

GEORGE MASON UNIVERSITY
College of Science

BIOL 695 and BIOL704: Precision Oncology Studies (1 credit Seminar Class)

Instructor: Mariaelena Pierobon, MD MPH

Associate Professor
School of Systems Biology
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: Friday 1:30-2:30 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: Friday 12:00-1:15. In person sections on the SciTech campus in K. Johnson Hall Room 256 or via Zoom

<https://gmu.zoom.us/j/98988808326?pwd=Z2VsVEJWMkxCL2l6RE1DenkvSGp3dz09&from=addon>

Meeting ID: 989 8880 8326

Passcode: 535500

One tap mobile

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+13017158592,,98988808326#,,,,*535500# US (Washington DC)

Pre-requisite: At least one Cancer Biology undergraduate course, or BIOL 682 Advanced Eukaryotic Cell Biology, or BIOL 566 Cancer Biology, or similar.

Catalogue Description: The purpose of this seminar is to provide an opportunity for students to understand how precision medicine has been developed and integrated in oncology practice. This class will use a journal club-based approach where each week we will have a discussion based on seminal peer-reviewed articles that have had a major impact on the field of precision oncology. Alongside we will also have the opportunity to discuss how the development of high throughput technologies like Next-Generation Sequencing has accelerated target identification and development on anti-cancer drugs able to specifically interfere with the activation of oncogenic signaling molecules.

Course Goal and Objectives:

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

- Explain the main principles of precision medicine in cancer;
- Illustrate how discoveries at the bench can become therapeutic solutions;
- Understand how cancer cells become resistant to treatment;
- Describe progression of precision medicine and its current state in cancer;
- Describe new trends and future directions of precision medicine in cancer;
- Critique a scientific manuscript;
- Share and discuss peer-reviewed research with peers and instructor.

Reading list

- Slamon et al. Human breast cancer: correlation of relapse and survival with amplification of the HER-2/neu oncogene.
- Hudziak et al. Increased expression of the putative growth factor receptor p185HER2 causes transformation and tumorigenesis on NIH 3T3 cells.
- Slamon et al. Use of chemotherapy plus a monoclonal antibody against HER2 for metastatic breast cancer that overexpresses HER2.
- Rusch Differential expression of the Epidermal Growth Factor Receptor and its ligands in primary Non-Small Cell Lung Cancers and adjacent benign lung.
- Lynch Activating Mutations in the Epidermal Growth Factor Receptor Underlying Responsiveness of Non–Small-Cell Lung Cancer to Gefitinib.
- Chabon et al. Circulating tumour DNA profiling reveals heterogeneity of EGFR inhibitor resistance mechanisms in lung cancer patients.
- Le et al. Mismatch repair deficiency predicts response of solid tumors to PD-1 blockade
- Flaherty et al. Molecular Landscape and Actionable Alterations in a Genomically Guided Cancer Clinical Trial: National Cancer Institute Molecular Analysis for Therapy Choice (NCI-MATCH).
- Clark et al. Neoadjuvant T-DM1/pertuzumab and paclitaxel/trastuzumab/pertuzumab for HER2+ breast cancer in the adaptively randomized I-SPY2 trial.
- Paraiso et al. Recovery of phospho-ERK activity allows melanoma cells to escape from BRAF inhibitor therapy.
- van 't Veer et al. Gene expression profiling predicts clinical outcome of breast cancer.
- Cardoso et al. 70-Gene Signature as an Aid to Treatment Decisions in Early-Stage Breast Cancer.
- Von Hoff et al. Pilot Study Using Molecular Profiling of Patients' Tumors to Find Potential Targets and Select Treatments for Their Refractory Cancers.
- Anderson et al. Long-Lasting Complete Responses in Patients with Metastatic Melanoma after Adoptive Cell Therapy with Tumor-Infiltrating Lymphocytes and an Attenuated IL2 Regimen.
- Sahin et al. Personalized RNA mutanome vaccines mobilize poly-specific therapeutic immunity against cancer.
- Ott et al. An immunogenic personal neoantigen vaccine for patients with melanoma.

Grading and Class structure

Paper presentations: 50 points

Discussion summaries: 20 points

Final Paper: 20 points

In-class active participation: 10 points.

Paper discussions:

In each session, 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. Non-presenters will be graded based on their active participation during the discussion.

Discussion summary:

By Tuesday following the discussion, each student is required to submit a 300-word summary explaining the study design, research question, methods, and results of the study. Students should also reserve one paragraph of the summary statement to what they consider the main take home message of the paper and how it has increased their knowledge on precision medicine compared to the paper analyzed the previous week.

