

1 A cell must continuously sort useful materials from its waste products and then remove or recycle the waste. One way a cell does this is to first put tiny tags on proteins that are no longer needed. These tags, which are small polypeptide chains 76 amino acids long, are called ubiquitin.

Ubiquitin tags direct proteins to compartments of the cell called proteasomes. Within each proteasome, ubiquitin-tagged proteins are deconstructed into their component amino acids. These pieces can be repurposed to build new proteins.

3 Sometimes organs stop processing waste effectively, allowing the waste to pile up and contributing to many diseases. Alzheimer's disease, for example, includes piles of waste proteins in the brain called tangles, while Parkinson's disease involves the accumulation of recyclable material into Lewy bodies. Mallory bodies are piles of waste proteins common in liver disease. These piles, known generically as inclusions, can be identified under the microscope because they are covered in tiny ubiquitin tags.

4 A problem in the breakdown of ubiquitin-tagged proteins may be one cause of spinocerebellar ataxia type 1. In this disease, a protein called ataxin-1 has an abnormal genetic mutation, and ubiquitin is able to attach to the mutant protein. Scientists believe that the mutated protein cannot be chopped up by the proteasome because of its shape, so ubiquitin-tagged ataxin-1 starts to accumulate, which leads to cell death. The cells most affected by this genetic mutation are neurons in a part of the brain associated with motor control and the spinal cord. So, a person with mutant ataxin-1 progressively loses muscle control as these cells die.

Why do individuals with spinocerebellar ataxia experience loss of muscle control, even though the ataxin-1 protein builds up only in the brain and spinal cord?

- ☐ A. Inclusions can build up in all body systems and can cause debilitating effects.
- ☐ B. Genetic mutations in the ataxin-1 protein cause muscular proteins to change shape.
- ☐ C. When the ubiquitin tagging system does not work effectively, cellular waste can build up in the muscles.
- ☒ D. The neurons affected by the ataxin-1 protein buildup are in a region of the brain that manages muscle control.

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