)

Self-reflection – 40 pts total

- Filling out self-reflection prompts for each corresponding module
- 5 pts per Module – graded for completion (*5 pts participation/0 pts no participation*)



Except for Scientific Presentation, all assignments are graded based on completion

Grading scale

91-100 pts – A	81-90 pts – B	71-80 pts – C	61-70 – D	0 – 60 – F

HOW TO SUCCEED IN THE COURSE

- **Attend all the course sessions** (lectures and group discussions, *see below for more details on Module structure*). Excused absences are allowed, and you can reach out directly to Jelena_Patrnogic@hms.harvard.edu for accommodation. If 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.
- **Ask questions & actively participate in all the sessions** – we want to make this a dynamic learning experience.
- **Read introductory papers** that support each Module to help you create foundation of the topics that will be covered in class
- **Come prepared for all small group discussions** (*see guidelines & rubrics for presentations and participation*)
- **Reflect on course content and learning** and how it relates to relevance of your own research projects and/or interests

MODULE STRUCTURE & ASSIGNMENTS

Each course modules consist of three sessions –

SESSION ONE – introductory lecture

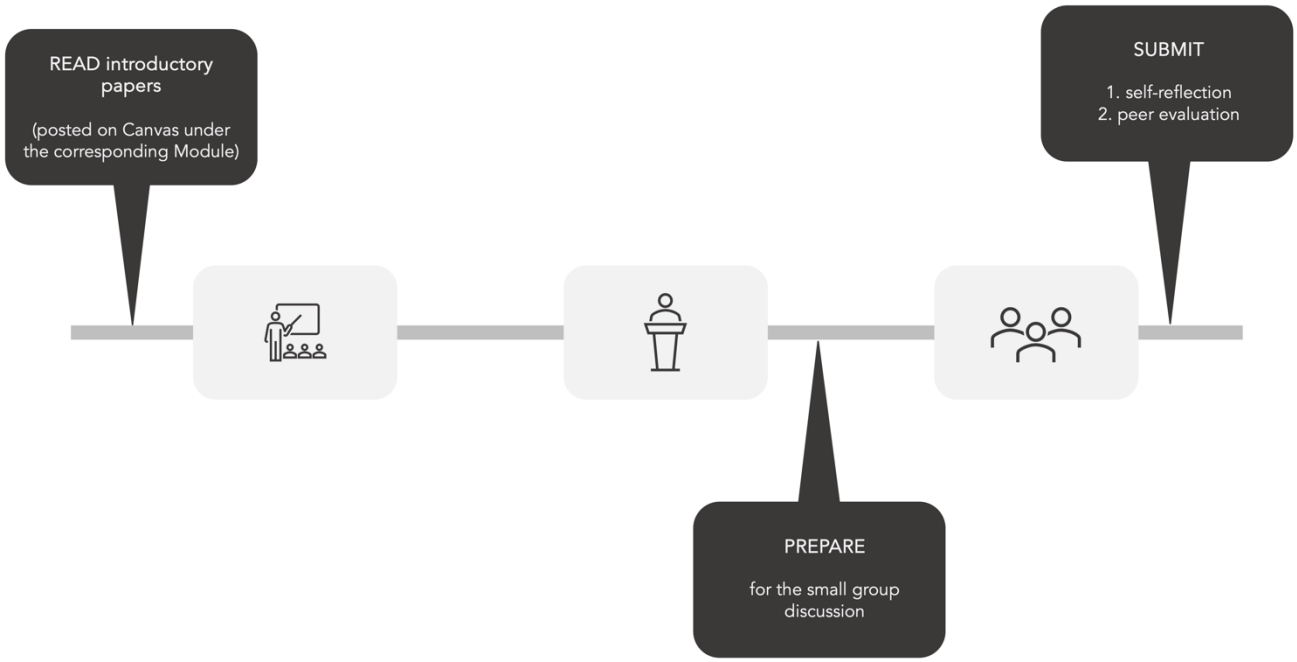
designed to provide you with an overview of the topic highlighting foundational research, main concepts, and future directions

