**BIOS 4500/BIOL 8803: Drug Discovery**

**Course Syllabus**

# Instructor: Prof. Jeffrey Skolnick

EBB, 950 Atlantic Drive, NW, Room 2151

*skolnick@gatech.edu*

***Course summary:*** In this course, you will learn about the entire drug discovery process by identifying a disease and disease target, designing a therapy to treat the disease which you will take from the early stage to preclinical testing and then though the entire FDA drug approval process. Of course, this will all be done in a virtual context as it is impractical to do in reality in the time constraints of this course.

BIOL 4803/8803 is a 3-credit course that meets on Monday, Wednesday and Friday with lectures/discussions from 10:10 -11:00 AM in Cherry Emerson room 320.

**Required text:** Supplied reading list – peer reviewed journal articles. All articles can be found in the Resources section in T-Square.

**Office hours:** By appointment. Please email or consult with the instructor during class to set up a meeting.

***Evaluation:***

**Oral Drug Discovery Topic Presentation 15%**

**Oral Presentation of Selected Drug Target 25%**

**Oral Presentation of Results 20%**

**Research Paper 30%**

**Supplemental Research paper presentation/critique 10%**

**Course Learning Outcomes:** By the end of this course you will be able to:

1. Describe the entire drug discovery process.
2. Articulate how one designs a therapy that can successfully cure a disease
3. Understand the various phases of drug discovery and the success rates associated with each phase.
4. Analyze what makes a good drug and a good causative target of the disease of interest

**Supplemental Research paper presentation/critique:** Graduate students, typically in groups of 2-3, will be assigned by the instructor and responsible for presenting one Supplemental research paper on a selected aspect of drug discovery (blue on the class schedule). Students work together to design a 40-45 min Powerpoint presentation on the paper and relevant background information, which is presented in class on the date assigned. About 5-10 minutes are allowed for questions. All students that are not presenting that day will fill out an oral presentation assessment form (available on Canvas) of the presentation and turn it in at the end of class. The presentation grade for each group will be derived from the average of the assessment grade from your peers (50%) and from the instructor (50%). The grade from your presentation represents 10% of your course grade. Graduate students unable to present due to an excused absence will be allowed to join a later group or have the opportunity to present a later paper alone to make up the missed assignment.

Each undergraduate in class will select one of the Supplemental research papers (blue on class schedule) and independently write a critical review of that paper. The instructor will indicate a date when undergraduates must decide on which paper they will write a critique. Undergraduates who do not choose a paper by that date will be assigned one by the instructor. A digital copy of the critique is to be sent to the instructor via e-mail by the beginning of class on the day of the presentation. The written critical review will be graded by the instructor using the critique rubric (available on Canvas). The critique represents 10% of your course grade. 10 points are deducted for each day the assignment is late.

**Oral Drug Discovery Topic Presentation:** Will consist of 15% of your grade. The presentation will consist of a PowerPoint presentation giving a synopsis of one of the required reading topics. You are expected to prepare a 10 minute presentation with 5-minutes for questions. The presentation will be timed and you will be held to the 10-minute time limit. The order of presentation will be assigned at random.

**Oral Presentation of Selected Drug Target:** Will consist of 25% of your grade. The presentation will consist of a PowerPoint presentation of what disease you are targeting and which molecular target you have selected. You are expected to prepare a 10 minute presentation with 5-minutes for questions. The presentation will be timed and you will be held to the 10-minute time limit. The order of presentation will be assigned at random.

**Oral Presentation of the Results:** Will consist of 30% of your grade. In this presentation, you will present the results from your computational analysis of your target protein, results from your representative small molecule library ligand screening and a justification of the top 5 molecules you have selected to move to animal screening and what time of animal model you have chosen to validate your molecules. You are expected to prepare a 20-minute presentation with 5-minutes for questions. The presentation will be timed and you will be held to the 20-minute time limit. The order of presentation will be assigned at random.

**Research Paper:** Will consist of 30% of your grade. You are expected to write up your results in a 5-page paper using the format of the Journal of Chemical Information and Modeling: http://pubs.acs.org/page/jcisd8/submission/authors.html You should describe the protein target selected, the relationship of this target to the disease you wish to treat, describe your modeling procedure, virtual screening results and results from a literature analysis that justifies which 5 ligands you believe would be most likely to bind experimentally, what animal model you selected, and how you would conduct Phase I-III clinical trials. Your conclusion should describe what you have done, what are the limitations and what you would do next.

