Fall 2005

BIOL/CHEM 6756 & BIOL 4746
DISCOVERY OF SIGNALING MOLECULES

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Course summary: The diversity of chemical signals between organisms and their structural specificities will be presented along with chemical and biological approaches for identifying signaling molecules.

This class meets on Tuesdays from 3:05 to 5:55 pm in EST L1175. There is no textbook for this course. Readings will be made available on WEBCT (webct.gatech.edu), and students are encouraged to use library databases and the scientific literature to pursue topics in more detail. Since there is no textbook and many of the sessions involve class discussion rather than formal lecture, attendance and class participation are required.

Evaluation:

Mid-term test	**20%**
Literature assignment	**20%**
Final test	**20%**
Student presentation	**20%**
Class participation	**20%**

The **mid-term test** will be based on material covered in lectures, class discussions, and readings up to the date of that exam. The **final test** will be based on material covered throughout the course.

The **literature assignment** will be a short paper written by each student (maximum 2 pages single spaced, 12 point font), reporting on a recent article from the scientific literature (not a review) that each student chooses by conducting their own literature search. The chosen article should be one that the student found particularly interesting and important, and can focus on any area of chemical signaling in living systems. In their paper, the student should present a brief overview of the field, report the important findings of the chosen article, argue why this article represents an important contribution, and critically evaluate its strengths and weaknesses.

The **student presentations** will be performed in groups of 2-3 students, with each group having 40 minutes to present and answer questions. Topics can be chosen by each group in consultation with the instructor, and should be related to recent developments and applications of chemical signaling. Examples from past years include: Natural Product-based Chemical Weapons; Signaling Molecules in Wound Healing; Chemical Sensors and Biosensors; The Use of Insect Pheromones to Protect Crops; Settlement Cues for Restoring Coral Reefs.

Class participation will be judged by the degree to which each student participates in class discussions (by asking questions, answering questions, offering ideas, opinions, and critiques of readings), during student presentations (by asking questions during others' presentations, by engaging the audience during their own presentation, by connecting their presentation to previous class discussions, by working successfully in a small group), and during lectures (by asking questions and offering ideas and opinions).

Please see www.honor.gatech.edu for Georgia Tech's Academic Honor Code, which you are required to uphold.

Class calendar:

Week	Date	Topic	Reading assignment (read BEFORE class)
1	Aug 23	Course overview and introduction: Molecules as information in nature (lecture)	
		General classes of natural products and their biological origins (lecture)	
2	Aug 30	Human sex pheromones: are there or aren't there? (discussion) - critical evaluation of experimental design	Read both: Wedekind et al 1995 Stern & McClintock 1998
		Sex pheromones & and receptor-ligand sensory systems in vertebrates (lecture & discussion) - what molecules are involved - where do these molecules come from - how do these molecules create a signal - how does this signal affect behavior and physiology	Read 1 of: Novotny et al 1999 Leinders-Zufall et al 2000 Leypold et al 2002 If you need background information: Buck et al 2000, Firestein 2001
3	Sept 6	Continued discussion on papers from week 2	
		Why capsaicin tastes hot and menthol is cool: molecular basis for taste, smell, and thermosensation (lecture & discussion)	Read both: McKemy et al 2002, Jordt & Julius 2002 Background: Lindemann 2001
4	Sept 13	Continued discussion on papers from week 3	
		Interactions of natural toxins with receptors: Ecological and evolutionary consequences (discussion)	Bricelj et al (2005)
5	Sept 20	Bacterial chemotaxis: How, why, and contrast with eukaryotic signal transduction (discussion)	Mao et al 2003 Background: Bourret & Stock 2002
		Chemically-mediated microbial-microbial interactions (discussion)	Read both: Kerr et al 2002, Queller et al 2003
6	Sept 27	How can we test for the involvement of specific signaling compounds: Bioassay-guided fractionation and chemical separations (lecture)	
		Chemical cues in host-pathogen interactions: Natural antibiotics – their structures and functions, with critique of separation methods (discussion)	Read both: Schittek et al 2001, Kubanek et al 2003
7	Oct 4	***Mid-term test***	
		The origin of signaling molecules: polyketide biosynthesis in plants, microbes, and animals (lecture)	Chapter by Herbert

8	Oct 11	***(literature paper due)*** Molecular approaches to polyketide biosynthesis, polyketide-peptide biosynthesis, and an example from host-symbiont interactions (discussion)	Read both: McDaniel et al 1999 Piel 2002 Background: Cane et al 1998
		The origin of signaling molecules: isoprenoid biosynthesis in plants, microbes, and animals (lecture)	Chapter by Torssell
9	Oct 25	Molecular approaches to isoprenoid biosynthesis and an example from plant-herbivore interactions (discussion)	Faldt et al 2003
		The origin of signaling molecules: shikimate biosynthesis in plants and microbes (lecture)	Chapter by Herbert
10	Nov 1	The biological activity of tannins (shikimate products): A critical evaluation (discussion)	Graduate students to bring abstracts and critiques of papers related to tannins for discussion
		So you have a signaling compound – how do you determine its structure? Overview of approaches (lecture)	
11	Nov 8	Synthesizing multiple types of spectral data to identify complex natural products – examples from microbial quorum sensing (discussion)	Read all 3: Boettcher & Ruby 1995, Chen et al 2002, Chen et al 2004 Background: Miller & Bassler 2001
12	Nov 15	The use of mass spectral data (including LC-MS) in chemical signaling research (lecture)	
		Student presentations	
13	Nov 22	Student presentations	
		Student presentations	
14	Nov 29	***Final test***	
		Student presentations	
15	Dec 6	Student presentations	
		Student presentations	

