Questions to Ponder

What is a prion? Describe the prion hypothesis. Prusiner is credited with developing the prion hypothesis. Describe the argument he puts forth in his article (2012) regarding the role of prions in neurodegenerative conditions beyond spongiform encephalopathies.

Describe two cellular/tissue characteristics of Alzheimer’s disease (AD). How do those characteristics relate to protein folding?

What hypothesis(es) did Morales et al. (2012) set out to test?

What is the difference between the two mouse models used by Morales et al. (2012) (*HuAPPwt* and *tg2576)*?

What does Figure 1 of the Morales et al. (2012) article demonstrate? What was the purpose of performing that analysis? In other words, how does it relate to the hypothesis(es) being tested?

Figure 2 shows results from an analysis of the brain tissue of a patient with AD. What characteristics were the authors expecting to see in that tissue? Did the results match up with the expectation? How so? Why was it important to conduct this analysis before moving forward with the subsequent experiments?

In Figure 3, explain why it was important to do a separate inoculation with control brain tissue? How does that impact the interpretation of the results? What was the purpose of doing this staining in addition to exposing the tissue to an anti-amyloid-β antibody?

Why did the authors choose to compare results from the HuAPPwt mouse with similar analyses using the tg2576? What did that analysis demonstrate?

Much of the analyses focused in on the hippocampus. Given the most common symptoms of AD, why does it make sense to look for cellular/tissue changes in that region of the brain?

Does the Morales et al. (2012) paper provide support for the hypothesis described by Prusiner (2012)? In what way?

Do you accept Morales et al.’s (2012) interpretation of their results? Are there alternative interpretations you would propose? What new questions emerged from this work?

What is the central argument put forth by Lahiri’s letter? Is it well grounded/supported?

In addition to learning about underlying mechanisms involved in Alzheimer’s disease, what other insights can be gleaned from this line of work?