7.61 Discussion #D1 Receptors : Growth Hormone & α_{1B}-adrenergic - Structure-Function Analysis/ Mutagenesis/ Surface Plasmon Resonance

Assigned Reading for Discussion #1, Wed. September 13, 2006

COME TO THE DISCUSSION READY TO LEAD THE DISCUSSION. YOU SHOULD BE READY TO:

1) REVIEW THE SCIENTIFIC BACKGROUND UPON WHICH THE KEY QUESTION(S) ADDRESSED WERE BASED – WHY WAS THE WORK DONE? YOU SHOULD BE ABLE TO SUCCINCTLY DESCRIBE THE KEY QUESTIONS ADDRESSED IN THE PAPER
2) SUMMARIZE BRIEFLY EACH EXPERIMENT – FIGURE BY FIGURE AND TABLE BY TABLE -(IN ORDER OF PRESENTATION IN THE 'RESULTS' SECTION), INCLUDING:
   WHAT QUESTION WAS ASKED, WHAT TECHNIQUE WAS USED AND WHY, HOW DOES THE TECHNIQUE WORK (E.G., SCANNING CALORIMETRY) AND WHAT CAN BE LEARNED BY USING THE TECHNIQUE, WHAT WERE THE RESULTS, WHAT CONCLUSIONS CAN BE DRAWN FROM THE RESULTS, DID THE AUTHORS DRAW REASONABLE CONCLUSIONS OR DID THEY GO TOO FAR OR NOT FAR ENOUGH IN INTERPRETING THE SIGNIFICANCE OF THEIR RESULTS
3) SUMMARIZE AND CRITICIZE THE DISCUSSION AND OVERALL CONCLUSIONS
4) PROVIDE A TWO OR THREE SENTENCE SUMMARY OF THE WHOLE PAPER

YOU SHOULD BE PREPARED TO GO TO THE BLACKBOARD TO CLEARLY SKETCH OUT ANY CONCEPT OR METHOD OR RESULT, IF THAT WILL HELP YOU PRESENT THIS INFORMATION SUCCINCTLY AND CLEARLY

BRING A FOLDED PIECE OF PAPER OR BOARD WITH YOUR NAME CLEARLY WRITTEN IN DARK, BOLD PRINT. THIS WILL SERVE AS A NAME PLATE FOR THE INSTRUCTORS AND YOUR FELLOW STUDENTS. PLEASE BRING THIS 'NAME PLATE' WITH YOU TO **ALL** DISCUSSIONS.

3 papers:

Biophysical studies of growth hormone interactions with its receptors - Is symmetry need for binding?

Paper 1. Cunningham, B. C., M. Ultsch, Vos A. M. De, M. G. Mulkerrin, K. R. Clauser, and J. A. Wells. "Dimerization of the extracellular domain of the human growth hormone receptor by a single hormone molecule." Science 254 (5033 1991): 821-5. What are the implications of a 2:1 ratio of receptor to ligand?

Paper 2. Cunningham, B. C. and J. A. Wells. "Comparison of a Structural and a Functional Epitope" J. Mol. Biol. 234: 554-563 (1993). Use of a very high tech method (Surface Plasmon Resonance) which allows the remarkably easy determination of association and dissociation rate constants. This method is one of the most powerful methods available today for analyzing protein binding reactions. We have provided you with a brief description of the SPR detection technique and we can talk about it in class. Don't worry about mastering the physical principles underlying the method.

Mutagenic analysis of G-coupled receptors to study the nature of the conformational changes associated with ligand binding and regulation of receptor activity.

Paper 3. Kjelsberg et al. "Constitutive activation of the α_{1B}-adrenergic receptor by all amino acid substitutions at a single site: evidence for a region which constrains receptor activation." J. Biol. Chem. 267:1430-1433 (1992). (you may want to scan some of the reading for Lecture 2 as background for this – but not essential).

Other papers of interest:

Liggett, S. B., N. J. Freedman, D. A. Schwinn and R. J. Lefkowitz. "Structural basis for receptor subtype-specific regulation revealed by a chimeric β_3/β_2-adrenergic receptor. PNAS 90: 3665-3669 (1993). This paper is an extension of the classic paper on chimeric receptors by the Lefkowitz group (Kobilka et al. "Chimeric α_2-,β_2-Adrenergic Receptors: Delineation of domains involved in effector coupling and ligand binding specificity" Science 240:1310-1316 (1988)).