

Chem 162/262 Midterm Exam Guide

The midterm exam in Chem 162/262 will test your *understanding* of topics covered up to, and including the function of receptors. You should be well familiar with the answers to questions in the first three homework assignments. Furthermore, you should be familiar with the biological concept of the disease that you are working on in this course. You can demonstrate your understanding by explaining concepts and techniques relevant to drug design and applying your knowledge to solve problems. Of course, understanding a topic requires good knowledge of the material.

The midterm is a mixture of knowledge and problem-solving type questions. An old sample exam key is available at http://www.chem.ucsb.edu/~kalju/chem162/private/Exam_162_Key.pdf

I believe that the following resources help you best in preparing for the exam:

- a) Lecture material. Was there anything that I said and was not clear? If so, please see if you can get answers by (i) asking me or (ii) asking our TA, or (iii) reading the textbook/literature/Internet.
- b) Required reading. First, make sure that you have some idea what is the main point of each of these papers. Then see if which papers you need to read more thoroughly to strengthen your understanding of the material.
- c) Textbooks. Our suggested textbook provides a good background on receptors but covers less about disease biology and target validation approaches. You may want to consult a general biochemistry or molecular biology text if you are not familiar with these methods.

Topics from lectures that I consider most important

1. General process from disease to the cure
 - Disease identification
 - Target identification and validation
 - Lead discovery
 - Lead optimization
 - The role of animal studies and clinical trials
2. Historical developments in drug discovery
 - The role of serendipity in drug discovery
 - Drugs to alter imbalance of chemicals in our body
 - Magic bullets against pathogens
 - Focus of target-guided drug discovery
 - Role of combinatorial chemistry and high-throughput screening
 - Advantages and limitations of biological macromolecules as drugs
3. Target validation technologies
 - Gene knockout
 - Phage display
 - Yeast two-hybrid system
 - Expression cloning
 - Gene chips, analysis of microarray data
 - Single nucleotide polymorphisms

- RNA Interference
 - Antisense oligonucleotides
 - Proteomics
4. Biological role / molecular mechanism of targets that we have discussed
- Tumor suppressor p53
 - Murine double minute oncogene and its human analog
 - Fumaroyl acetoacetate hydrolase
 - HIV fusion machinery
 - OMP decarboxylase
 - Nicotinic acetylcholine receptor
 - NMDA receptor
 - H^+ / K^+ ATP-dependent transporter
 - β -adrenergic receptors
 - G-proteins
5. Receptor structure and functions studies
- Important types of receptors
 - Functional assays for ion channels
 - Functional assays for GPCRs
 - Binding studies w/ membrane receptors: practical considerations
 - Displacement assay
 - Hydrophathy analysis
 - Protease protection assay
 - Determination of 3D structure of membrane receptors
6. Key concepts
- Receptors, agonists, antagonists, inverse agonists
 - Basics of enzyme catalysis and inhibition
 - Signal transduction cascades
 - Metabolic pathways, their regulation
 - Differences between higher eukaryotes, parasites, bacteria, and viruses
 - Lead compound, why a lead is not a drug, lead optimization