I. Course Information

1. Drug Discovery and Development

2. April 11 - June 19

   Distance Learning Course Week: Wednesday through Tuesday

3. Instructor's Name and Contact Information

   John J. Keilty
   Adjunct Instructor, Rabb School of Continuing Studies, Brandeis University
   Email: jkeilty@brandeis.edu
   Phone: 978.590.8131
   Skype: john.keilty
   Office Hours/Availability: Via phone or Skype by appointment.

4. Document Overview

   This syllabus contains all relevant information about the course: its objectives and outcomes, the grading criteria, the texts and other materials of instruction, and of weekly topics, outcomes, assignments, and due dates.

   Consider this your roadmap for the course. Please read through the syllabus carefully and feel free to share any questions that you may have. Please print a copy of this syllabus for reference.

5. Course Description

   There are high expectations for bioinformatics to contribute to drug discovery. This course explores issues faced during drug discovery and development. Topics include the drug discovery process, its major players and its origins; scientific principles behind drug properties and actions; target product profiles; disease and drug target selection, sources of drug-like molecules; assays and screening; medicinal chemistry; pharmacology; toxicology; discovery and application of biomarkers and clinical trials. At the end of the course, students will be able to:

   i  Apply bioinformatics strategies to identify, characterize, assess and prioritize drug targets and compounds.

   ii Determine the core information needs that support drug discovery decision making from lab to clinic to market.

   iii Communicate the organization of the drug discovery and development process and the related informatics needs within the process.
b. Additional Description

Students will learn about applications of bioinformatics and cheminformatics to drug discovery and development. The primary project work by students will be the selection of drug targets, screening strategies, and chemical compounds for cancer treatment. Lectures and readings will cover additional diseases, including inflammation, cardiovascular diseases, as well as various infectious diseases.

6. Relevant Programs: This is an elective for the Bioinformatics Graduate Program.

7. Prerequisites:

RCHE 101, RBIO 102, and (RBIF 102 or RBIF 101). RBIF 103 is recommended, but not required. Familiarity with relational databases (MySQL), R and Perl scripting will be important to success in this class.

a. Recommended Text

None. Journal articles will be supplied for class participants.

b. Required Software

a. R, Perl

b. Students need to have access to basic bioinformatics software including BLAST and other tools available through the National Center for Biotechnology Information (NCBI - http://www.ncbi.nlm.nih.gov), Clustal or other alignment application, PyMol or other structure visualization software. Genome workbench and/or Integrative Genomics Viewer (IGV) as well as the Broad connection map may also be useful.

c. Recommended Text(s) / Journals

Students will be expected to identify literature relevant to their assignments and projects using PubMed and the Brandeis Library resources. In addition to this work, students are encouraged to seek out relevant articles from the following journals, which often present significant developments in a concise manner applicable to scientists from different disciplines.

- Science (http://www.sciencemag.org)
- Nature (http://www.nature.com)
- Nature Reviews Drug Discovery (http://www.nature.com/nrd)
- BMC Bioinformatics (http://www.biomedcentral.com/bmcbioinformatics/)
- Cell (http://www.cell.com/)
- Cancer Cell (http://www.cell.com/cancer-cell/)
- New England Journal of Medicine (http://www.nejm.org/)

The following websites may also provide important information:

- DrugBank: http://www.drugbank.ca
- Cancer Genome Atlas (http://cancergenome.nih.gov/)
- Catalogue Of Somatic Mutations In Cancer (http://www.sanger.ac.uk/genetics/CGP/cosmic/)
- FDA (http://www.fda.gov/Drugs/default.htm)
- Therapeutic Targets Database (http://bidd.nus.edu.sg/group/TTD/TTD.asp)

Online Course Content
This course will be conducted completely online using Brandeis’ LATTE site, available at http://latte.brandeis.edu. The site contains the course syllabus, assignments, our discussion forums, links/resources to course-related professional organizations and sites, and weekly checklists, objectives, outcomes, topic notes, self-tests, and discussion questions. Access information is emailed to enrolled participants before the start of the course. To begin participating in the course, review the Welcoming Message and the Week 1 Checklist.

