

## COURSE OUTLINE: BS3028

Course Title	<b>Natural products in medicinal chemistry</b>		
Course Code	<b>BS3028</b>		
Offered	Study Year 3, Semester 2		
Course Coordinator	Liang Zhao-Xun (Assoc Prof)	ZXLiang@ntu.edu.sg	6592 7736
Pre-requisites	BS1003 Organic Chemistry & BS1005 Biochemistry I & BS1006 Principles of Genetics OR BS1013 Foundations of Chemistry II & BS1005 Biochemistry I & BS1006 Principles of Genetics OR CM2031 Organic and Bioorganic Chemistry		
AU	3		
Contact hours	Lectures: 26, Tutorials: 13		

### Course Aims

The module will expose the students to fundamental concepts and frontiers in modern biochemistry and natural product biosynthesis, with the objective of equipping the students with essential analytical skills for dissecting the structure-function relationship in natural products enzymes and analyzing and annotating biosynthetic pathways. Textbooks and reading materials were chosen accordingly to foster the students' interest in the research areas of drug discovery and natural product biosynthesis.

### Intended Learning Outcomes

Upon successfully completing this course, you should be able to:

1. Apply genomics and recombinant DNA technologies to studying natural product biosynthesis and facilitate discovery of new natural products
2. Manipulate protein or cell-based biological systems to create new chemistry.
3. Analyze and assess primary literature in the field of enzymology and natural product biosynthesis.
4. Recognize, draw and analyze chemical structures of major classes of secondary metabolites.
5. Compare and contrast how biomolecules are synthesized by living cells and by chemists.
6. Propose reasonable biosynthetic mechanism
7. Propose biosynthetic mechanism for major classes of natural products

### Course Content

Major classes of biosynthetic enzymes.

Classification of major classes of secondary metabolites.

Mechanism of action of natural product-based drugs

The role of organic cofactor in enzyme catalysis

Biosynthesis of polyketide

Biosynthetic mechanism of terpenoids

Biosynthetic mechanism of ribosome-derived peptide natural products

Biosynthetic mechanism of non-ribosome-derived peptide natural products

Biosynthetic gene cluster and its regulation

Engineering of biosynthetic pathways

#### Assessment

Component	Course ILOs tested	SBS Graduate Attributes tested	Weighting	Team / Individual	Assessment Rubrics
<b>Continuous Assessment</b>					
<b>Tutorials</b>					
Presentation	1, 3, 4, 5, 6, 7	1. b 2. e, f 3. a, b, c 5. a, c 7. a, c	20	both	See Appendix for rubric
<b>Mid-semester Quiz</b>					
Essay	1, 2, 3, 4, 5, 6, 7	1. b 2. a 3. c, e 5. a, c 7. a, c	20	individual	See Appendix for rubric
<b>Examination (2.5 hours)</b>					
Essay	1, 2, 4, 5, 6, 7	1. b 2. e, f 3. c 5. a 7. a	20	individual	See Appendix for rubric

Short Answer Questions	1, 2, 4, 5, 6, 7	1. b 2. e 3. c, e 5. a 7. a	40	individual	See Appendix for rubric
<b>Total</b>			<b>100%</b>		

These are the relevant SBS Graduate Attributes.

