



Nanocourse | Applying the Concepts from Translational Discoveries

Course Director | Nilay Sethi, MD, PhD

Curriculum Fellow | Jelena Patnogić, PhD

Course Objectives

- Recognize the translational impact of thoughtful and rigorous basic science research
- Describe examples of successful translational research and conceptual advances that led to biomedical breakthroughs
- Analyze problem-solving in translational research
- Connect translational research with your own project

Course Description

Translational research has many definitions. Broadly, it is considered any investigation that can lead to clinical impact. In this course, we will use bench to bedside vignettes as a backdrop for interactive discussions. We will emphasize cancer dependency, targeted therapy, and resistance mechanisms to help facilitate problem-solving discussions. In particular, we will walk through the discovery of BCR-ABL inhibitors for chronic myelogenous leukemia and next generation anti-androgens for prostate cancer. The course will include group discussions and assignments designed to reinforce the key concepts from each session.

Session dates, times & location

In order to receive credit, registered students must attend all sessions and complete the assignments. The course will take place in person.*

Session One Monday March 21, 2:30-4pm, TMEC 106

Session Two Tuesday March 22, 2:30-4pm, TMEC 306

Session Three Monday March 28, 2:30-4pm, TMEC 106

Session Four Tuesday March 29, 2:30-4pm, TMEC 306

Detailed information about sessions can be found below.

***Physical Distancing**

The HMS policy for in-person courses is that vaccinated individuals need not maintain any physical distancing, but that masks are required for indoor activities. Students who are not comfortable with this arrangement are asked to approach the course director or a member of the instructional staff before the first meeting to discuss alternate arrangements. Reasons not to be comfortable may include not being vaccinated, having a medical issue that makes one more vulnerable, or being in close contact with an immunocompromised individual.



Session One | How Gleevac earned the title “magic bullet”

Objectives

- Understand key concepts in cancer biology (e.g., oncogene addiction and cancer dependency)
- Understand how critical discoveries led to translational impact
- Applying concepts to design targeted therapy

We will begin Session one by briefly learning about each student’s research and any translational component (~15-30 mins depending on the number of students); I will share my translational research goals to start. We will then introduce chronic myelogenous leukemia (CML) and the seminal discoveries that elucidated the importance of BCR-ABL (20 mins). We will then open a discussion on how one would develop a targeted therapy to treat CML (20 mins); this will be an interactive discussion about translational research. We will wrap up the first session with the studies that led to the first BCR-ABL inhibitor Gleevac (20 mins).

Session 2 | Second generation BCR/ABL Inhibitors

Objectives

- Understand how resistance mechanisms to targeted therapy emerge
- Understand the methodical approach to defining resistance mechanisms
- Recognize strategies to overcome resistance mechanisms

Session two will begin with a group discussion on potential resistance mechanisms to Gleevac based on the pre-session assignment submissions (30 mins). We will then describe the translational studies that led to elucidation of Gleevac resistance mechanisms (20 mins). We will then have a group discussion on how we would overcome these resistance mechanisms (20 mins). We will then close by reviewing the translational studies that led to second generation BCR-ABL inhibitors (20 mins).



Session 3 | Prostate cancer: new cancer, old paradigm

Objectives

- Apply the understanding of cancer dependency to prostate cancer
- Understand translational research in prostate cancer
- Apply a translational research concepts to a different cancer

Session three will pivot towards prostate cancer. We will follow the same narrative of translational research in CML except apply it to prostate cancer. First, we will discuss the biology of prostate cancer and define its dependency in discussion format (15 mins). Second, we will review first generation targeted therapy and define the emergency of resistance (15 mins). Third, we will then breakout into discussion about possible approaches to pinpoint the mechanism of resistance (30 mins). We will close by discussing the translational research underlying next generation targeted therapy to overcome resistance in prostate cancer (30 mins)

Session 4 | Lineage plasticity: new mechanism of resistance and start of a new cancer

Objectives

- Understand the concept of lineage plasticity
- Understand newer resistance mechanisms to targeted therapy
- Apply all the principles of translational research to colorectal cancer

Session four will start with a group discussion on resistance mechanisms to targeted therapy in prostate cancer (15 mins). We will then discuss the translational research that defined this resistance mechanisms (15 mins). We will then engage in active discussion about cancer dependency in colorectal cancer (1 hour).