Syllabus SIO 264 – Spring 2016

Biosynthesis of Marine Natural Products
9:00 – 11:00 AM Tues/Thurs, Vaughn Hall 100
(4 Units)

Instructors: Bradley Moore (bsmoore@ucsd.edu) and Bill Gerwick (wgerwick@ucsd.edu)

This course will explore natural product biosynthesis and will focus on metabolic pathways associated with prominent marine products to illustrate major metabolic trends in the marine environment. A diversity of marine natural products will be examined in a multidimensional discussion of structure, biological activity, and biosynthesis at the mechanistic, enzymological and genomic levels. Students will gain deep insights into the major classes of marine secondary metabolites and the biosynthetic processes used in their creation. Significant in class and homework assignments will provide students opportunities to develop their skills in deducing origins of natural products, the process for their assembly, and deduction of structures from genetic sequence information.

| Date | Topic | Lecturer |
|---|---|---|
| Mar 29 | Biosynthesis – general principles / pathways | Moore |
| Mar 31 | Redox reactions common in secondary metabolism | Moore |
| Apr 5 | Polyketide synthase assembly line biochemistry I | Moore |
| Apr 7 | Polyketide synthase assembly line biochemistry II | Moore |
| Apr 12 | Ladder ether dinoflagellate polyketides | Gerwick |
| Apr 14 | PUFA synthase and marine lipids | Gerwick |
| Apr 19 | Oxylipin biosynthesis | Gerwick |
| Apr 21 | Aromatic polyketide biosynthesis | Moore |
| Apr 26 | Nonribosomal peptide synthetase assembly line biochemistry I | Gerwick |
| Apr 28 | Nonribosomal peptide synthetase assembly line biochemistry II | Gerwick |
| May 3 | Hybrid PKS-NRPS biosynthesis | Gerwick |
| May 5 | RiPP peptides | Gerwick |
| May 10 | Terpene biosynthesis | Gerwick |
| May 12 | Terpene cyclases | Gerwick |
| May 17 | Biohalogenation | Moore |
| May 19 | Biosynthetic diversification reactions | Moore |
| May 24 | Cyanobacterial alkaloids | Gerwick |
| May 26 | Sponge alkaloids | Moore |
| May 31 | Genome mining | Moore |
| Jun 2 | Synthetic biology | Moore |

Course Goal

Understand and predict how nature assembles complex (marine) organic molecules from basic primary metabolic building blocks.

Big Picture Ideas

1. **Retrobiosynthesis** – problem-solving technique for transforming the structure of a natural product to a sequence of progressively simpler structures along a pathway which ultimately leads to primary or common metabolic precursors. This "reflective" reasoning parallels EJ Corey's retrosynthetic analysis (ACIE, 455-612, 1991).
2. **Genome mining** – outcome-based method to convert genetic information to chemical prediction. This "constructive" thinking approach applies biosynthetic logic to discovery chemistry.
3. **Bioengineering and synthetic biology** – biosynthetic application to reprogram natural metabolic pathways to designer bio-based molecules. Also "forward" thinking.

Essential questions

- How do marine organisms synthesize NPs?
- How are primary and secondary metabolism similar and different?
- How can genomic data be used to solve chemistry problems?
- How can you engineer / design unnatural NPs or manipulate metabolism?

Learning goals

Students will know how to apply biosynthetic principles / knowledge to MNPs (discovery, structure elucidation, enzymology, genetics, synthesis, etc.)

Teaching goals

Inverted classroom approach will be followed. Five main teaching goals to be achieved:

1. Develop ability to apply principles and generalizations already learned to a new problem and situation.
2. Develop problem-solving skills.
3. Develop ability to synthesize and integrate information and ideas.
4. Develop ability to think holistically to see the whole as well as the parts.
5. Develop ability to think creatively.

Grading

**Homeworks – 10 @ 10pts = 100 points total**

Assigned each Thursday and due following Tuesday in class – for the final June 2 HW assignment, please return to Dr. Moore's mailbox in Scholander Hall by June 7.

**Reading reflection – 5 @ 10pts = 50 points total**

After completing the reading assignments, write brief responses of ~150 words to 2 of the 3 questions:

1. What is the main point of this reading?
2. What information did you find surprising? Why?
3. What did you find confusing? Why?

These are due the following class period. Only 5 reading reflections will be graded during the quarter. Be prepared to discuss daily with class.

**Presentation – 50 points**
Students should select a MNP for which nothing has yet been reported on its biosynthesis and propose a biosynthetic pathway for its construction. Topics should be chosen by April 19 and confirmed with Drs. Moore and Gerwick. We suggest reviewing the annual Marine Natural Products review by Blunt et al in the journal *Natural Product Reports* for newly reported MNP structures. You will prepare and print a 1-page summary for each class member and present a 20-minute lecture (to be followed by 10-minute discussion. Date TBD during the end of the quarter; details to follow.

Text
No required text. Primary literature to be assigned in class and posted in a course Dropbox folder.