SESSION TWO – keynote lecture

designed to provide you with an overview of recent discoveries and research being done in the lab of the faculty member joining us and can be a great opportunity for you when considering your rotation labs

SESSION THREE – small group discussion

designed to give you the opportunity to explore a specific topic of interest and lead a group discussion, while practicing both your presentation and feedback & evaluation skills. During small group discussions the class will be divided into sections of 6-8 students (*details will be posted on Canvas in a timely manner*). Small group discussions will be led by one student presenter and moderated by lecturers, postdocs from lecturers' labs, and/or course directors.



How to prepare for the sessions

For sessions one & two

Read introductory papers posted on Canvas under the corresponding module. Write down your questions and/or misconceptions and ask them during the lectures.

For session three

All 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 *(see Canvas for participation guidelines & rubric for more details).*

For presenters

Student presentations will give you the opportunity to present a research paper related to the topics covered in the lectures. This will allow you to synthesize and implement the knowledge that you have gained while practicing your presentation skills. In addition, you will run the session the follow up discussion *(see Canvas for presentation guidelines & rubric for more details).*

Post session three/Post module

You will receive written feedback on your presentation skills from the moderator that facilitated your session, as well as combined peer evaluation & critique rubrics from the group (anonymous). Following session three, and the Module, you are expected to fill out self-reflection prompts posted on Canvas.

Scientific communication office hours

If you need help in preparing your presentation (outline, slides, message, *etc.*), you can reach out directly to Jelena_Patrnogic@hms.harvard.edu and set up a meeting.

SCHEDULE *(see below detailed schedule with module descriptions, and session locations)*

Date	Faculty & Module Topic
Mon Jan 22	Intro & Cell Cycle Machinery, Peter Sicinski, in TMEC 209
Wed Jan 24	Building Your Presentation Skills, Jelena Patrnogić, in TMEC 106
Mon Jan 29	Module One | Cancer Metabolism & How We Study It, Naama Kanarek
Wed Jan 31	
Mon Feb 5	
Wed Feb 7	Module Two | Cancer Cell Interactomes, Marc Vidal
Mon Feb 12	
Wed Feb 14	
Wed Feb 21	Module Three | Functional Proteomics, Jarrod Marto
Mon Feb 26	
Mon Feb 19	*No Class – Presidents' Day*
Wed Feb 28	
Mon Mar 4	Module Four | Cancer Epigenetics, Zuzana Tothova
Wed Mar 6	
Mon Mar 11	*No Classes – Spring Break*
Wed Mar 13	
Mon Mar 18	
Wed Mar 20	Module Five | Decoding Tumor Heterogeneity, Kornelia Polyak
Mon Mar 25	
Wed Mar 27	
Mon Apr 1	Module Six | Advances in Cancer Drug Development, Geoff Shapiro
Wed Apr 3	
Mon Apr 8	
Wed Apr 11	Module Seven | Immune Therapy in Cancer, Stephanie Dougan
Mon Apr 15	
Wed Apr 17	
Mon Apr 22	Module Eight | Using Chemistry to Conquer Cancer, Jun Qi
Wed Apr 24	

COURSE MODULES | Schedule & Information

Module One: Cancer Metabolism and How We Study It
Instructor: Naama Kanarek, naama.kanarek@childrens.harvard.edu

