

CHEM 4803/8853: Bioorganic Chemistry – Spring 2009

MWF 9:00 am – 9:55 am
MSE G021

Course Website available on T-Square: <https://t-square.gatech.edu/portal>

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Week of:	Topic:	Suggested Reading:
Jan 5	Review of amino acids, proteins, enzymes Enzyme catalysis Enzyme inhibition	Bugg; CH 2-5 (p. 2.1-2.10; 3.1-3.8; 4.1-4.4; 5.1-5.3) (<i>This should mostly be a review of Biochemistry; the text and chapters are short; don't let the number of chapters and pages the first two weeks startle you...</i>)
Jan 12	Cofactor and coenzyme chemistry <i>...a blitz through cofactors...</i>	Bugg, CH5-7, 9-10; (5.4-5.8; 6.1-6.4, 6.6-6.10; 7.1-7.2; 9.1-9.6; 10.1-10.4)
Jan 19	<i>January 19 – MLK Day; No Class</i> Introduction to biosynthetic research	Bugg, CH 4 (p. 4.4-4.5; 4.7) Koehn, 2005
Jan 26	Biosynthesis of isoprenoids Biosynthesis of shikimic acid and derivatives	Bugg, CH7 (p. 158-169) CH 8 (p. 180-184) CH 10 (10.5)
Feb 2	Biosynthesis of alkaloids Biosynthesis of fatty acids	Bugg, CH 7 (7.3-7.4) CH 9 (9.7) O'Connor, 2006 Weismann, 2008
Feb 9	<i>Feb 9 and Feb 11 – Topics TBA</i> Feb 13 Biosynthesis of polyketides	Sattely, 2008
Feb 16	Biosynthesis of polyketides and nonribosomal peptides Protein engineering, biosynthetic engineering	Sattely, 2008 Felnagle, 2008 Wilkinson, 2007
Feb 23	Exam I – Monday, February 23 Biosynthetic engineering, metabolic engineering	Chang, 2006 Hawkins, 2008 Ro, 2006
March 2	Principles of medicinal chemistry	Koehn, 2005
March 9	Antibacterial agents	Excerpts from Walsh Book

March 16	<i>Spring Break – No Class</i>	
March 23	Antibacterial agents Antifungal agents	Excerpts from Walsh Book Foye's CH 36
March 30	Anticancer agents	Foye's CH 38
April 6	Anticancer agents and misc. natural products of note TBA/Presentations	
April 13	Presentations	

Final Exam: Thursday, April 30; 2:50 pm - 5:40 pm in MSE G021 (regular room)

Grading:

Midterm Exam (100 pts)

Final Exam (200 pts) will be comprehensive for the course.

Problem Sets (up to 70 pts): There will be up to 7 problem sets to be handed in and graded throughout the semester. Feel free to work with each other on these, but it should be clear that you are turning in your own work. Verbatim answers of items accessible from the internet, reserve material, primary literature are not acceptable.

Class Participation (up to 30 pts): You are expected to fully participate in class discussions, including those associated with presentations.

Project (100 pts): You will prepare an original research proposal based on a topic from a current literature paper in the past year. Topics will be cleared with the instructor no later than March 13. The written proposal (10 pages *maximum*) is due April 8 and presentations will begin that week or the following week.

Required Text:

"An Introduction to Enzyme and Coenzyme Chemistry", 2nd Edition, Tim Bugg
(on reserve at the library under CHEM 8853)

Additional Assigned Readings:

Additional articles may be provided throughout the course, if not currently included in the syllabus. Whenever possible, the PDF will be posted to T-Square. Otherwise, arrangements can be made with Dr. Kelly. Please check T-Square regularly for updates.

Chang, M. C. Y.; Keasling, J. D. Production of isoprenoid pharmaceuticals by engineered microbes, *Nat. Chem. Biol.* **2006**, 2, 674-681.

Felnagle, E. A.; Jackson, E. E.; Chan, Y. A.; Podevels, A. M.; Berti, A. D.; McMahon, M. D.; Thomas, M. G. Nonribosomal peptide synthetases involved in the production of medically relevant natural products, *Mol. Pharmaceut.* **2008**, 5, 191-211.

Hawkins, K. M.; Smolke, C. D. Production of benzyloquinoline alkaloids in *Saccharomyces cerevisiae*, *Nat. Chem. Biol.* **2008**, 4, 564-573.

Koehn, F. E.; Carter, G. T. The evolving role of natural products in drug discovery. *Nat. Rev. Drug. Disc.* **2005**, 4, 206-220.

O'Connor, S. E.; Maresh, J. J. Chemistry and biology of monoterpene indole alkaloid biosynthesis, *Nat. Prod. Rep.* **2006**, 2, 532-547.

Ro, D.-K.; Paradise, E. M.; Ouellet, M.; et al ; Production of the antimalarial drug precursor artemisinic acid in engineered yeast, *Nature*, **2006**, 440, 940-943.

Sattely, E. S.; Fischbach, M. A.; Walsh, C. T.; Total biosynthesis: *in vitro* reconstitution of polyketide and nonribosomal peptide pathways, *Nat. Prod. Rep.* **2008**, 25, 757-793.

Weissman, K. J. Taking a closer look at fatty acid biosynthesis, *ChemBioChem*, **2008**, 9, 2929-2931.

Wilkinson B.; Micklefield, J. Mining and engineering natural-product biosynthetic pathways, *Nat. Chem. Biol.* **2007**, 3, 379-386.

Other Useful Sources of Information:

Any Organic Chemistry Text is highly recommended

Any Biochemistry Text is highly recommended (e.g. Voet and Voet or Lehninger)

"The Organic Chemistry of Enzyme-Catalyzed Reactions", Revised edition, Richard B. Silverman, Academic Press, 2002

"Medicinal Natural Products: A Biosynthetic Approach", Second Edition, Paul M. Dewick

"The Organic Chemistry of Biological Pathways", John, McMurray and Tadgh Begley

"Foye's Principles of Medicinal Chemistry", 5th Edition, David A Williams and Thomas L. Lemke

"Antibiotics: actions, origins, and resistance", Christopher Walsh

Missed Exams: There is no scheduled makeup exam. Planned absences for exam dates for an Institute Approved Activity must be cleared with Prof. Kelly **no later** than three weeks prior to the date of the exam. (see <http://www.deanofstudents.gatech.edu/#> for information on Institute Approved Activities).

Background: You should have an understanding of the functional groups, their properties, and fundamental reaction mechanisms common in organic chemistry and be able to draw a reaction mechanism using curved arrows to show electron flow. You should be able to draw the structure of each proteinogenic amino acid.

Re-grade Requests: Requests must be in writing and directly handed to Dr. Kelly no later than the Friday of the week in which exams are returned (by 5 pm). ***In all cases, the entire exam is subject to a reassessment, not just the item in question.***

Please refer to Georgia Tech's Academic honor code: www.honor.gatech.edu, which you are required to uphold. Academic dishonesty will **NOT** be tolerated.