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 nuclear 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.

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
   - Common types of drugs
   - Common mechanisms of actions of drugs

2. Historical developments in drug discovery
   - Nature as a source of drugs and drug leads
   - The role of serendipity in drug discovery
   - Drugs to alter imbalance of chemicals in our body
   - Magic bullets against pathogens
   - Treatment with focus of restoring balance of chemicals in human body
   - Focus of target-guided drug discovery
   - Role of combinatorial chemistry and high-throughput screening
   - Advantages and limitations of biological macromolecules as drugs

3. General considerations in choosing a disease to work with
   - Prevalence and disease seriousness measures
   - Existing treatments and disease response to these
   - Technological feasibility of success
4. 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

5. Biological role / molecular mechanism of targets that we have discussed
   - Tumor suppressor p53
   - Murine double minute oncogene and its human analog
   - HIV fusion machinery
   - RANK–RANKL system
   - Nicotinic acetylcholine receptor
   - NMDA receptor
   - H⁺ / K⁺ ATP-dependent transporter
   - Cystic fibrosis transmembrane conductance regulator
   - Chemistry and regulation of (nor)adrenaline biosynthesis
   - β-adrenergic receptors
   - Adenosine receptors
   - G-proteins
   - Estrogen receptor

6. Receptor structure and functions studies
   - Important types of receptors
   - Functional assays for ion channels
   - Functional assays for GPCRs
   - cAMP AlphaScreen™ technology
   - Binding studies w/ membrane receptors: practical considerations
   - Displacement assay
   - Hydropathy analysis
   - Protease protection assay
   - Determination of 3D structure of membrane receptors

7. Key concepts
   - Receptors, agonists, antagonists, inverse agonists
   - Receptor subtypes: drug selectivity and side effect issues
   - Signal transduction cascades
   - Differences between higher eukaryotes, parasites, bacteria, and viruses
   - Lead compound, why a lead is not a drug, lead optimization