Date	Location
Monday January 29	TMEC 227
Wednesday January 31	TMEC 227

Description

Metabolism is the front line of all cellular functions. It is what we research when we study cells at the higher resolution. Metabolites are the little workers that actually do what needs to be done in a cell; when a cell grows, nutrients feed that growth, when a signaling event happens – metabolites provide the materials (such as phosphates), and the energy to allow it, and when cell fate decisions are made – metabolite sensing is often a critical part in that decision making. Therefore, it is not surprising that cancer cells reprogram metabolism to feed their own needs, and metabolic rewiring drives tumor initiation, progression, and metastasis. In some cases, specific mutations in metabolic genes are sufficient to cause cancer, emphasizing the critical role played by metabolic rewiring in the tumor transformation. The cancer metabolism field incorporates research of metabolic adaptations of cancer cells, unique and targetable metabolic needs of cancer cells, and the cancer microenvironment from the nutritional perspective. A relatively new and exciting frontier is the competition between cancer and immune cells over limiting nutrients in the tumor microenvironment. In our class we will review cancer metabolism and discuss how unique metabolic traits are, or can be, targeted to treat cancer.

Objectives

- Review cancer cell metabolism
- Introduce metabolomics as a tool to study Cancer Metabolism
- Identify how cancer metabolism can be exploited to define tumor vulnerabilities
- Discuss the metabolic competition between cancer and immune cells and its implications in tumor immunity

Module Two: Cancer Cell Interactomes
Instructor: Marc Vidal, marc_vidal@dfci.harvard.edu

Date	Location
Monday February 5	TMEC 227
Wednesday February 7	TMEC 227
Monday February 12	See Canvas for group assignments

Description

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.

Objectives

- Describe how cellular systems get perturbed in cancer
- Compare and contrast – cellular functions in normal and diseased states

Module Three: Functional Proteomics
Instructor: Jarrod Marto, jarrod_marto@dfci.harvard.edu

Date	Location
Wednesday February 14	TMEC 227
Wednesday February 21	TMEC 227
Monday February 26	See Canvas for group assignments

Description

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.

Objectives

- Understand the approaches for interrogating functional proteome
- Describe how proteomic data allows us to decipher the impact of cancer genomes on individual proteins

Module Four: Cancer Epigenetics
Instructor: Zuzana Tothova, zuzana_tothova@dfci.harvard.edu

Date	Location
Wednesday February 28	TMEC 227
Monday March 4	Modell 100A
Wednesday March 6	See Canvas for group assignments

Description

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. 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 functional genomics, transcriptomics, proteomics and immunopeptidomics, as well as *in vivo* experimental approaches in primary mouse and patient-derived models as strategies to mechanistically interrogate chromatin-associated protein and protein complex activity and therapeutic targeting in cancer.

Objectives

- Understand the various mechanisms by which chromatin architecture and gene expression is established and maintained
- Describe experimental approaches used in the mechanistic study of chromatin-associated proteins and protein complex activity

Module Five: Decoding Tumor Heterogeneity
Instructor: Kornelia Polyak, kornelia_polyak@dfci.harvard.edu

Date	Location
Monday March 18	TMEC 227
Wednesday March 20	TMEC 227
Monday March 25	See Canvas for group assignments

Description

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.

Objectives

- Compare and contrast various types of intratumor heterogeneity
- Understand the methods of assessing various types of heterogeneity
- Describe the functional and the clinical relevance of tumor heterogeneity

Module Six: Advances in Cancer Drug Development
Instructor: Geoff Shapiro, geoffrey_shapiro@dfci.harvard.edu

Date	Location
Wednesday March 27	TMEC 227
Monday April 1	TMEC 227
Wednesday April 3	See Canvas for group assignments

Description

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.

Objectives

- Understand the principles of targeted therapies from inhibitors of signal transduction, cell cycle and DNA repair
- Understand the results from recent clinical trials
- Describe approaches to overcome mechanisms of resistance to these agents

Module Seven: Immune Therapy in Cancer
Instructor: Stephanie Dougan, stephanie_dougan@dfci.harvard.edu

Date	Location
Monday April 8	Modell 100A
Wednesday April 10	Modell 100A
Monday April 15	See Canvas for group assignments

Description

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. Dougan will review the different cellular and molecular mechanisms through which immune cells can eliminate cancer cells and how cancer cells can acquire resistance. Furthermore, she will discuss results from clinical trials, which have shown that immunotherapies can induce durable responses in patients with metastatic disease.