## Academic Integrity

Georgia Tech aims to cultivate a community based on trust, academic integrity, and honor. Students are expected to act according to the highest ethical standards. For information on Georgia Tech's Academic Honor Code, please visit http://www.catalog.gatech.edu/policies/honor-code/ or <http://www.catalog.gatech.edu/rules/18/>.

Any student suspected of cheating or plagiarizing on a quiz, exam, or assignment will be reported to the Office of Student Integrity, who will investigate the incident and identify the appropriate penalty for violations.

Each student is expected to work separately on their drug discovery projected as these are unique to each student in the class. Students are encouraged to collaborate about information regarding on-line resources and aspects of the general drug discovery process.

## Accommodations for Students with Disabilities

If you are a student with learning needs that require special accommodation, contact the Office of Disability Services at (404)894-2563 or <http://disabilityservices.gatech.edu/>, as soon as possible, to make an appointment to discuss your special needs and to obtain an accommodations letter. Please also e-mail me as soon as possible in order to set up a time to discuss your learning needs.

**Attendance and participation**

While your attendance in each class is strongly encouraged as essential material may be provided during the lectures of either the professor or the presentations of your classmates, it will not be required nor graded.

## Extensions, Late Assignments, & Re-Scheduled/Missed Exams

Class assignments for oral presentations are made well in advance of the presentation and you are expected to present at the assigned time. If for some reason, you cannot do so, please contact me in advance so that your presentation can be rescheduled. The paper describing your project is due on the last day of class at midnight, with no extensions given.

## Student-Faculty Expectations Agreement

At Georgia Tech we believe that it is important to strive for an atmosphere of mutual respect, acknowledgement, and responsibility between faculty members and the student body. See <http://www.catalog.gatech.edu/rules/22/> for an articulation of some basic expectation that you can have of me and that I have of you. In the end, simple respect for knowledge, hard work, and cordial interactions will help build the environment we seek. Therefore, I encourage you to remain committed to the ideals of Georgia Tech while in this class.

## Collaboration & Group Work

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## Student Use of Mobile Devices in the Classroom

Students are expected to refrain from using mobile devices in the classroom with the exception of using said devices to search for course related information.

**Statement of Intent for Inclusivity**

As a member of the Georgia Tech community, I am committed to creating a learning environment in which all of my students feel safe and included. Because we are individuals with varying needs, I am reliant on your feedback to achieve this goal. To that end, I invite you to enter into dialogue with me about the things I can stop, start, and continue doing to make my classroom an environment in which every student feels valued and can engage actively in our learning community.

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| **BIOL 4803/8803 PROPOSED CLASS SCHEDULE 2019** | | | |
| Week 1 | Monday, January 7, 2019  10:10 – 11:00 AM  LECTURE | Wednesday, January 9, 2019  10:10 – 11:00 AM  LECTURE | Friday, January 11, 2019  10:10 - 11:00 AM  LECTURE |
| Week 2 | Monday, January 14, 2019  10:10 – 11:00 AM  LECTURE | Wednesday, January 16, 2019  10:10 – 11:00 AM  LECTURE | Friday, January 18, 2019  10:10 - 11:00 AM  LECTURE |
| Week 3 | Monday, January 21, 2019  10:10 – 11:00 AM  **MLK DAY – NO CLASS** | Wednesday, January 23, 2019  10:10 – 11:00 AM  **TOPIC PRESENTATIONS**  *Reading Assignments – Section* | Friday, January 25, 2019  10:10 - 11:00 AM  **TOPIC PRESENTATIONS**  *Reading Assignments – Section* |
| Week 4 | Monday, January 28, 2019  10:10 – 11:00 AM  **TOPIC PRESENTATIONS**  *Reading Assignments – Section* | Wednesday, January 30, 2019  10:10 – 11:00 AM  **TOPIC PRESENTATIONS**  *Reading Assignments – Section* | Friday, February 1, 2019  10:10 - 11:00 AM |
| Week 5 | Monday, February 4, 2019  10:10 – 11:00 AM  LECTURE | Wednesday, February 6, 2019  10:10 – 11:00 AM  LECTURE | Friday, February 8, 2019  10:10 - 11:00 AM  LECTURE |
| Week 6 | Monday, February 11, 2019  10:10 – 11:00 AM  **TARGET PRESENTATIONS** | Wednesday, February 13, 2019  10:10 – 11:00 AM  **TARGET PRESENTATIONS** | Friday, February 15, 2019  10:10 - 11:00 AM  **TARGET PRESENTATIONS** |
| Week 7 | Monday, February 18, 2019  10:10 – 11:00 AM  **TARGET PRESENTATIONS** | Wednesday, February 20, 2019  10:10 – 11:00 AM  **TARGET PRESENTATIONS** | Friday, February 22, 2019  10:10 - 11:00 AM  LECTURE |

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| Week 8 | Monday, February 25, 2019  10:10 – 11:00 AM  LECTURE | Wednesday, February 27, 2019  10:10 – 11:00 AM  LECTURE | Friday, March 1, 2019  10:10 - 11:00 AM  LECTURE |
| Week 9 | Monday, March 4, 2019  10:10 – 11:00 AM  LECTURE | Wednesday, March 6, 2019  10:10 – 11:00 AM  LECTURE | Friday, March 8, 2019  10:10 - 11:00 AM  LECTURE |
| Week 10 | Monday, March 11, 2019  10:10 – 11:00 AM  LECTURE | Wednesday, March 13, 2019  10:10 – 11:00 AM  LECTURE | Friday, March 15, 2019  10:10 - 11:00 AM  LECTURE |
|  | Monday, March 18, 2019  **SPRING BREAK - NO CLASS** | Wednesday, March 20, 2019  **SPRING BREAK - NO CLASS** | Friday, March 22, 2019  **SPRING BREAK - NO CLASS** |
| Week 11 | Monday, March 25, 2019  10:10 – 11:00 AM  LECTURE | Wednesday, March 27, 2019  10:10 – 11:00 AM  LECTURE | Friday, March 29, 2019  10:10 – 11:00 AM  LECTURE |
| Week 12 | Monday, April 1, 2019  10:10 – 11:00 AM | Wednesday, April 3, 2019  10:10 – 11:00 AM  **RESULTS PRESENTATIONS** | Friday, April 5, 2019  10:10 - 11:00 AM  **RESULTS PRESENTATIONS** |
| Week 13 | Monday, April 8, 2019  10:10 – 11:00 AM | Wednesday, April 10, 2019  10:10 – 11:00 AM  **RESULTS PRESENTATIONS** | Friday, April 12, 2019  10:10 - 11:00 AM  **RESULTS PRESENTATIONS** |
| Week 14 | Monday, April 15, 2019  10:10 – 11:00 AM  **RESULTS PRESENTATIONS** | Wednesday, April 17, 2019  10:10 – 11:00 AM  **RESULTS PRESENTATIONS** | Friday, April 19, 2019  10:10 - 11:00 AM  **RESULTS PRESENTATIONS** |
| Week 15 | Monday, April 22, 2019  10:10 – 11:00 AM  **RESEARCH PAPER DUE** |  |  |

**BIOS 4500/BIOL 8803: Topics by Week**

**Required Reading:**

**Instructor: Jeff Skolnick**

# 1. Week 1: Overview of the drug discovery process

1. Hughes J, Rees S, Kalindjian S, Philpott K. Principles of early drug discovery. *British Journal of Pharmacology*. 2011;162(6):1239-1249.
2. RM Plenge, EM Scolnick, D. Altschuler. Validating therapeutic targets through human genetics, *Nature Reviews Drug Discovery*. 2013;12:581-594.
3. An overview of the drug discovery process; see <http://blog.aptuit.com/blog/an-overview-of-the-drug-discovery-process>
4. A short overview drug Discovery; see <http://rbharath.github.io/a-short-overview-of-drug->discovery.