- 1. Recognize the relationship and complexity between structure and function of all forms of life, resulting from an academically rigorous in-depth understanding of biological concepts**
  - b. Explain the relationship between structure and function of all forms of life at the molecular level
- 2. Critically evaluate and analyze biological information by applying the knowledge, scientific methods and technical skills associated with the discipline**
  - a. Identify the assumptions behind scientific problems and issues
  - e. Analyze the validity of qualitative and quantitative scientific data
  - f. Evaluate results in primary biological literature
- 3. Develop and communicate biological ideas and concepts relevant in everyday life for the benefit of society**
  - a. Simplify and explain scientific concepts and results of experiments to a non-biologist (avoiding jargon)
  - b. Display and explain scientific results clearly and persuasively to peers both verbally and in writing (includes the ability to graph data appropriately and accurately).
  - c. Demonstrate an understanding of the recursive nature of science, where new results continually modify previous knowledge
  - e. Discuss current critical questions in the field of biology
- 5. Develop communication, creative and critical thinking skills for life-long learning**
  - a. Learn independently and then share that knowledge with others
  - c. Demonstrate critical thinking skills such as analysis, discrimination, logical reasoning, prediction and transforming knowledge
- 7. Demonstrate information literacy and technological fluency**
  - a. Locate and evaluate information needed to make decisions, solve problems, design experiments, and understand scientific data
  - c. Evaluate and use biological databases (literature and public datasets)

### Formative Feedback

Because it's a small class, there is plenty of time and opportunities for you to discuss the lecture material and tutorial questions/answers with me after the lecture or tutorials. The discussions will have significantly positive impact on all the intended learning outcomes.

Besides the post-lecture/tutorial discussion, feedback will be provided in the form of Examiner's report at the end of the semester.

Feedback on your mid-term essay report and student presentation will also be provided.

### Learning and Teaching Approach

<b>Lectures</b> (26 hours)	The lectures are designed to bridge chemistry and biology and to highlight the use of biological tools in discovering new chemistry. You will have the opportunities to draw structures and biosynthetic mechanisms on the white board and inspect protein structures using computational software during class. These approaches are the means for achieving objectives 1-7.
<b>Tutorials</b> (13 hours)	The tutorial questions are designed to reinforce the fundamental concepts in chemical biology and natural product biosynthesis. Through the interactive tutorial sessions within a small class, objectives 1-7 can be achieved.

## Reading and References

Although no textbooks are formally required, some of the material in the lecture notes can be found in the book Natural Product Biosynthesis (Ref 1). Research articles will be provided to you throughout the semester as additional reading materials to broaden and deepen your understanding of the topics. You are NOT required to know or remember all the details of the research articles. Instead, apply the critical reading skill to grasp the important and relevant concepts. Below are several recommended reference books that you may find useful. The books can be found on the reservation shelf in the library. Many fundamental Biochemistry textbooks that contain relevant information are also available in the library.

- 1) Natural Product Biosynthesis by Christopher Walsh and Yi Tang, royal Society of Chemistry, 2017
- 2) Antibiotics: actions, origins, resistance, by Christopher Walsh. 2003.
- 3) The Organic Chemistry of Enzyme-catalyzed Reactions by Richard B. Silverman, Academic Press, 2002
- 4) Structure and Mechanism in Protein Science: A Guide to Enzyme Catalysis and Protein Folding by Alan Fersht
- 5) Principles of Bioinorganic Chemistry by Stephen J. Lippard and Jeremy M. Berg

## Course Policies and Student Responsibilities

You are expected to complete all assigned readings and activities, attend all lectures and tutorials punctually and take all scheduled assignments by due dates. You are expected to take responsibility to follow up with course notes, assignments and course related announcements for lectures you have missed. You are expected to participate in discussions and activities in class.

Absence from class without a valid reason will affect your overall course grade. Valid reasons include falling sick supported by a medical certificate and participation in NTU's approved activities supported by an excuse letter from the relevant bodies. There will be no make-up opportunities for tutorial activities.

## Academic Integrity

Good academic work depends on honesty and ethical behaviour. The quality of your work as a student relies on adhering to the principles of academic integrity and to the NTU Honour Code, a set of values shared by the whole university community. Truth, Trust and Justice are at the core of NTU's shared values.

As a student, it is important that you recognize your responsibilities in understanding and applying the principles of academic integrity in all the work you do at NTU. Not knowing what is involved in maintaining academic integrity does not excuse academic dishonesty. You need to actively equip yourself with strategies to avoid all forms of academic dishonesty, including plagiarism, academic fraud, collusion and cheating. If you are uncertain of the definitions of any of these terms, you should go to the [Academic Integrity website](#) for more information. Consult your instructor(s) if you need any clarification about the requirements of academic integrity in the course.