Objectives

- Describe molecular and cellular mechanisms by which immune cells eliminate transformed cells
- Understand the results from recent clinical trials

Module Eight: Using Chemistry to Conquer Cancer
Instructor: Jun Qi, jun_qi@dfci.harvard.edu

Date	Location
Wednesday April 17	TMEC 227
Monday April 22	TMEC 227
Wednesday April 24	See Canvas for group assignments

Description

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 inhibitors provide an excellent opportunity to combat this reprogramming; targeting epigenetic proteins involved in these gene regulatory pathways. The small molecule probes also offered unique opportunity to both understand the biological rationale for potential cancer therapeutics 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 targeted proteins in cancer as well as the drug development.

Objectives

- Describe the molecule probe design and development
- Identify how molecule probe design is used in biological function of targeted proteins in cancer and drug development

Academic Integrity

All work in this course is governed by the academic integrity policies of

- Harvard Kenneth C. Griffin GSAS (https://gsas.harvard.edu/policy/academic-integrity) and
- HMS (https://issuu.com/hmsgraduateeducation/docs/handbook_updates_all_22-23_gc?fr=sNzY5YTUxODU3Njk – 3.09 Academic Dishonesty and Plagiarism).

It is your responsibility to be aware of these policies and to ensure that your 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 your own effort and understanding. You are expected to clearly distinguish your own ideas and knowledge from information derived from other sources, including from conversations with other people. When working with others you must do so in the *spirit of collaboration*, not via a unidirectional transfer of information. Note that, unless it is part of the assignment, sharing or sending completed assignments to others will nearly always violate this collaborative standard. If you have a question about how best to complete an assignment in light of these policies, ask the instructor for clarification.

Community Standards

HMS is committed to supporting inclusive learning environments that value and affirm the diverse ideas and unique life experiences of all people. An equitable, inclusive classroom is a shared responsibility of both instructors and students, and both are encouraged to consider how their own experiences and biases may influence the learning environment. This requires an open mind and respect for differences of all kinds. You are encouraged to contact the course director if you are experiencing bias or feel that their learning experience – including a course's content, manner of instruction, or learning environment -- is not inclusive. Curriculum Fellows, program administrators and directors, the Harvard Kenneth C. Griffin GSAS Office of Equity, Diversity, Inclusion & Belonging (https://gsas.harvard.edu/diversity), the Office for Gender Equity (https://oge.harvard.edu/), and the Ombuds Office (https://harvardombuds.harvard.edu/) are also available to discuss your experiences and provide support. Additionally, you can utilize Harvard's Anonymous Reporting Hotline (https://reportinghotline.harvard.edu/) to report issues related to bias.

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, you must first connect with their local disability office. The primary point of contact for Harvard Kenneth C. Griffin GSAS students is the Disability Access Office (https://aeo.fas.harvard.edu/). 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 to initiate the accommodation process as soon as possible, preferably at least two weeks before accommodations are needed in a course or immediately following an injury or illness. Students are strongly encouraged to discuss their 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 inside or outside of class, there are resources available to help. The Harvard Kenneth C. Griffin GSAS Student Services Office, stuserv@fas.harvard.edu or 617-495-5005 is available to assist students navigating academic or personal difficulties and connect you to university resources. HILS PhD students have access to free academic tutoring, arranged through the DMS office. A variety of academic support services are also available to Harvard Kenneth C. Griffin GSAS students through the Academic Resource Center (https://academicresourcecenter.harvard.edu) and the Writing Center and Communications Lab (https://communicate.gse.harvard.edu/).

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 at https://camhs.huhs.harvard.edu or by calling the main office at 617-495-2042. Urgent care can be reached 24/7 at 617-495-5711.