# 2. Week 2: Major classes of drug targets/biological role-kinases, proteases, phosphatases, GPCRs, others

1. R Santos, O Ursu, AP Bento, RS Donadi, CG Bologna, A Karlsson, B Al-Lazalini, A Hershey, TI Oprea & JP Overington. A comprehensive map of molecular drug targets. *Nature Reviews Drug Discovery*. 2016;16:19-34.
2. Bull SC, Doig AJ. Properties of Protein Drug Target Classes. Yamanishi Y, ed. *PLoS ONE*. 2015;10(3):e0117955. doi:10.1371/journal.pone.0117955.
3. Gashaw, P. Ellinghaus, A Sommer, K Asadulla, What makes a good drug target? *Drug Discovery Today.* 2012: 175; S24-30.

# 3. Week 5:Computational Approaches to drug discovery

1. Shoichet BK (2004) Virtual screening of chemical libraries. *Nature* 432(7019):862-865; see also <http://dock.compbio.ucsf.edu/DOCK_6/index.htm2>.
2. H. Zhou and J. Skolnick. FINDSITEcomb: A threading/structure-based, proteomic-scale virtual ligand screening approach. Journal of Chemical Information and Modeling 2013: 53(1): 230-240.
3. Roy, A, Srinivasan B, Skolnick J. 2015. PoLi: A Virtual Screening Pipeline Based on Template Pocket and Ligand Similarity. Journal of Chemical Information and Modeling. 55(8):1757-1770.
4. Zhou, H, Gao M, Skolnick J. 2016. ENTPRISE: An Algorithm for Predicting Human Disease-Associated Amino Acid Substitutions from Sequence Entropy and Predicted Protein Structures. PLOS ONE. 11(3):e0150965.

# 4. Week 8:Methods for drug target identification

1. Zhao S & Li S (2010) Network-based relating pharmacological and genomic spaces for drug target identification. *PloS one* 5(7):e11764
2. Chan JN, Nislow C, & Emili A (2010) Recent advances and method development for drug target identification. *Trends Pharmacol Sci* 31(2):82-88.
3. Congreve M, Murray CW, & Blundell TL (2005) Structural biology and drug discovery. *Drug Discov Today* 10(13):895-907.

# 5. Week 9:Types of drugs and their properties –Lipinski rules

1. Lipinski CA (2000) Drug-like properties and the causes of poor solubility and poor permeability. *J Pharmacol Toxicol Methods* 44(1):235-249.

# 6. Week 9:Prediction/Identification of Drug side effects/off-target interactions

1. Evans WE & McLeod HL (2003) Pharmacogenomics--drug disposition, drug targets, and side effects. *N Engl J Med* 348(6):538-549.
2. Campillos M, Kuhn M, Gavin AC, Jensen LJ, & Bork P (2008) Drug target identification using side-effect similarity. *Science* 321(5886):263-266.
3. Zhou, H, Gao M, Skolnick J. 2015. Comprehensive prediction of drug-protein interactions and side effects for the human proteome. Scientific Reports. 5:11090.

# 7. Week 10: Methods of drug lead identification: Natural products versus rational drug discovery versus high throughput screening

1. Carr RA, Congreve M, Murray CW, & Rees DC (2005) Fragment-based lead discovery: leads by design. *Drug Discov Today* 10(14):987-992.
2. Ramstrom O & Lehn JM (2002) Drug discovery by dynamic combinatorial libraries. *Nat Rev Drug Discov* 1(1):26-36
3. Harvey AL, Edrada-Ebel R, & Quinn RJ (2015) The re-emergence of natural products for drug discovery in the genomics era. *Nature reviews. Drug discovery* 14(2):111-129.

# 8. Week 11:Role of genomics, proteomics, metabolomics in drug discovery

1. Arakaki AK, Skolnick J, & McDonald JF (2008) Marker metabolites can be therapeutic targets as well. *Nature* 456(7221):443.
2. Arakaki AK*, et al.* (2008) Identification of metabolites with anticancer properties by computational metabolomics. *Mol Cancer* 7:5

# 9. Week 12: Rise of personalized medicine

1. Collins FS & Varmus H (2015) A new initiative on precision medicine. *The New England journal of medicine* 372(9):793-795.
2. Jameson JL & Longo DL (2015) Precision medicine--personalized, problematic, and promising. *The New England journal of medicine* 372(23):2229-2234.