8. Overall Course Outcomes

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

- Apply bioinformatics strategies to identify, characterize and prioritize drug targets.
- Understand the evolving role of biomarkers in the drug discovery process.
- Determine the core information needs that support drug discovery decision making.
- Understand the organization of the drug discovery and development process and the related informatics needs within the process.

The course is intended to provide students with hands-on experience in the identification and assessment of potential drug targets and compounds.

10. Course Grading Criteria

a. Description of Components and Percentages

<table>
<thead>
<tr>
<th>Component</th>
<th>Description</th>
<th>% Final Grade</th>
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</thead>
<tbody>
<tr>
<td>Homework</td>
<td>Approximately five assignments focused on practical application of topics and tools covered in class. All assignments must be submitted in pdf format and follow the name convention lastname_hwX.pdf.</td>
<td>40</td>
</tr>
<tr>
<td>Discussions/Online Participation</td>
<td>Each week respond to one discussion question by 11:55pm EST Saturday and post at least two substantive responses to posts by your colleagues by 11:55pm EST Tuesday (see grading criterion for responses below).</td>
<td>40</td>
</tr>
<tr>
<td>Final Project*</td>
<td>You and a partner will create a Target Product Profile for a target of your choice. This must contain all of the key components that we have discussed throughout the course.</td>
<td>20</td>
</tr>
</tbody>
</table>

b. Grading Criteria for Discussions/Online Participation

Discussion responses to instructor posts will be graded on a 50-point scale according to the criterion outlined below:

An exceptional post (50 points):
Provides original, substantive, and thought provoking analysis of the course material.
Is coherent and has a central thesis.
Contains properly cited references.
Is grammatically correct and contains no spelling errors.

**A good post (40-49 points):**
Contains most elements of an exceptional post, but may lack coherency and/or have a couple minor spelling/grammatical errors.

**A fair post (30-39 points):**
Provides only a surface-level analysis of the course material. 
Contains properly cited references. 
Contains a few grammatical and/or spelling errors 

**A poor post (20-29 points):**
Provides only a surface-level analysis of the course material. 
Does not properly cite references. 
Contains several grammatical and/or spelling errors.

Similarly, substantive responses to peer posts will be graded on a 50-point scale. In addition to the grading metric outlined above, to earn full credit the responses must (1) address the author of the post directly and highlight texts/ideas from the original post and 2) provide constructive insight (i.e. not simply “I agree/disagree with you”).

**c. Homework**
Each will contribute equally to the final grade
Late homework will lose 20 percent for each day it is late. Most of the homework will be directly related to the advancement of a student-directed target assessment, and it will be important to keep up with this process.
Up to two extra-credit homework assignments may be offered as an opportunity to make up for low scores.

**d. Final Project**
As a final project, students will propose (as a Word document) a specific target for drug development, along with a strategy for selecting compounds and ushering them through the drug discovery pipeline.

11. **Weekly Information**

<table>
<thead>
<tr>
<th>Week 1</th>
<th>4/11 - 4/17</th>
<th>A War of Attrition: Introduction to the Drug Discovery and Development Process</th>
</tr>
</thead>
</table>
| **Objectives** | | - Overview of course expectations, requirements and resources.  
  - Review of bioinformatics basics  
  - Introduction to the overall drug discovery and development process 
  - Review expectations for the class for the upcoming semester 
  - Introduction to the concept of a Target Product Profile |
| **Outcomes** | | - Ability to distinguish benefits of potential drug discovery from other strategies to improve health. 
  - Understanding of informatics “touch points” in the drug discovery process 
  - Ability to understand a basic Target Product Profile. |
| Week 2  | Disease elucidation in the Genomics Era |
| 4/18 - 4/24 | |
| Objectives | • Review of basic molecular, cell and developmental biology concepts  
• Discussion of ‘omics and mechanisms of disease  
• Overview of key cancer pathways and disease relevance |
| Outcomes | • Understand relevant resources for oncology research, including software, databases and algorithms.  
• Understanding common cancer drug therapies, including recent targeted drugs.  
• Consider how tools and approaches developed in cancer genomics can be applied to other diseases |
| Readings | • Listed in Latte |
| Assignments / Assessments / Self-Assessments | • Response to one discussion topic, two substantive responses  
• Submit Homework 1 |

| Week 3  | Target Identification and Validation |
| 4/25 - 5/1 | |
| Objectives | • Understand various approaches to target identification and validation  
• Review approaches to recognizing structure elements of proteins, classify proteins, predict binding sites, and build homology models.  
• Introduction to commonly-used target databases.  
• Understand the use of ‘omics technologies for target ID and validation  
• Discuss strategies for target validation |
| Outcomes | • Understand how to apply informatics principles to evaluate viable drug targets  
• Ability to relate disease and drug target information from literature to genome data, in particular for exploration of drug targets and mechanisms of drug action  
• Ability to identify and summarize target validation evidence for a given target |
| Readings | • Listed in Latte |
| Assignments / Assessments / Self-Assessments | • Response to one discussion topic, two substantive responses |
| Assessments/ Self-Assessments | Begin Homework 2 (Draft target portion of a Target Product Profile which must contain criteria to be used for defining a “good” drug target)  
| Response to one discussion topic, two substantive responses |
|---|---|
| **Week 4**  
5/2 – 5/8 | **Finding the “Right” Molecules and Therapeutic Modality** |
| **Objectives** | Understand the various approaches to finding appropriate therapeutics for a known target, including HTS and rational drug design.  
Reinforce concepts of target product profile, drug target, and drug properties from the first two lectures  
Discuss other therapeutics modalities, including biologics and gene therapy |
| **Outcomes** | Understand how to apply informatics principles to evaluate viable drug molecules  
Understand the hit-to-lead process.  
Ability to create and evaluate a SAR table. |
| **Readings** | Listed in Latte |
| **Assignments / Assessments/ Self-Assessments** | Submit Homework 2  
Begin homework assignment 3 (Draft of the drug selection strategy portion of their TPP)  
Response to one discussion topic, two substantive responses |
| **Week 5**  
5/9 – 5/15 | **From Lead to Clinical Testing - Pharmacology, Toxicology, Pharm Dev and DMPK** |
| **Objectives** | Understand the use and limitations of animal models  
Introduce approaches to modeling human toxicity  
Understand Pharmaceutical Development and DMPK in the DD&D process  
Toxicogenomics growing role in understanding human toxicology |
| **Outcomes** | Ability to apply informatics principles to the Toxicology  
Ability to evaluate and interpret toxicology output  
Understanding of in vitro, in silico and in vivo approaches to toxicology assessment  
Ability to evaluate and interpret DMPK output, including cMax, AUC and volume of distribution |
| **Readings** | Listed in Latte |
| **Assignments / Assessments/ Self-Assessments** | Begin Homework 4 (Draft of the biomarker strategy portion of their TPP)  
Response to one discussion topic, two substantive responses |
<table>
<thead>
<tr>
<th>Week 6</th>
<th>Personalizing therapy: Biomarker Development</th>
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<tbody>
<tr>
<td>5/16 - 5/22</td>
<td><strong>Objectives</strong></td>
</tr>
</tbody>
</table>
| | • Understanding of the role of biomarker development in drug discovery, including genomic, proteomic, metabolomic and other approaches.  
• Discuss approaches to analyze, interpret and integrate biomarker data |
| | **Outcomes** |
| | • Ability to develop a robust biomarker strategy, including approaches for companion diagnostics  
• Ability to analyze and interpret biomarker data, including genomic and proteomic data. |
| | **Readings** |
| | • Listed in Latte |
| | **Assignments / Assessments / Self-Assessments** |
| | • Response to one discussion topic, two substantive responses  
• Submit homework 3 |

<table>
<thead>
<tr>
<th>Week 7</th>
<th>Regulatory obligations in clinical trails</th>
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<tbody>
<tr>
<td>5/23 - 5/29</td>
<td><strong>Objectives</strong></td>
</tr>
</tbody>
</table>
| | • Understanding how the evolution of the regulatory agencies and their role in the development process.  
• Discuss the incorporation of regulatory strategy into drug development planning.  
• Understand the IND, PMA and NDA process in clinical and biomarker development.  
• Interpret relevant FDA guidances on drug development |
| | **Outcomes** |
| | **Readings** |
| | • Listed in Latte |
| | **Assignments / Assessments / Self-Assessments** |
| | • Response to one discussion topic, two substantive responses  
• Begin Homework 4  
• Work on Final Project |

