

**GEORGE MASON UNIVERSITY**  
**College of Science**  
**BIOL 508-003** (3 credits)  
**Signaling & Precision Oncology**  
**Instructor: Mariaelena Pierobon, MD MPH**  
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**Office hours:** Monday 3:30-4:30 (IABR Room 2016) and by appointment.

**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

**Course Goal and Objectives:**

This course will explore the role of alternated signaling networks in promoting tumor initiation and progression. Students will learn about different signaling networks and their effect on modulating tumor cells' ability to proliferate, evade death, and disseminate locally and systemically. Given the increased interest in precision oncology, this course will emphasize how alterations of these signaling networks have become direct targets of the new generation of anti-cancer compounds.

Learning objectives will be achieved through a combination of lectures and in-class discussions of scientific papers covering different aspects of tumor biology and their clinical applications. Classes will be structured as a traditional lecture and students lead paper discussions on topics covered in previous classes.

**Grading and Class structure**

1 Interim Exams: 25 points  
1 Paper discussion: 15 points  
1 Group Oral Presentation: 15 points  
1 Final exams: 40 point  
Class participation: 5 points

*Paper discussion:*

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 and lead an in-class discussion.

*Group presentation:*

Each group will consist of 5-6 students (groups will be established the first week of class). Each group will select a specific tumor type and a signaling pathway that represent a therapeutic target for that specific type of cancer. Each group will identify: 1) a review paper that provided background information on the specific tumor and signaling pathway to be analyzed; 2) a basic or translational research paper that highlight the therapeutic role of the signaling pathway in that specific tumor type; 3) a paper describing the efficacy of targeting the selected specific signaling pathway in cancer patients (e.g. clinical trial, biomarker analysis etc.). Papers will be presented at week 11 of the course. Articles should be

identified by the groups at the end of week 6 to allow for proper preparation. Presentations will be 20 minutes long followed by a 5 minutes Question & Answer. Presentations should be prepared in PowerPoint.

### **Grading scale**

90-100 points: A

89-80 points: B

79-75 points: C

<74 points: D

### **Classroom Policies**

Students are expected to attend all lectures and participate during discussions. Cell phones should be turned off during class and internet surfing should be limited to discussions. Make-up exams will be given only for excused absences where supporting documentation is provided.

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.

Please familiarize yourself the GMU honor code at <http://www.gmu.edu/facstaff/handbook/aD.html>

If you are a Student 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.

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).

### **Recommended Text:**

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

### **Reading list (list will be updated based on number of students and novel literature):**

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 Oncol. 2018;4(11):1527-1534.

Sandra M et al. KRAS G12C NSCLC Models Are Sensitive to Direct Targeting of KRAS in Combination with PI3K Inhibition. Clin Cancer Res. 2019;25(2):796-807.

Choi HJ et al. A novel PI3K/mTOR dual inhibitor, CMG002, overcomes the chemoresistance in ovarian cancer. Gynecol Oncol. 2019

Turner NC 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

Jayson GC et al. Plasma Tie2 is a tumor vascular response biomarker for VEGF inhibitors in metastatic colorectal cancer. Nat Commun. 2018;9(1):4672.

Liu PH et al. An IRAK1-PIN1 signalling axis drives intrinsic tumour resistance to radiation therapy. Nat Cell Biol. 2019;21(2):203-213.

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.

Week	Topic
Lecture 1	Course overview. Lecture: Fundamental of signal transduction and overview of cancer treatment.
Lecture 2	Lecture: Growth Factors and Receptor Tyrosine Kinases. Paper Discussion: How to read a scientific article.
Lecture 3	Lecture: Cell growth and differentiation: the MAPK signaling pathways Paper Discussion: Targeting EGFR mutations in Non-Small Cell Lung Cancers.
Lecture 4	Lecture: Translational control and cell survival: The PIK3CA/AKT/mTOR signaling pathway. Paper Discussion: Targeting the “undruggable” KRAS.
Lecture 5	Lecture: Cell cycle regulation in cancer cells. Paper Discussion: PI3K/AKT inhibitors in chemo-resistant ovarian cancer.
Lecture 6	Mid-term Lecture: Nuclear receptors and transcriptional regulation.
Lecture 7	Lecture: Mechanisms of cell death and their role in cancer. Paper Discussion: Cdk4/6 inhibitors in breast cancer.
Lecture 8	Lecture: Hypoxia inducible factor and cancer metabolism. Paper Discussion: Autophagy in pancreatic cancer.
Lecture 9	Lecture: NFkB signaling and inflammation. Paper Discussion: Blocking angiogenesis in metastatic colorectal cancer
Lecture 10	Lecture: Cancer dissemination, and principles of immunotherapies. Paper Discussion: Role of inflammation in response to treatment.
Lecture 11	Lecture: Wnt, NOTCH, and Hedgehog signaling in cancer. Paper Discussion: Targeting inflammation in the tumor microenvironment.
Lecture 12	PRESENTATIONS
	Final exam.

### Course Schedule: