

Chemistry 315/515-Medicinal Chemistry

Instructions for Student Presentations

The last six class sessions, Nov. 18, 23, 30 and Dec. 2, 7 9, will be devoted to student-led presentations. Here are some guidelines.

- 1) Group organization: select 6 groups (4 groups of 3 and 2 groups of 2 students) and date of presentation in class on October 19. Each group will have one class period to present their articles.
- 2) Number of articles per presentation: undergraduate groups need to select two scientifically related articles. The undergraduate groups of 2 students may select two shorter articles or communications. Graduate student groups need to select three scientifically related articles.
- 3) Article selection tips: the groups may choose any topic related to medicinal chemistry but you should make sure that your presentation includes material on lead compounds, biochemical targets, and a systematic discussion of how drug discovery occurred or failed. You are welcome to discuss topics that we have touched upon in class or in your papers, but make sure that you cover new material. Your article selection must be made in consultation with Dr. Mal and it must be communicated to the entire class at least two weeks before your presentation date, so that everyone can read the article.
- 4) Presentation organization tips: your presentation should include some introductory material prepared from textbook and review article sources and then a presentation of the primary literature articles. In a given partnership, one person might deal with the target and biochemical assays while the other presents drug development.
- 5) Interactive elements to the presentation: design an evaluation form that asks at least one question of substance and seeks feedback about the presentation/discussion itself. You are also encouraged to ask questions to stimulate discussion and you may elect to “quiz” the class at the beginning of your talk.
- 6) Talking time and discussion time: each student should aim to speak for 20 minutes; that will leave ~20 minutes for discussion or questions. Remember to practice your talk to have the correct pace. Start early and consult Dr. Mal when appropriate!
- 7) Evaluation: You will be graded on four categories: Speaking/Presentation, Organization/Clarity, Visuals/Handouts, and Audience Questions/Discussion.
- 8) Relevance to final exam: approximately 25-40% of the final exam will come from material in these articles and presentations.

Group	Data of Presentation	Topic and Literature Articles
Andrew Krasley, Sarah Burke, Maria Winters (grad students)	Nov. 18	<i>HCV Protease inhibitors</i> , articles #1, 2, and 3 (below)
Sung Eun Kim and Natalia Mavrogiannis	Nov. 23	<i>Anti-cancer (kinase) inhibitors</i> articles #4 and 6 (below) and a NY Times article
Eesha Sheikh, Margaux Kearney, and Alison Panosian	Nov. 30	<i>Parkinson's disease therapies</i> articles #1 and 3 (below)
Jon Witt, Michael Ross, and Julia Anderson	Dec. 2	<i>Anti-malarials</i> articles #2 and 3 (below)
Asha Mahajan, Andrew Mumma, and Shwetha Manjunath	Dec. 7	<i>Diabetes (type II) treatment</i> articles #1 and 3 (below)
Ariana Hall and Laura Alexander	Dec. 9	<i>Alzheimer's disease drugs (γ-secretase inhibitors)</i> articles #1 and 3 (below)

Article selection ideas:

Topic	Article Link
antibiotics/bacterial resistance	<ol style="list-style-type: none"> 1. "Bacterial charity work leads to population-wide resistance" Henry H. Lee, Michael N. Molla, Charles R. Cantor & James J. Collins, <i>Nature</i>, 2010, 467, 82-85. 2. "Design, Synthesis, and Crystal Structures of 6-Alkylidene-2'-Substituted Penicillanic Acid Sulfones as Potent Inhibitors of Acinetobacter baumannii OXA-24 Carbapenemase" Robert A. Bonomo,* Antonio Romero,* John D. Buynak* et al. <i>J. Am. Chem. Soc.</i> 2010 ASAP, DOI: 10.1021/ja104092z. 3. "Type IIA topoisomerase inhibition by a new class of antibacterial agents" Benjamin D. Bax, Michael N.

	<p>Gwynnmick et al. <i>Nature</i>, 2010, 466 , 935–940.</p> <p>4. “Synthetic Analogs Tailor Native AI-2 Signaling Across Bacterial Species” William E. Bentley,* Herman O. Sintim* et al. <i>J. Am. Chem. Soc.</i>, 2010, 132 (32), 11141–11150.</p>
anti-malaria drugs	<p>1. “Identification and Characterization of Small Molecule Inhibitors of a Class I Histone Deacetylase from <i>Plasmodium falciparum</i>” Vishal Patel, Jon Clardy* et al. <i>J. Med. Chem.</i>, 2009, 52 (8), 2185–2187.</p> <p>2. “Spiroindolones, a Potent Compound Class for the Treatment of Malaria” Matthias Rottmann,* Case McNamara,* Bryan K. S. Yeung,* Thierry T. Diagana,* et al. <i>Science</i> 2010, 329 (5996), 1175 – 1180.</p> <p>3. ”Identification of an antimalarial synthetic trioxolane drug development candidate” Jonathan L. Vennerstrom et al. <i>Nature</i> 2004, 430, 900-904.</p>
Alzheimer’s drugs	<p>1. “Discovery and Evaluation of BMS-708163, a Potent, Selective and Orally Bioavailable γ-Secretase Inhibitor” Kevin W. Gillman,* John E. Starrett, Jr.,* et al. <i>ACS Med. Chem. Lett.</i> 2010, 1, 120–124.</p> <p>2. (Merck) “The Discovery of Pyridone and Pyridazone Heterocycles as γ-Secretase Modulators” Xianhai Huang*, Robert Aslanian*, Wei Zhou, Xiaohong Zhu, et al. <i>ACS Med. Chem. Lett.</i>, 2010, 1 (4), 184–187.</p> <p>3. (Wyeth) “Discovery of Begacestat, a Notch-1-Sparing γ-Secretase Inhibitor for the Treatment of Alzheimer’s Disease” Scott C. Mayer*, Anthony F. Kreft*, Boyd Harrison, Magid Abou-Gharbia, et al. <i>J. Med. Chem.</i>, 2008, 51 (23), 7348–7351.</p>
anti-cancer (kinase inhibitors)	<p>1. (Cephalon) “Discovery of a Potent Inhibitor of Anaplastic Lymphoma Kinase with in Vivo Antitumor Activity” Gregory R. Ott*, Rabindranath Tripathy*, et al. <i>ACS Med. Chem. Lett.</i>, 2010, Article ASAP DOI: 10.1021/ml100158s.</p> <p>2. (GlaxoSmithKline) “Discovery of GSK2126458, a Highly Potent Inhibitor of PI3K and the Mammalian Target of Rapamycin” Steven D. Knight*, Nicholas D.</p>

	<p>Adams, Joelle L. Burgess, et al. <i>ACS Med. Chem. Lett.</i>, 2010, <i>1</i> (1), 39–43.</p> <p>3. (OSI Pharmaceuticals) “Discovery of an Orally Efficacious Imidazo[5,1-f][1,2,4]triazine Dual Inhibitor of IGF-1R and IR” Meizhong Jin*, Prafulla C. Gokhale, Mark J. Mulvihill* et al. <i>ACS Med. Chem. Lett.</i>, 2010, <i>ASAP</i>.</p> <p>4. (Plexxikon) “Clinical efficacy of a RAF inhibitor needs broad target blockade in BRAF-mutant melanoma” Gideon Bollag, Peter Hirth, James Tsai, Jiazhong Zhang, et al. <i>Nature</i>, 2010, <i>ASAP</i>, doi:10.1038/nature09454.</p> <p>5. (Merck/Schering-Plough/Ligand) “Discovery of Dinaciclib (SCH 727965): A Potent and Selective Inhibitor of Cyclin-Dependent Kinases” Kamil Paruch, Michael P. Dwyer, Carmen Alvarez, Timothy J. Guzi* et al. <i>ACS Med. Chem. Lett.</i>, 2010, <i>1</i> (5), 204–208.</p> <p>6. (Imperial College, London) “A Novel Pyrazolo[1,5-a]pyrimidine Is a Potent Inhibitor of Cyclin-Dependent Protein Kinases 1, 2, and 9, Which Demonstrates Antitumor Effects in Human Tumor Xenografts Following Oral Administration” Simak Ali, et al. <i>J. Med. Chem.</i> 2010 <i>ASAP</i>.</p>
anti-cancer (other targets)	<p>1. “A class of hybrid polar inducers of transformed cell differentiation inhibits histone deacetylases” VICTORIA M. RICHON*†, STEPHANE EMILIANI, RICHARD A. RIFKIND*, PAUL A. MARKS* et al. <i>Proc. Natl. Acad. Sci. USA</i> 1998, <i>95</i>, 3003–3007.</p> <p>2. “Selective inhibition of BET bromodomains” Panagis Filippakopoulos, Christopher A. French, Olaf Wiest, Andrew L. Kung, Stefan Knapp, James E. Bradner, et al. <i>Nature</i> 2010, doi:10.1038/nature09504 Published online 24 September 2010.</p>
anti-viral (HCV protease inhibitors)	<p>1. (Schering-Plough) “Challenges in Modern Drug Discovery: A Case Study of Boceprevir, an HCV Protease Inhibitor for the Treatment of Hepatitis C Virus Infection” F. George Njoroge, Kevin X. Chen, Neng-Yang Shih and John J. Piwinski <i>Acc. Chem. Res.</i>, 2008, <i>41</i> (1), 50–59.</p>

