Recitation Reading Assignment

Purpose:
Skills: The purpose of this assignment is to help you practice interpreting the scientific literature, a skill which is essential to your success in any scientific discipline. Specifically, you will practice how to:

- Interpret and contextualize data presented in the primary literature
- Critique data and arguments presented in the primary literature
- Use review papers to learn about a topic new to you

Knowledge: This assignment will also help you to become familiar with the following content knowledge related to our lectures on proteins:

- Protein folding and misfolding pathways
- How protein misfolding causes disease
- Therapeutic strategies for neurodegenerative diseases
- Protein chaperones

Task: Read the papers below. For the review paper (Soto 2003), you are required to read only the listed sections but are encouraged to read the entire paper at your leisure. Based on your reading of the papers, consider the questions in this assignment. While you are not required to answer these questions, doing so will guide your reading of the papers and prepare you for classroom discussion.


- Introduction
- Determinants of misfolding and aggregation
- The mechanism of misfolding and aggregation
- Mechanisms of neuronal death: skim loss-of-function hypothesis and gain-of-toxic-activity hypothesis
- A common therapy for conformational diseases?


Criteria: You will be graded on your active participation during recitation discussion of these papers. The discussion will be based on the questions in this assignment; however, you will not turn in any written work.
Questions for Soto 2003

1. What neurodegenerative diseases are associated with misfolded proteins? In each, what protein is misfolded/aggregated?

2. Do all aggregates have similar structures? Explain.

3. Explain how misfolded proteins form insoluble protein aggregates. What intramolecular interactions make this pathway thermodynamically favorable?

4. How might protein aggregates lead to neuronal death? What is some experimental evidence for and against these hypotheses?

5. What general strategies are being used to treat protein misfolding diseases? How might the efficacy of these strategies differ depending on the cause of neuronal death?

Questions for Parsell et al. 1994

1. What was known previously about Hsp104? What question(s) did the authors set out to answer in this paper?

2. For each figure, consider the following:
   a. What question were the authors asking in this experiment?
   b. What methods do the authors employ to answer this question?
   c. What controls were included in the experiment?
   d. What conclusions can be drawn from the data?
   e. Are there any alternate hypotheses that could explain the data?

3. From the data presented in the paper, what can the authors conclude about the role of Hsp104 versus that of Hsp70 in response to heat stress?