Scissors? A truck? Or BOTH? Moonlighting proteins can do it all

Proteins are the molecular machines that perform millions of different jobs throughout the body. Everything we do requires specific kinds of proteins, from cutting molecules into smaller pieces when we digest our food, to carrying oxygen from our lungs to our muscles, to smelling a rose. A few decades ago we used to think that each protein evolved to perform a specific job, much like scissors can cut paper or trucks can drive around and carry packages for delivery. Surprisingly, more and more proteins are being found that can perform multiple, sometimes very different jobs. It's like having a pair of scissors that cuts paper when inside the house but can turn into a truck when it is outside of the house! We call these multitalented proteins "moonlighting proteins", and we and other labs are determining their three-dimensional structures and testing their functions to learn how they can be so versatile. It turns out some proteins bend and change into a different shape in order to perform a second function, like the characters in the Transformers movies.

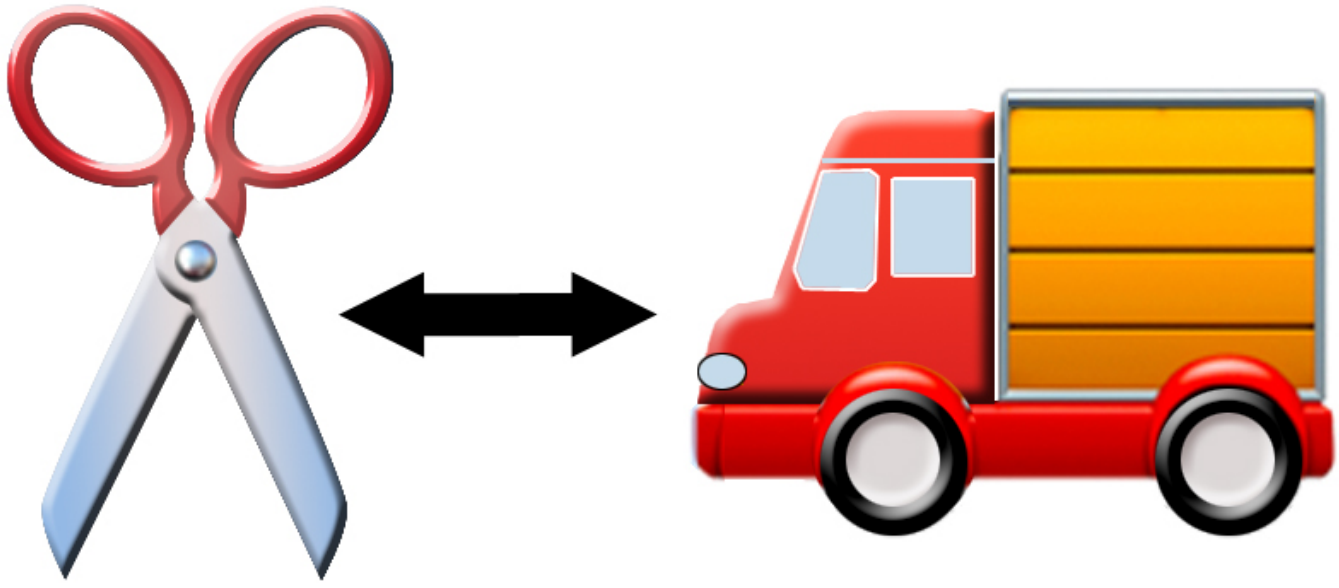

Fig. 1. Moonlighting Proteins are versatile machines that can do two very different jobs, often in different places in a cell, like a pair of scissors that can cut paper while inside the house but can turn into a truck and deliver packages when outside of the house.

Other proteins have one pocket on the surface in which one action takes place and another pocket on the surface to interact with other molecular machines in the cell. One group of moonlighting proteins that we focus on in the lab includes proteins that have one function inside of the cell and then have another function when they are placed on the outside surface of the cell. We don't know yet how proteins like this get from inside of the cell to outside of the cell or how they get attached onto the cell's surface. We do know, however, that having all of our moonlighting proteins doing all of their jobs at the right places and at the right times is important for maintaining our health and preventing disease. When a moonlighting protein can't perform all of its jobs correctly, we can become sick. Part of what we do in the lab is find out which proteins are damaged and aren't working well when there is a disease. If we can figure out what is going wrong, we can sometimes develop a new drug that fixes the activity of the damaged protein. But if a protein is a moonlighting protein with more than one activity, we need to make sure that we fix the function that is damaged and do not interfere with the other functions of the protein. Adjusting the level of activity of the wrong function can lead to side effects. We are working on learning how moonlighting proteins perform all of their jobs, switch between their different jobs, and move to different places in the cell so that they can do their jobs in the right places and at the right time, as well as how these characteristics of the proteins are altered in disease. Learning all these things can help lead to developing new drugs that are more effective in treating disease and with fewer side effects than current drugs.

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