### Course Instructors

Instructor	Office Location	Phone	Email
Liang Zhao-Xun (Assoc Prof)	03s-53	6592 7736	ZXLiang@ntu.edu.sg

### Planned Weekly Schedule

Week	Topic	Course ILO	Readings/ Activities
1	Natural products as drugs	1, 2, 4, 7	
2	Biosynthesis of natural product	1, 5, 6	
3	Enzymes in natural product biosynthesis	1, 2, 3, 4	
4	Bio-synthetic enzymes with organic cofactor	2, 3, 5, 6	
5	Metalloenzymes	1, 3, 5, 6, 7	
6	Terpene biosynthesis	1, 3, 5, 6, 7	
7	Polyketide biosynthesis	1, 3, 5, 6, 7	
8	Biosynthesis of peptide-based natural products	2, 3, 5, 6, 7	
9	Alkaloid biosynthesis	1, 2, 3, 4, 5, 6, 7	
10	Biosynthetic pathway	1, 3, 5, 6, 7	
11	Engineering of biosynthetic pathways	4, 5, 6, 7	
12	Student presentation	3, 4, 6, 7	
13	Review, consultation & discussion	1, 2, 3, 4, 5, 6, 7	

### Appendix 1: Assessment Rubrics

#### Rubric for Tutorials: Presentation (20%)

The score will be determined solely by the course coordinator. The presentation will be scored as:

**10%** of the assessment will be based on the clarity of the presentation, and demonstration that you understanding the material.

10% of the assessment will be based on how you answer the questions from the course coordinator and other students.

Scoring is as follows:

Criteria	Score
Clearly articulated the experimental design, results and conclusions.	5
Background of the studies	2
The presentation style is clear and well organized	3
Answer the questions from the coordinator and other students in a professional manner	10
<b>Total</b>	<b>20</b>

#### **Rubric for Mid-semester Quiz: Essay (20%)**

The assignment will require you to write up a short essay on the biosynthetic mechanism of a chosen natural product from recent literature. Assessment and feedback on the assignment will be by the course coordinators, using the following criteria:

Criteria	Score
The essay has a brief introduction on the scientific or biomedical importance of the natural product	5
Explain the biosynthetic mechanism in a clear manner	5
The essay contains correct molecular structures and reaction schemes	5
The essay is well organized with correct referencing, style, grammar and spelling	5
<b>Total</b>	<b>20</b>

#### **Rubric for Examination: Essay (20%)**

The final exam will consist of a combination of short answer questions and large essay questions.

For the large essay questions (20%), it will require you to answer questions based on a good understanding of the chemical and biological mechanisms discussed in lectures and tutorials. The answers, which can be written text or a series of chemical structures used to illustrate biosynthetic mechanism, is expected to be provided by you.

The exam will contain 2-3 such essay questions. Each question is worth equal marks.

#### **Rubric for Examination: Short Answer Questions (40%)**

The final exam will consist of a combination of short answer questions and large essay questions.

For the short answer questions (40%), it will require you to solve problems based on the understanding of the material discussed in lectures and tutorials. A short answer, which can be one or two short sentences or a chemical structure, is expected to be provided by you.

The exam will contain 6-8 each questions. Each question is worth equal marks.

### **Appendix 2: Intended Affective Outcomes**

As a result of this course, it is expected you will develop the following "big picture" attributes:

Appreciate the complex structure of natural products underlying their bioactivity

Appreciate the power of DNA technology in discovering new chemistry

Appreciate the use the genomic information in modern chemical biology research

Awareness of different biosynthetic origin of natural products

Appreciate the biological roles of secondary metabolites

Appreciate the role of natural products in modern medicine