	<p>2. (Boehringer Ingelheim) “Discovery of a Potent and Selective Noncovalent Linear Inhibitor of the Hepatitis C Virus NS3 Protease (BI 201335)” Montse Llins-Brunet*, Murray D. Bailey, et al. <i>J. Med. Chem.</i>, 2010, <i>53</i> (17), 6466–6476.</p> <p>3. (Schering-Plough) “Discovery of Narlaprevir (SCH 900518): A Potent, Second Generation HCV NS3 Serine Protease Inhibitor” Ashok Arasappan*, Frank Bennett*, Stephane L. Bogen, Srikanth Venkatraman, Melissa Blackman, et al. <i>ACS Med. Chem. Lett.</i>, 2010, <i>1</i> (2), 64–69.</p> <p>4. (Vertex) “Discovery and Development of VX-950, a Novel, Covalent, and Reversible Inhibitor of Hepatitis C Virus NS3.4A Serine Protease” Lin, C.1; Kwong, A. D.1; Pemi, R. B. <i>Infectious Disorders - Drug Targets</i>, 2006, <i>6</i> (1), 3-16. (article)</p>
anti-viral (influenza)	<p>1. “Influenza Neuraminidase Inhibitors Possessing a Novel Hydrophobic Interaction in the Enzyme Active Site: Design, Synthesis, and Structural Analysis of Carbocyclic Sialic Acid Analogues with Potent Anti-Influenza Activity” Choung U. Kim,* Willard Lew, and Raymond C. Stevens et al. <i>J. Am. Chem. Soc.</i>, 1997, <i>119</i> (4), 681–690.</p> <p>2. “Rational design of potent sialidase-based inhibitors of influenza virus replication” Mark von Itzstein*, Wen-Yang Wu*, Gaik B. Kok*, Michael S. Pegg*, Jeffrey C. Dyason*, Betty Jin*, Tho Van Phan*, Mark L. Smythe*, Hume F. White*, Stuart W. Oliver*, et al. <i>Nature</i> 1993, <i>363</i>, 418 – 423.</p>
anti-inflammatory	<p>1. (Merck) “Discovery of a Potent and Orally Bioavailable CCR2 and CCR5 Dual Antagonist” Alexander Pasternak*, Stephen D. Goble, Mary Struthers, et al. <i>ACS Med. Chem. Lett.</i>, 2010, <i>1</i> (1), 14–18.</p>
diabetes (type II) treatment	<p>1. (Metabasis Therapeutics) “A Potent and Selective AMPK Activator That Inhibits de Novo Lipogenesis” Jorge E. Gmez-Galeno*, Qun Dang, Thanh H. Nguyen, Serge H. Boyer, et al. <i>ACS Med. Chem. Lett.</i>, 2010, <i>Article ASAP</i>.</p>

	<p>2. <u>"Anti-diabetic drugs inhibit obesity-linked phosphorylation of PPARγ by Cdk5"</u> Jang Hyun Choi, Alexander S. Banks, Jennifer L. Estall, Bruce M. Spiegelman et al. <i>Nature</i>, 2010, 466, 451–456.</p> <p>3. (Amgen and Japan Tobacco) <u>"T2384, a Novel Antidiabetic Agent with Unique Peroxisome Proliferator-activated Receptor γ Binding Properties"</u> Yang Li et al. <i>J. Biol. Chem.</i> 2008, 283 (14), 9168-9176.</p>
antihypertensive	<p>1. <u>"Structural Modification of the P2' Position of 2,7-Dialkyl-Substituted 5(S)-Amino-4(S)-hydroxy-8-phenyl-octanecarboxamides: The Discovery of Aliskiren, a Potent Nonpeptide Human Renin Inhibitor Active after Once Daily Dosing in Marmosets"</u> Jürgen Maibaum,* Stefan Stutz, Richard Göschke, Pascal Rigollier, et al. <i>J. Med. Chem.</i>, 2007, 50 (20), 4832–4844.</p>
Parkinson's disease therapies	<p>1. <u>"Discovery of 4-(4-(2-((5-Hydroxy-1,2,3,4-tetrahydronaphthalen-2-yl)(propyl)amino)ethyl)piperazin-1-yl)quinolin-8-ol and Its Analogues as Highly Potent Dopamine D2/D3 Agonists and as Iron Chelator: In Vivo Activity Indicates Potential Application in Symptomatic and Neuroprotective Therapy for Parkinson's Disease"</u> Balaram Ghosh, Tamara Antonio, Maarten E. A. Reith and Alope K. Dutta. <i>J. Med. Chem.</i>, 2010, 53 (5), 2114–2125.</p> <p>2. <u>"Dopamine D2, D3, and D4 Selective Phenylpiperazines as Molecular Probes To Explore the Origins of Subtype Specific Receptor Binding"</u> Katharina Ehrlich, Angela Gutz, Stefan Bollinger, Nuska Tschammer, Laura Bettinetti, Steffen Hurterich, Harald Hubner, Harald Lanig and Peter Gmeiner. <i>J. Med. Chem.</i>, 2009, 52 (15), 4923–4935.</p> <p>3. <u>"Design, Synthesis, and Evaluation of Potent and Selective Ligands for the Dopamine 3 (D3) Receptor with a Novel in Vivo Behavioral Profile"</u> Shaomeng Wang et al. <i>J. Med. Chem.</i> 2008, 51 (19), 5905–5908.</p>