Reading list – articles available on WEBCT

Boettcher KJ, Ruby EG (1995) Detection and quantification of *Vibrio fischeri* autoinducer from symbiotic squid light organs. J Bacteriol 177:1053-1058

Bourret RB, Stock AM (2002) Molecular information processing: lessons from bacterial chemotaxis. J Biol Chem 277:9625-9628

Bricelj VM, Connel L, Konoki K, MacQuarrie SP, Scheuer T, Catterall WA, Trainer VL (2005) Sodium channel mutation leading to saxitoxin resistance in clams increases risk of PSP. Nature 434:763-767

Buck LB (2000) The molecular architecture of odor and pheromone sensing in mammals. Cell 100:611-618

Cane DE, Walsh CT, Khosla C (1998) Harnessing the biosynthetic code: combinations, permutations, and mutations. Science 282:63-68

Chen H, Fujita M, Feng Q, Clardy J, Fink GR (2004) Tyrosol is a quorum-sensing molecule in *Candida albicans*. PNAS 101:5048-5052

Chen X, Schauder S, Potier N, Dorsselaer AV, Pelczer I, Bassler BL, Hughson FM (2002) Structural idenfication of a bacterial quorum-sensing signal containing boron. Nature 415:545-549

Faldt J, Martin D, Miller B, Rawat S, Bohlmann J (2003) Traumatic resin defense in Norway spruce (*Picea abies*): methyl jasmonate-induced terpene synthase gene expression, and cDNA cloning and functional characterization of (+)-3-carene synthase. Plant Molec Biol 51:119-133

Firestein S (2001) How the olfactory system makes sense of scents. Nature 413:211-218

Jordt SE, Julius D (2002) Molecular basis for species-specific sensitivity to "hot" chili peppers. Cell 108:421-430

Kerr B, Riley MA, Feldman MW, Bohannah BJM (2002) Local dispersal promotes biodiversity in a real-life game of rock-paper-scissors. Nature 418:171-174

Kubanek J, Jensen PR, Keifer PA, Sullards MC, Collins DO, Fenical W (2003) Seaweed resistance to microbial attack: a targeted chemical defense against marine fungi. PNAS 100:6916-6921

Leinders-Zufall T, Lane AP, Puche AC, Ma W, Novotny MV, Shipley MT, Zufall F (2000) Ultrasensitive pheromone detection by mammalian vomeronasal neurons. Nature 405:792-796

Leypold BG, Yu RC, Leinders-Zufall T, Kim MM, Zufall F, Axel R (2002) Altered sexual and social behaviors in trp2 mutant mice. PNAS 99:6376-6381

Lindemann (2001) Receptors and transduction in taste. Nature 413:219-225

Mao H, Cremer PS, Manson MD (2003) A sensitive, versatile microfluidic assay for bacterial chemotaxis. PNAS 100:5449-5454

McDaniel R, Thamchaipenet A, Gustafsson C, Fu H, Betlach M, Betlach M, Ashley G (1999) Multiple genetic modifications of the erythromycin polyketide synthase to produce a library of novel "unnatural" natural products. PNAS 96:1846-1851

McKemy DD, Neuhausser WM, Julius D (2002) Identification of a cold receptor reveals a general role for TRP channels in thermosensation. Nature 416:52-58

Miller MB, Bassler BL (2001) Quorum sensing in bacteria. Annu Rev Microbiol 55:165-199

Novotny MV, Jemiolo B, Wiesler D, Ma W, Harvey S, Xu F, Xie TM, Carmack M (1999) A unique urinary constituent, 6-hydroxy-6-methyl-3-heptanone, is a pheromone that accelerates puberty in female mice. Chem Biol 6:377-383

Piel J (2002) A polyketide synthase-peptide synthetase gene cluster from an uncultured bacterial symbiont of *Paederus* beetles. PNAS 99:14002-14007

Queller DC, Ponte E, Bozzaro S, Strassmann JE (2003) Single-gene greenbeard effects in the social amoeba *Dictyostelium discoideum*. Science 299:105-106

Schittek B, Hipfel R, Sauer B, Bauer J, Kalbacher H, Stevanovic S, Schirle M, Schroeder K, Blin N, Meier F, Rassner G, Garbe C (2001) Dermcidin: a novel human antibiotic peptide secreted by sweat glands. Nature Immunol 2:1133-1137

Stern K, McClintock MK (1998) Regulation of ovulation by human pheromones. Nature 392:177-179

Wedekind C, Seebeck T, Bettens F, Paepke AJ (1995) MHC-dependent mate preferences in human. Proc R Soc Lond B 260:245-249