Georgia STATE UNIVERSITY

Department of Chemistry

Nucleic Acid Synthesis, Drug Design, Mechanism, and Detection

Chem4650/6650 (Syllabus)

Fall 2016

INSTRUCTOR: **Prof. Zhen Huang, Ph.D.**

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PREREQUISITE: For Chem4650: Chem 3410 (Organic Chemistry II) with grade of B or higher and consent of instructor; for Chem6650: consent of instructor.

SUGGESTED TEXT:

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

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

C: Biochemistry (Text book), Zubay

D: The RNA World (by Gesteland, Cech, and Atkins)

E: Nucleic Acid Structure (by Stephen Neidle)

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

LABORATORY: None

EXAMINATIONS AND QUIZZES/HOMEWORK:

Three examinations/quizzes will be given during class time. Exams for 4650and 6650 will not be identical and exams for 6650 students will be graded more rigorously to reflect graduate-level. There will also be homework/project assignments in addition to a final examination. Again, homework and project assignments for 6650 will be more intensive and will be graded more rigorously to reflect graduate level.

GRADING:

Class Participation:	10%
Homework/projects	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

1. Nucleic acid (DNA and RNA), a chemical molecule
2. Importance and significance of nucleosides, nucleotides, and nucleic acids
3. Modification of nucleosides, nucleotides, and nucleic acids
4. General introduction of nucleic acid chemical, biochemical & biological synthesis
5. Synthesis of unnatural nucleosides, nucleotides, and nucleic acids
6. General introduction of nucleic acid structure
7. General introduction of nucleic acid function

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

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. 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 IV. Targeting Nucleic Acids: DNA-Interactive Agents and Inhibition

1. Natural killers of genes
2. Nucleic acids 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

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

1. Gene expression profile and drug discovery

2. Gene silencing 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 levels
4. RT-PCR strategy
5. Gene Chip and Microarray strategies
6. RNA Microchip Development