<table>
<thead>
<tr>
<th>Week 8</th>
<th>Clinical Trial Design and Execution</th>
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<tbody>
<tr>
<td>5/30 - 6/5</td>
<td><strong>Objectives</strong></td>
</tr>
</tbody>
</table>
| | • Gain strong understanding of the design and execution of clinical trials, including:  
• Integration of biomarker data  
• Adaptive trial design  
• Bayesian versus frequentist approaches  
• Operational and execution challenges  
• Fundamental understanding of alternatives for clinical data capture, storage and analyses. |
### Outcomes
- Ability to formulate and interpret objective, effective clinical trial
- Working knowledge of basic clinical trial analysis approaches, including Kaplan-Meier curves and Hazard Ratios.

### Readings
- Listed in Latte

### Assignments / Assessments / Self-Assessments
- Response to one discussion topic, two substantive responses
- Submit homework 4
- Work on final project

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### Week 9
**6/6 - 6/12**

**Getting the “Plumbing” right: Data Management in Drug Discovery**

### Objectives
- Understanding common mechanisms for organizing data generated in the discovery process.
- Discuss the common mechanisms and approaches to managing data workflows.

### Outcomes
- Ability to utilize common strategies and standards in the storage, vetting, analysis and reporting of discovery and clinical data.

### Readings
- Listed in Latte

### Assignments / Assessments / Self-Assessments
- Response to one discussion topic, two substantive responses
- Submit Homework 5

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### Week 10
**6/13 - 6/19**

**Commercial**

### Objectives
- Understand the role of commercial in the drug discovery process including:
  - Determining Patient populations
  - Evaluating competition
  - Assessing viability of the drug in the open market

### Outcomes
- Ability to evaluate the impact of commercial considerations on drug success
- Understanding the value of early commercial estimates in drug development

### Assignments / Assessments / Self-Assessments
- Listed in Latte

### Assignments / Assessments / Self-Assessments
- Submit Final Project
III. Course Policies and Procedures

1. Late Policies

- Discussion responses will be accepted up to 3 days late with a 5-point deduction per day.
- Homework assignments will be accepted up to one week late with a 20 percent deduction per day.
- Substantive responses to discussion posts and the final project will NOT be accepted late.

2. Grading Standards

A. Work expectations

Students are responsible to explore each week's materials and submit required work by their due dates. On average, a student can expect to spend approximately 3-5 hours per week reading and approximately 4-8 hours per week completing assignments and posting to discussions (3-5 hours for the former and 1-2 hours for the latter). Exams are designed to take 3-5 hours to complete, and the final project is estimated to take 10-15 hours. The calendar of assignments and due dates is located at the end of this syllabus, and all assignments are due by the close of the associated week (Tuesday evenings, 11:55 EST).

B. Grading Scale

<table>
<thead>
<tr>
<th>Score Range</th>
<th>Grade</th>
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<tbody>
<tr>
<td>100–94</td>
<td>A</td>
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<tr>
<td>93–90</td>
<td>A-</td>
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<tr>
<td>89–87</td>
<td>B+</td>
</tr>
<tr>
<td>86–83</td>
<td>B</td>
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<tr>
<td>82–80</td>
<td>B-</td>
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<tr>
<td>79–77</td>
<td>C+</td>
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<tr>
<td>76–73</td>
<td>C</td>
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<tr>
<td>72–70</td>
<td>C-</td>
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<tr>
<td>69–67</td>
<td>D+</td>
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<tr>
<td>66–63</td>
<td>D</td>
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<tr>
<td>62–60</td>
<td>D-</td>
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<td>&lt; 60</td>
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3. Feedback

I will provide weekly feedback on your participation. Your homework and exams will be graded within 1 week of receipt and grades will be posted on Latte.

4. Confidentiality

We can draw on the wealth of examples from our organizations in class discussions and in our written work. However, it is imperative that we not share information that is confidential, privileged, or proprietary in nature. We must be mindful of any contracts we have agreed to with our companies. In addition, we should respect our fellow classmates and work under the assumption that what is discussed here (as it pertains to the workings of particular organizations) stays within the confines of the classroom.

