SYLLABUS
BIOL-667

GEORGE MASON UNIVERSITY
College of Science
BIOL-667 (3 credits)
Signal transduction in cancer
Instructor: Mariaelena Pierobon, MD MPH
Associate Professor
Institute for Advanced Biomedical Research
10920 George Mason Circle, Room 2016
Manassas, VA 20110
Phone: 703-993-9839
Email: mpierobo@gmu.edu (preferred method)

Office hours: Wednesday 3:30-4:30 by appointment (link for office hours will be sent when after appointments have been scheduled). For urgent communications, please email at mpierobo@gmu.edu

Course type: Asynchronous and Synchronous online activities. Synchronous activities will be held via Blackboard Ultra or in person.

Catalogue Description: Principles of signal transduction in cancer with an emphasis on their biological and clinical implications. The course will explore the role of different signaling pathways in modulating inter- and intra-cellular communication, tumor development, and therapeutic interventions.

Pre-requisite: At least one Cell or Molecular Biology undergraduate course, or BIOL 682 Advanced Eukaryotic Cell Biology, or BIOL 566 Cancer Biology. Due to the online format of the class, students will need a computer, internet connection, and the ability to actively participate to weekly activity. Use of a webcam is highly recommended during live sessions.

Course Goal and Objectives:

At the end of the course students will be able to:

- Explain the main principles of signaling transduction;
- Illustrate the biochemical mechanisms by which different members of these signaling networks operate;
- Describe signaling pathways involved in cancer initiation and progression;
- Define at least three post-translational modifications;
- Describe the effect of post-translational modifications on signal transduction cascades;
- Connect signaling activities and corresponding biological functions;
- Explain the principles underlying tumor dissemination and metastasis;
- Explain the role of signaling pathway in precision medicine;
- Distinguish between three main classes of anti-cancer treatments;
- Compare the mechanisms of action of targeted compounds used in cancer treatment;
- Critique a scientific manuscript;
- Report peer-reviewed research to peers.

Learning objectives will be achieved through a combination of lectures and life discussions of scientific papers covering different aspects of tumor biology and their clinical applications. Classes will be structured as asynchronous online lectures and synchronous students' lead paper discussions on topics covered in previous lectures.

Grading and Class structure -Graduate level-
1 Interim Exams: 20 points
Paper presentation(s): 20 points
1 Final exams: 30 points
Feedback and participation to paper discussions: 6 points
Online discussion board: 24 points; each discussion will be graded on a scale of 0-4.

Grading and Class structure -Undergraduate level-
1 Interim Exams: 30 points
Paper presentation(s): 20 points
1 Final exams: 32 points
Feedback and participation to paper discussions: 6 points
Online discussion board: 12 points; each discussion will be graded on a scale of 0-4.

Exams:
Exams will be structured using a combination of multiple choices and open questions. The final exam will cover the material of the entire course. After a paper presentation, each presenter will submit 3 questions relevant to the presented article; a few of these questions will be included in the exams. **Group exams or exams containing plagiarized material will not count toward the final grade.**

Paper discussions:
Students will lead the discussion of a scientific paper. List of papers and sign-up sheet will be provided during the first week of class. Students will analyze the assigned paper(s) and lead an in-class discussion. Non-presenters will be grated based on their active participation during the discussion.

Online discussions:
On selected weeks a question will be posted on the discussion board (See class calendar for dates); students can use the discussion board as an opportunity to exchange knowledge, provide opinions on a specific topic, elaborate solutions for scientific problems, and share relevant previously published findings. Students are also encouraged to use the discussion board to ask peers questions on the material covered in the lectures or during paper presentations.

Make up exams will be discussed on a case-by-case basis for students facing emergencies and health related issues. Supporting documentation may be required.

Grading scale -Graduate level-

A+	4.00	Satisfactory/Passing
A	4.00	Satisfactory/Passing
A-	3.67	Satisfactory/Passing
B+	3.33	Satisfactory/Passing

B	3.00	Satisfactory/Passing
B-	2.67	Satisfactory*/Passing
C	2.00	Unsatisfactory/Passing
F	0.00	Unsatisfactory/Failing

* Although a B- is a satisfactory grade for a course, students must maintain a 3.00 average in their degree program and present a 3.00 GPA for the courses listed on the graduation application. Information about additional grade notations that apply to graduate students including "IN" Incomplete and "IP" In Progress as well as grading for undergraduate students may be found in the Academic Policies section of the catalog under Grading System. Graduate students are not required to take midterm exams.

