Request for Review of New Course

Course Number: MCB 88

Instructor: Nilabh Shastri, Prof. MCB

Course Title: Immunotherapy of Cancer: Success and failures

Description: Recent years have seen remarkable success in immunotherapy of cancer. We analyze data that reveals how cancer develops and how it can be eliminated by the immune system.

Division: MCB/Immunology and Pathogenesis

Effective Start Term: Spring 2017

Units: 2

Grade: Letter grade or P/NP with instructor's permission

Final exam or other assessment: Final project (group project involving quantitative analysis of data on clinical trials of cancer immunotherapy). Students can choose to conduct original analysis or explain and evaluate previously published work.

Instructional Format: Laboratory, Discussion, Lecture. 2 hours integrated lab/lecture (1 hr LEC, 1 hr LAB)

Estimated number of hours students will be expected to spend doing work outside of class: 4 per week

TIE Code: LECS

Prerequisites and Restrictions (if any): Co-requisite or Prerequisite: Foundations of Data Science (COMPSCI C8 / DATASCI C8 / INFO C8 / STAT C8)

Repeat Rules: Not repeatable

Justification remarks in final section: This course is a connector course for the Foundations of Data science class.

Course Description: (500 space limit; this is what will appear in the Catalog)

In this course, we will work with a variety of datasets that describe a molecular view of cells and how they divide. We will learn about the processes that cause cells to become specialized (differentiate) and to give rise to cancer (transform). We will analyze data on genetic mutations in cancer that distinguish tumor cells from normal cells. We will learn how mutations are detected by the immune system and the basis of cancer immunotherapy. Finally we will analyze data on clinical trials of cancer immunotherapy to define the correlates of success in curing the disease. The students are expected to gain an understanding of data that reveals the basics of cell physiology and cancer, how immunotherapies of cancer work and their current limitations.

Data Science Connector: how will this course connect to, i.e., build up or enrich, the Foundations of Data Science course:

This connector course will make use of the skills taught in the main course as well as introduce material specific to the application of data science to cell biology, immunology and cancer. For example, students will apply their knowledge of tables and data visualization to explore quantitative characteristics of basic cellular components, such as DNA, RNA transcripts and proteins. They will apply statistical principles to define mutations and outcomes of clinical trials.

Data on biological systems is far more complex than the datasets students use in the foundations course. This connector will show students how to find and use the available data sets on biological systems, as well as the underlying ethical issues of data ownership and use.

Syllabus:

● <u>Outline of the topics to be covered in the course.</u>

Meetings 1 & 2   Cell biology basics

Students enrolled in this course are not expected to have taken any undergraduate biology courses. Therefore, the first two meetings will aim at bringing everyone on the same page. These two meetings will cover following topics:

• What is a cell….. cellular components, macromolecules and metabolites
• The central dogma…… information flow, DNA — RNA — Protein
• Multicellular organisms …. specialized cell functions.

Genetic concepts will be illustrated by a short movie on the evolution of skin color. The assignments will analyze a news item or a popular science article that uses these concepts. The goal is to get students to use credible sources to look up unfamiliar biological concepts as they will do throughout the course.

Meeting 3   Genome analysis

We will analyze some simple data sets from the UC Santa Cruz genome browser that illustrate the genetic composition of cells and the relationship between DNA sequence, RNA transcript and primary sequence of proteins.

Meeting 4   Cell differentiation

In this meeting we will analyze how cells become different and gain specialized functions – a process called "differentiation". We will examine gene expression profiles from Immgen databases of differentiated cells that arise from a common progenitor. We will use the examples from the immune system to also provide background for later discussions of immunotherapy.

Meeting 5   How cells divide

We will discuss the cell cycle and how it is regulated. We will explore the various phases of the cell cycle and their check-points. Because cancer is associated with disruption of the normal control of cell cycle, we will analyze genomic data for variations in the regulators of cell cycle. We will use the p53 and/or Rb as key examples of cell cycle regulators which are often mutated in cancer. These examples also provide an interesting entry for the next meeting on polymorphisms versus mutations.

Meeting 6:   Polymorphisms versus mutations

Both polymorphisms and mutations are naturally occurring variations in DNA sequences. To illustrate these we will take examples of known genes that are highly conserved, versus those that are highly polymorphic versus those that commonly mutated in cancer (e.g. p53). We will analyze protein sequences from public databases to illustrate how sequence substitutions alter the function of proteins that confer selective advantages to our immune systems versus cancer cells.

Meeting 7:   The cancer genome

A typical cancer cell harbors numerous mutations that allow it to grow and to evade the immune system. We will analyze some of these mutations that typically define cancer cells by analysis of datasets from the cancer genome project. The analysis will focus on cancer mutations that are common to most cancers versus those that are peculiar to certain kinds of cancers only.

Meeting 8:   How the immune system detects mutations

Beginning with this meeting, we will discuss how the immune system detects and responds to mutations through antigen presentation and by eliciting killer T cell responses. We will use the algorithms of the "Immune epitope database (IEDB)" to analyze the predicted epitopes in proteins commonly mutated in cancer in different individuals.

Meeting 9:   Immune response and checkpoints of regulation

The immune response involves both cell division and cell differentiation. We will use datasets on gene expression at different stages of the immune response to understand the cellular changes that occur during an immune response and control its specificity, magnitude and duration. Introduce the concept of checkpoints in the immune response developed by gene expression analysis of cellular activation and immunological memory.

Meeting 10: Cancer therapy

We begin our analysis of how cancer therapies work. We focus on the use of check-point inhibitors to regulate the magnitude of the immune response to cancer cells. We will make use of gene expression profiles of immune cells that distinguish their behavior towards recognizing and eliminating cancer cells.

Meeting 11 & 12:   Immunotherapy clinical trials

We begin our analysis of cancer progression in immunotherapy clinical trials. We analyze published data on the genomes, RNA transcripts and mutations from patients undergoing treatment. These data will be used to identify the potential epitopes that could be detected by the immune system. Finally, we analyze the correlates of success in immunotherapy.

Meetings 13 and 14:   Group project presentations

These two meetings are reserved for presentations of group projects or extra discussions.

Some online resources:

- NIH National Human Genome Research Institute glossary of genetic terms: https://www.genome.gov/Glossary/index.cfm
- Open SNP database: opensnp.org
- Cancer genome project: https://genome-cancer.ucsc.edu
- Immunological genome: Immgen.org (http://www.immgen.org)
- Immune Epitope Data Base: IEDB.org (http://www.iedb.org)

Course readings:

• Articles will be assigned from popular press and on-line resources relating to the topics discussed in class. For example on the biology of cells, students will read the information on the topic available on the Howard Hughes Medical Institute's web site (http://www.hhmi.org/biointeractive/biology-cells). Later readings will include discussion of articles on cancer immunotherapy from the

New York Times (http://www.nytimes.com/2016/07/31/health/what-is-immunotherapy-cancer-treatment.html) as well as other sources (The future of immune check-point therapy, *Science* (2015) vol 348, page 56-61; The odds of immunotherapy success, *Science*, vol 350m 6257-6259)

- Requirements and grading. A list of what students will be required to do to pass the class, and the relative weight of each requirement toward the final grade. Usually expressed as percentages (25% 10-page paper, 25% midterm, etc.)

Grading elements:

Weekly exercises and participation   50%
-   Attendance (25%)
-   Lab participation or quiz (25%)
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Mid-semester assessment (project proposal)   10%
Final project (presentation 20%, written report 20%)   40%