Small Proteins Help Misplaced Proteins Return to their Proper Location

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Small proteins, now called targeted relocalization activating molecules (TRAMs), help relocate proteins to their correct location. Normally, proteins are directed to their proper place by biological regulators in the cell. These regulators need a signal to form the proteins that indicate where they are supposed to go. Even though different proteins send different signals to go to different places, some of the signals can be degenerate, causing them to appear as other signals. This results in mislocation of proteins, which is the reason TRAMs are necessary.

TRAMs, the small proteins, occur with the appearance of a shuttle protein and target protein. A nucleocytoplasmic shuttling protein takes molecules from the nucleus (import) to the cytoplasm (export) through nuclear pores. Shuttling proteins recognize the export and import signals to figure out where to go. Additionally, there are two different kinds of shuttle proteins: Mammalian and Bacteria protein shuttles. A target protein is a protein that is a part of a diseased area. This protein embedded in the diseased area is “targeted” by a drug that binds to it. TRAMs use ligands, molecules that bind with proteins, to connect ecDHFR, a protein that turns into a shuttle protein by attaching an amino-acid sequence called a nuclear export sequence (NES) and adding a fluorescent tag to a target protein. One ligand connects to the shuttle protein and the other connects to the target protein. Once they are connected, the target protein rides along with the shuttle protein and gets relocated.

The mislocation of proteins is the cause of many significant human diseases today. Proteins are responsible for gene transcription. So, biological regulators directing proteins to the incorrect location can cause cancers, neurodegenerative diseases, and viral infections. TRAMs were found to be able to shuttle from the cytoplasm to the nucleus, specifically in amyotrophic

lateral sclerosis (ALS), a disease caused by the mislocation of protein from the nucleus to the cytoplasm. Even though this discovery seems promising, it is not complete. All of these shuttles have been engineered to result in higher expression, while the non-engineered shuttle proteins have low expression, seldom resulting in function. Additionally, TRAMs still need to be explained stoichiometrically. Specifically, there needs to be a molecule for every target protein and shuttle protein.

In summary, TRAMs, when completed, could aid in the relocation of target proteins, therefore minimizing diseases like cancers, neurodegenerative diseases, and viral infections.

References

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