Members of the University’s technical staff have access to all course sites to aid in course setup and technical troubleshooting. Program Chairs and a small number of Graduate Professional Studies (GPS) staff have access to all GPS courses for oversight purposes. Students enrolled in GPS courses can expect that individuals other than their fellow classmates and the course instructor(s) may visit their course for various purposes. Their intentions are to aid in technical troubleshooting and to ensure that quality course delivery standards are met. Strict confidentiality of student information is maintained.

5. DL Class Calendar: Online class weeks begin on Wednesday and end at midnight on the following Tuesday. Assignments are due by 11:55pm EST on the last day of the course week unless otherwise indicated.

<table>
<thead>
<tr>
<th>Week</th>
<th>Online Week Start/End Dates</th>
<th>Assignment(s) due in addition to discussion forums (see Course Grading Criteria for discussion deadlines).</th>
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<tbody>
<tr>
<td>1</td>
<td>4/11 - 4/17</td>
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<tr>
<td>2</td>
<td>4/18 - 4/24</td>
<td>Homework 1</td>
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<tr>
<td>3</td>
<td>4/25 - 5/1</td>
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<tr>
<td>4</td>
<td>5/2 - 5/8</td>
<td>Homework 2</td>
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<tr>
<td>5</td>
<td>5/9 - 5/15</td>
<td>Homework 3</td>
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<td>6</td>
<td>5/16 - 5/22</td>
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<tr>
<td>7</td>
<td>5/23 - 5/29</td>
<td>Homework 4</td>
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<tr>
<td>8</td>
<td>5/30 - 6/5</td>
<td>Homework 5</td>
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<td>9</td>
<td>6/6 - 6/12</td>
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<tr>
<td>10</td>
<td>6/13 - 6/19</td>
<td>Final Project</td>
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IV. University and Division of Graduate Professional Studies Standards

{These are policies and procedures set at the University and Division level. An instructor may not remove these sections. All instructors must make these policies unquestionably clear to students by posting related announcements to the online classroom.}

Please review the policies and procedures of Graduate Professional Studies, found at http://www.brandeis.edu/gps/current-students/academic-information/student-handbook.html. We would like to highlight the following.

Learning Disabilities

If you are a student with a documented disability on record at Brandeis University and wish to have a reasonable accommodation made for you in this course, please contact the Rabb School Disability Coordinator immediately.

Academic Honesty and Student Integrity

Academic honesty and student integrity are of fundamental importance at Brandeis University and we want students to understand this clearly at the start of the term. As stated in the Brandeis Rights and Responsibilities handbook, “Every member of the University Community is expected to maintain the highest standards of academic honesty. A student shall not receive credit for work that is not the product of the student’s own effort. A student’s name on any written exercise constitutes a statement that the work is the result of the student’s own thought and study, stated in the student’s own words, and produced without the assistance of others, except in quotes, footnotes or references with appropriate acknowledgement of the source.” In particular, students must be aware that material (including ideas, phrases, sentences, etc.) taken from the Internet and other sources MUST be appropriately cited if quoted, and footnoted in any written work turned in for this, or any, Brandeis class. Also, students will not be allowed to collaborate on work except by the specific permission of the instructor. Failure to cite resources properly may result in a referral being made to the Office of Student Development and Judicial Education. The outcome of this action may involve academic and disciplinary sanctions, which could include (but are not limited to) such penalties as receiving no credit for the assignment in question, receiving no credit for the related course, or suspension or dismissal from the University.

Further information regarding academic integrity may be found in the following publications: "In Pursuit of Excellence - A Guide to Academic Integrity for the Brandeis Community", "(Students') Rights and Responsibilities Handbook", AND " Graduate Professional Studies Student Handbook". You should read these publications, which all can be accessed from the Graduate Professional Studies Web site. A student that is in doubt about standards of academic honesty (regarding plagiarism, multiple submissions of written work, unacknowledged or unauthorized collaborative effort, false citation or false data) should consult either the course instructor or other staff of the Rabb School Graduate Professional Studies.

University Caveat

The above schedule, content, and procedures in this course are subject to change in the event of extenuating circumstances.