Spring 2018

Bio-Organic Chemistry CHEM 6410 (CRN: 22016)

Co-listed: Bioorganic Chemistry CHEM 4410 (CRN: 22015)

Tuesday and Thursday from 5:30-8:15 PM in 302 Adhold

Instructors

Professor Zhen Huang: huang@gsu.edu (office hour: by appointment and immediately after the lecture)

Course Content

This course will cover the three important classes of biomolecules (Nucleic Acids, Proteins, and Carbohydrates) for drug discovery and biomedical applications.

PREREQUISITE: For Chem4410: Chem 3410 (Organic Chemistry II) with grade of B or higher and consent of instructor; for Chem6410: consent of instructor.

Textbook

A: Biochemistry (Text book), Zubay

B: The Organic Chemistry of Drug Design and Drug Action by Richard Silverman, Academic Press, ISBN 0-12-643732-7

C: Handbook of Nucleoside Synthesis, Helmut Vorbruggen and Carmen Ruh-Pohlenz, Wiley-Interscience Publication, ISBN 0-471-09383-1;

D: Nucleic Acid Structure (by Stephen Neidle)

E: Ribozymes and RNA Catalysis (by Lilley and Eckstein).

EXAMINATIONS AND QUIZZES/HOMEWORK:

Three examinations/quizzes will be given during class time. There will also be homework/project assignments in addition to a final examination. Homework and project assignments for 6410 will be more intensive and will be graded more rigorously to reflect graduate level.

GRADING:

Class Participation:	10%
Homework/Projects/Presentation	30%
Quizzes/examinations	30%
Final	30%
Total	100%

A+: ≥96%; **A:** ≥90%; **A-:** ≥87%; **B+:** ≥84%; **B:** ≥80%; **B-:** ≥77%;
C+: ≥73%; **C:** ≥70%; **C-:** ≥66%, etc.

LECTURE

Part I. Introduction of Nucleic Acids, Proteins, and Carbohydrates

1. Nucleic acid (DNA and RNA), protein and carbohydrate: chemical molecules
2. Importance and significance of nucleosides, nucleotides, and nucleic acids
3. Nucleosides, amino acids and sugars
4. General introduction of nucleic acid chemical, biochemical & biological synthesis
5. Synthesis of unnatural nucleosides, nucleotides, and nucleic acids
6. General introduction of structures of nucleic acids, proteins and carbohydrates
7. General introduction of functions of nucleic acids, proteins and carbohydrates

Part II. Chemical & Biochemical Synthesis of Nucleosides, Nucleotides, Nucleic Acids, and Proteins

1. Synthesis of nucleosides by direct synthesis
2. Synthesis of pyrimidine and purine nucleosides via glycosidation and glycosylation
    a) Via activation of 1'-position by X-, Ms-, Ts-, -OAc, -OMe
    b) Activation of pyrimidines and purines by TMS-
    c) Using Lewis acid as catalysts
    d) Using Greenard reagents
3. Synthesis of nucleosides via conversion
4. Synthesis of unnatural nucleosides
5. Synthesis of nucleosides with C-C instead of C-N glycosidic bond
6. Synthesis of nucleotides by phosphorylation
7. Synthesis of nucleoside triphosphates
8. Synthesis of nucleic acids by solution phase and solid phase
9. Synthesis of nucleic acids using biochemical strategies

Part III. Why are Nucleic Acids, Proteins and Carbohydrates Essential for Life?

1. Functional requirements for nucleic acids, proteins and carbohydrates
2. Atoms and functional groups of nucleic acids, proteins and carbohydrates

3. Structure comparison of nucleic acids, proteins and carbohydrates
4. Function comparison of nucleic acids, proteins and carbohydrates

Part IV. Enzymatic Catalysis, Inhibition and Inhibitor Mechanisms

1. Proteins as catalysts
2. Catalytic RNAs (ribozymes) and ribosome.
3. What cause catalysis?---- mechanisms of enzyme catalysis
4. Coenzymes: small molecules that help enzymes
5. Why and how to inhibit an enzyme, especially nucleic acid-based enzymes
6. Reversible and irreversible enzyme inhibitors and how to design them
7. Drug resistance: a war provoked by microorganisms

Part V. Targeting Nucleic Acids and Proteins: DNA-Interactive Agents and Inhibition

1. Natural killers of genes and proteins
2. Nucleic acids and their protein complexes as drug targets
3. Disrupting diseases at gene expression and regulation levels
4. Targeting DNA and chromosome with small molecules
5. Gene function disruptors: DNA-binding agents and protein function inhibition

Part VI. Nucleic Acids and Proteins as Potential Diagnostic Targets and Tools for Diseases and Pathogen Identification

1. Gene expression profile and drug discovery
2. Gene silencing and protein synthesis inhibition by oligonucleotides (NA therapeutics) at RNA level (such as antisense molecules, siRNA, microRNA) and DNA level [such as CRISPR-RNA (crRNA)]
3. Advantage of disease and pathogen detection at nucleic acid and protein levels
4. RT-PCR strategy
5. Gene Chip and Microarray strategies of nucleic acids and proteins
6. Advantage of RNA Microchip Development