Medicinal Chemistry (CHEM 315/515)

Guidelines for Literature Article selection for Paper Assignment

1. The article should be from the primary scientific literature which means there should be new experimental results described. A secondary literature article, which is a review/summary of a selection of primary literature articles, may be used to inform your paper by providing a context, but it should not be the focus of your paper.
2. The *Journal of Medicinal Chemistry or ACS Medicinal Chemistry Letters* is not the only source for articles describing drug development. There are a variety of good journals that describe new drug development. A partial list of other journals that communicate drug development research includes: *Science, Nature, Journal of the American Chemical Society, Biochemistry, Journal of Biological Chemistry, Journal of Molecular Biology,* and *Angewandte Chemie International Edition*.
3. Your literature article may describe any stage of the drug development process, but should not be too clinical, nor too synthetic, in nature, i.e. some chemistry and biochemistry should be described, not just results of patient studies or simply a total synthesis of a biologically active molecule. A selection of papers is listed below to assist you. You do not need to chose one of these articles, but they are provided as examples and possible selections. References in these articles are another source of literature article.

Guidelines for Writing the Paper Assignment

1. Your paper should be a 3-5 page summary of the research described in the literature article.
2. Please refrain from quoting your article. You should use your own words and descriptions as much as possible.
3. Along with a description of the research, you should attempt to be critical in your analysis of the literature article. Does the data presented in the article support the conclusions that are reported? Are the conclusions supported by the data that is presented in figures or tables? Are there other experiments that should have been done? A good paper will address these issues and will support answers to these questions with brief explanations.
4. Graduate students taking the 515 course must select two articles in the same area and compare and contrast the articles and reported research. Again, a review article may be used to assist in understanding the field, but the two articles for the paper must be from the primary literature.
5. You must let me know of your paper selection by Thurs., Oct. 7. Your paper will be due in class on Thurs., Nov. 4. More than one student can review a particular paper but your analysis and writing must be independent.

Selection of Potential articles

Topic	Article Link
antibiotics/bacterial resistance	1. "Bacterial charity work leads to population-wide resistance" Henry H. Lee, Michael N. Molla, Charles R. Cantor & James J. Collins, *Nature*, **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. *J. Am. Chem. Soc.* **2010** *ASAP*, DOI: 10.1021/ja104092z. 3. "Type IIA topoisomerase inhibition by a new class of antibacterial agents" Benjamin D. Bax, Michael N. Gwynnmick et al. *Nature*, **2010**, *466* , 935–940. 4. "Synthetic Analogs Tailor Native AI-2 Signaling Across Bacterial Species" William E. Bentley,* Herman O. Sintim* et al. *J. Am. Chem. Soc.*, **2010**, *132 (32)*, 11141–11150.
anti-malaria drugs	1. "Identification and Characterization of Small Molecule Inhibitors of a Class I Histone Deacetylase from Plasmodium falciparum". Vishal Patel, Jon Clardy* et al. *J. Med. Chem.*, **2009**, *52 (8)*, 2185–2187. 2. "Spiroindolones, a Potent Compound Class for the Treatment of Malaria" Matthias Rottmann,* Case McNamara,* Bryan K. S. Yeung,* Thierry T. Diagana,* et al. *Science* **2010**, *329 (5996)*, 1175 – 1180.
Alzheimer's drugs	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. *ACS Med. Chem. Lett.* **2010**, *1*, 120–124. 2. (Merck) "The Discovery of Pyridone and Pyridazone Heterocycles as γ-Secretase Modulators" Xianhai Huang*, Robert Aslanian*, Wei Zhou, Xiaohong Zhu, et al. *ACS Med. Chem. Lett.*, **2010**, *1 (4)*, 184–187. 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. *J. Med. Chem.*, **2008**, *51 (23)*, 7348–7351.
anti-cancer (kinase inhibitors)	1. (Cephalon) "Discovery of a Potent Inhibitor of Anaplastic Lymphoma Kinase with in Vivo Antitumor Activity" Gregory R. Ott*, Rabindranath Tripathy*, et al. *ACS Med. Chem. Lett.*, **2010**, *Article ASAP* DOI: 10.1021/ml100158s. 2. (GlaxoSmithKline) "Discovery of GSK2126458, a Highly Potent Inhibitor of PI3K and the Mammalian Target of Rapamycin" Steven D. Knight*, Nicholas D. Adams, Joelle L. Burgess, et al. *ACS Med. Chem. Lett.*, **2010**, *1 (1)*, 39–43. 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. *ACS Med. Chem. Lett.*, **2010**, *ASAP*. 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. *Nature*, **2010**, *ASAP*, doi:10.1038/nature09454. 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. *ACS Med. Chem. Lett.*, **2010**, *1 (5)*, 204–208.
anti-cancer (HDAC inhibitors)	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. *Proc. Natl. Acad. Sci. USA* **1998**, *95*, 3003–3007.
anti-viral (HCV protease inhibitors)	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 *Acc. Chem. Res.*, **2008**, *41 (1)*, 50–59.

	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. *J. Med. Chem.*, **2010**, *53 (17)*, 6466–6476. 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. *ACS Med. Chem. Lett.*, **2010**, *1 (2)*, 64–69. 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; Perni, R. B. *Infectious Disorders - Drug Targets*, **2006**, *6 (1)*, 3-16. (see me for copy of article)
anti-viral (influenza)	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. *J. Am. Chem. Soc.*, **1997**, *119* (4), 681–690. 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. *Nature* **1993**, *363*, 418 – 423.
anti-inflammatory	1. (Merck) "Discovery of a Potent and Orally Bioavailable CCR2 and CCR5 Dual Antagonist" Alexander Pasternak*, Stephen D. Goble, Mary Struthers, et al. *ACS Med. Chem. Lett.*, **2010**, *1 (1)*, 14–18.
diabetes (type II) treatment	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. *ACS Med. Chem. Lett.*, **2010**, *Article ASAP*.

	2. "Anti-diabetic drugs inhibit obesity-linked phosphorylation of PPARγ by Cdk5" Jang Hyun Choi, Alexander S. Banks, Jennifer L. Estall, Bruce M. Spiegelmanbruce et al. *Nature*, **2010**, *466* , 451–456.
antihypertensive	1. 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" Jürgen Maibaum,* Stefan Stutz, Richard Göschke, Pascal Rigollier, et al. *J. Med. Chem.*, **2007**, *50 (20)*, 4832–4844.