Grading scale -Undergraduate level-

A+	4.00	Passing
A	4.00	Passing
A-	3.67	Passing
B+	3.33	Passing
B	3.00	Passing
B-	2.67	Passing
C+	2.33	Passing
C	2.00	Passing
C-	1.67	Passing
D	1.00	Passing
F	0.00	Failing

Basic Course Technology Requirements
Activities and assignments in this course will regularly use web-conferencing software (Blackboard Ultra Collaborate/Zoom). Students are required to have regular, reliable access to a computer with an updated operating system and a stable broadband Internet connection.
In addition, students are required to have a device with a functional camera and microphone. In an emergency, students can connect through a telephone call, but video connection is the expected norm.

Plagiarism
Plagiarism is the presentation of someone else's ideas or work as one's own. Students must give credit for any information that is not the result of original research or common knowledge. If a student borrows ideas or information from another author, the author must be acknowledged in the body of the text and on the reference page. Plagiarisms are subject to the penalties outlined in the Policies and Procedures section of the University Catalog, which include a hearing by the Honor Code Committee and may include a failing grade for the work in question or for the entire course. The following website provides helpful information concerning plagiarism for both students and faculty: http://oai.gmu.edu/the-mason-honor-code-2/plagiarism/

Group exams or exams containing plagiarized material will not be counted toward the final grade and will be reported to the Honor Code Committee.

Classroom Policies
Students are expected to attend live session and to participate during discussions. Internet surfing

should be limited during our discussion time.

Students must use their MasonLive email account to receive important University information, including communications related to this class. I will not respond to messages sent from or send messages to a non-Mason email address.

As a faculty member and designated "Responsible Employee," I am required to report all disclosures of sexual assault, interpersonal violence, and stalking to Mason's Title IX Coordinator per university policy 1412. If you wish to speak with someone confidentially, please contact the Student Support and Advocacy Center (703-380-1434) or Counseling and Psychological Services (703-993-2380). You may also seek assistance from Mason's Title IX Coordinator (703-993-8730; titleix@gmu.edu).

Familiarize yourself the GMU honor code at http://www.gmu.edu/facstaff/handbook/aD.html.
The honor code requires all members of this community to maintain the highest standards of academic honesty and integrity. Cheating, plagiarism, lying, and stealing are all prohibited. All violations of the Honor Code will be reported to the Honor Committee. More information can be found at http://oai.gmu.edu/the-mason-honor-code-2/ for more detailed information.

Course Materials and Student Privacy
All course materials posted to Blackboard or other course site are private; by federal law, any materials that identify specific students (via their name, voice, or image) must not be shared with anyone not enrolled in this class. **All recordings and class material are private and should not be shared with anyone outside the class**.

Students with Disabilities
Students with a disability requiring academic accommodations should talk to the instructor and contact the Disability Resource Center (DRC). Under the administration of University Life, Disability Services (DS) implements and coordinates reasonable accommodations and disability-related services that afford equal access to university programs and activities. If you are seeking accommodations, please visit https://ds.gmu.edu for detailed information about the Disability Services registration process.
Disability Services is located in Student Union Building I (SUB I), Suite 2500; Email: ods@gmu.edu Phone: (703) 993-2474. All academic accommodations must be arranged through the DRCS.

Ethics
Ethical behavior in all class related activities is required of every student.

Diversity
Learning to work with and value diversity is essential in every class. Students are expected to exhibit an appreciation for multinational, multiracial, and gender diversity in the classroom.

As a diverse community of learners, students must strive to work together in a setting of civility, tolerance, and respect for each other and for the instructor. Rules of classroom behavior (which apply to online as well as onsite courses) include but are not limited to the following:

- Conflicting opinions among members of a class are to be respected and responded to in a professional manner;

- Side conversations or other distracting behaviors including cell phone use or non-class online access are not to be engaged in during lectures, class discussions or presentations;
- There are to be no offensive comments, language or gestures.