Final Paper:

Students will submit a final paper where using the papers discussed throughout the semester they will provide a summary and personal re-elaboration of how precision medicine has been integrated in oncology, how it has change clinical practice and the clinical trial conception and design, its major limitation and future directions, and how laboratory work and practice is at the basis of precision oncology.

Grading scale

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.

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/>

Classroom Policies

Students are expected to attend live session and to participate during discussions and group activities. 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).

Please familiarize yourself the GMU honor code at <http://www.gmu.edu/facstaff/handbook/aD.html>. The 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 and should not be shared with anyone not enrolled in this class. By federal law, any materials that identify specific students (via their name, voice, or image) must also not be shared with anyone not enrolled in this 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;
- Offensive comments, language or gestures will not be tolerated at any time; students not complying with class policies will be asked to cease immediately or leave the class session.

Course Schedule:

Week	Topic
Lecture 1 Jan 19 -Online-	Course overview. Introduction to the course objectives and presentations.
Lecture 2 Jan 26 -Online-	Finding a “Magic Bullet” Part 1: Overexpression of Her2 in breast cancer affect patients’ outcomes. (Slamon et al. Human breast cancer: correlation of relapse and survival with amplification of the HER-2/neu oncogene)
Lecture 3 Feb 2 -Online-	Finding a “Magic Bullet” Part 2: Activation of Her2 has oncogenic effects in non-cancerous cells (Hudziak et al. Increased expression of the putative growth factor receptor p185HER2 causes transformation and tumorigenesis on NIH 3T3 cells)
Lecture 4 Feb 9 -Online-	Finding a “Magic Bullet” Part 3: Targeting Her2 in combination with chemotherapy increases survival in patients with overexpressing Her2 (Slamon et al. Use of chemotherapy plus a monoclonal antibody against HER2 for metastatic breast cancer that overexpresses HER2)
Lecture 5 Feb 16 -Online-	Redefining a “Magic Bullet” during the drug development process Part 1 (Rusch Differential expression of the Epidermal Growth Factor Receptor and its ligands in primary Non-Small Cell Lung Cancers and adjacent benign lung)
Lecture 6 Feb 23 -Online-	Redefining a “Magic Bullet” during the drug development process Part 2 (Lynch Activating Mutations in the Epidermal Growth Factor Receptor Underlying Responsiveness of Non–Small-Cell Lung Cancer to Gefitinib)
Lecture 7 March 1 -Online-	Redefining a “Magic Bullet” during the drug development process Part 3 (Chabon et al. Circulating tumour DNA profiling reveals heterogeneity of EGFR inhibitor resistance mechanisms in lung cancer patients)
No Class March 8	Spring Break
Lecture 8 March 15 -Online-	New trial design in the precision oncology era: Basket Trial. (Le et al. Mismatch repair deficiency predicts response of solid tumors to PD-1 blockade or Flaherty et al. Molecular Landscape and Actionable Alterations in a Genomically Guided Cancer Clinical Trial: National Cancer Institute Molecular Analysis for Therapy Choice (NCI-MATCH))
Lecture 9 March 22 -Online-	New trial design in the precision oncology era: Umbrella trial (Clark et al. Neoadjuvant T-DM1/pertuzumab and paclitaxel/trastuzumab/pertuzumab for HER2+ breast cancer in the adaptively randomized I-SPY2 trial)
Lecture 10 March 29 -Online-	Development of resistant to targeted agents through activation of off-target mechanisms (Paraiso et al. Recovery of phospho-ERK activity allows melanoma cells to escape from BRAF inhibitor therapy)
Lecture 11 April 5 -Online-	Beyond genomic in precision medicine Part 1. Gene signatures for outcome prediction in breast cancer (background reading van 't Veer et al. Gene expression profiling predicts clinical outcome of breast cancer; Cardoso et al. 70-Gene Signature as an Aid to Treatment Decisions in Early-Stage Breast Cancer)
Lecture 12 April 12	Beyond genomic in precision medicine Part 2; the Bisgrove trial (Von Hoff et al. Pilot Study Using Molecular Profiling of Patients’ Tumors to Find Potential Targets and Select Treatments for Their Refractory Cancers)
Lecture 13 April 19	Cellular targeted therapy in cancer to enhance immunosurveillance and tumor-immune interactions (Anderson et al. Long-Lasting Complete Responses in Patients with Metastatic Melanoma after Adoptive Cell Therapy with Tumor-Infiltrating Lymphocytes and an Attenuated IL2 Regimen)
Lecture 14 April 26	New personalized vaccines in cancer (Sahin et al. Personalized RNA mutanome vaccines mobilize poly-specific therapeutic immunity against cancer; or Ott et al. An immunogenic personal neoantigen vaccine for patients with melanoma)
Lecture 15 May 3	Final paper due