Ubiquitination: The Garbage Cycle of a Cell

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Abstract
Within every cell, there exists a system known as the ubiquitin-proteasome system (UPS) that eliminates damaged, misfolded or excess proteins. Unwanted proteins are tagged with ubiquitin, a small protein that identifies other proteins as being ready for degradation. The process of activating and transferring the ubiquitin to the protein is referred to as ubiquitination. Three proteins involved in this process are the ubiquitin activating enzyme (E1), the ubiquitin conjugating enzyme (E2), and the ubiquitin ligase (E3). Ubiquitination begins with ubiquitin being activated by and attaching to E1. E1 transfers ubiquitin to E2. Then E2 delivers ubiquitin to the unwanted protein, either directly or through E3. Finally, the tagged protein is broken down by the proteasome, which is the cell's protein-degrading complex.

Ubiquitin-Proteasome System

- **E1 activates ubiquitin**
- **Activated ubiquitin is transported by E2**
- **E2 passes ubiquitin on to E3**

Got Mad Cow?

Bovine Spongiform Encephalopathy (BSE), also referred to as "Mad Cow Disease", is an illness that attacks the brain and spinal cord. The name "Mad Cow Disease" comes from the strange behaviors, including aggression and lack of coordination, that are associated with infected cattle. BSE is the result of prion infection within the brain.

Prion Formation

- Normally folded form
- Misfolded prion form
- Normally folded form induced into the prion form
- Prion aggregate

A prion is a unique, misfolded form of a normal protein. As illustrated in the diagram above, the prion form initiates a chain reaction by causing other normal proteins of the same type to mis-fold and aggregate together. Though misfolded proteins are targeted to the ubiquitin system (shown in the diagram to the right), the prion escapes this targeting, causing these prion misfolds to accumulate in the cell. Prions are not only present in mammalian cells, but also in yeast cells which has made prion research easier.

What is the connection between the UPS and prions?

In yeast, when Ubch5b(E2) is removed from the ubiquitination process, an increase in prion formation has been observed. The easiest explanation would be that a decrease in E2 leads to an increase in misfolded protein, which might lead to increased prion formation. However, as the protein is not normally seen to associate with ubiquitin, the effect of deletion of Ubch5b is probably mediated indirectly.