Students not complying will be asked to cease immediately or leave the class session.

Recommended Text

Wagener C., Stocking C., & Mueller O (2017) Wiley-VCH. Cancer Signaling: From Molecular Biology to Targeted Therapy.

Reading list:

- Gerlinger et al. Intratumor heterogeneity and branched evolution revealed by multiregion sequencing. NEJM 2021.
- Oxnard GR et al. Assessment of resistance mechanisms and clinical implications in patients with EGFR T790m-positive lung cancer and acquired resistance to osimertinib. JAMA Oncology 2018.
- Amodio V. et al. EGFR blockade reverts resistance to KRAS G12C inhibition in colorectal cancer. Cancer Discovery 2020.
- Choi HJ et al. A novel PI3K/mTOR dual inhibitor, CMG002, overcomes the chemoresistance in ovarian cancer. Gynecol Oncol. 2019.
- Turner N et al. Cyclin E1 expression and palbociclib efficacy in previously treated hormone receptor-positive metastatic breast cancer. J Clin Oncol. 2019.
- Kinsey CG et al. Protective autophagy elicited by RAF→MEK→ERK inhibition suggests a treatment strategy for RAS-driven cancers. Nat Med. 2019*
- Ando Y et al. Necroptosis in pancreatic cancer promotes cancer cell migration and invasion by release of CXCL5. PlosOne. 2020
- Kawano M et al. Interaction between human osteosarcoma and mesenchymal stem cells via an interleukin-8 signaling loop in the tumor microenvironment. Cell Commun Signal. 2018; 16(10):13.
- Duan et al. Use of immunotherapy with Programmed Cell Death 1 vs Programmed Cell Death Ligand 1 inhibitors in patients with Cancer. JAMA 2019

Course Schedule:

Week	Topic
Lecture 1 Aug 24	Lecture: Fundamentals of signal transduction. Live Discussion: Course overview.
Lecture 2 Aug 31	Lecture: Overview of cancer treatment and tumor heterogeneity. Live Discussion: How to read a scientific article.
Lecture 3 Sept 7	Lecture: Growth Factors and Receptor Tyrosine Kinases. Live Discussion: Tumor heterogeity: implications for precision medicine.
Lecture 4 Sept 14	Lecture: Cell growth and differentiation: the MAPK signaling pathways. Live Discussion: Targeting EGFR mutations in Non-Small Cell Lung Cancers. Online Discussion: Principle and regulation of signal transduction pathways.
Lecture 5 Sept 21	Lecture: Translational control & cell survival: The AKT/mTOR signaling pathway. Live Discussion: Targeting the “undruggable” KRAS.
Lecture 6 Sept 28	Lecture: The many players in cell cycle control and regulation. Live Discussion: PI3K/AKT inhibitors in chemo-resistant ovarian cancer and review material for mid-term (if requested by students)
Lecture 7 Oct 5	Mid-term Online Discussion: PI3K/AKT inhibitors in cancer treatment: challenges and opportunities.
Lecture 8 Oct 12	Lecture: Mechanisms of cell death and their role in cancer. Live Discussion: Cdk4/6 inhibitors in breast cancer.
Lecture 9 Oct 19	Lecture: Mechanisms of cell death and their role in cancer. Live Discussion: Autophagy in cancer. Online Discussion: The dual role of autophagy in cancer.
Lecture 10 Oct 26	Lecture: NF-kB pathway and inflammation. Live Discussion: Necroptosis and tumor invasion.
Lecture 11 Nov 2	Lecture: Wnt signaling pathway. Live Discussion: Targeting inflammation in the tumor microenvironment. Online Discussion: Transcription factors as druggable molecules.
Lecture 12 Nov 9	Lecture: Role of methylation and ubiquitination in signal transduction. Live Discussion: Immuno-checkpoints blockade in cancer treatment. Online Discussion: Can cancer cells change phenotype?
Lecture 13 Nov 16	Lecture: Tumor-immune interactions. Online Discussion: Challenge with biomarker analysis in cancer research.
Lecture 14 Nov 30	Live Discussion: Review material for final exam.
Lecture 15 Dec 7	Final exam