The Transportation System Inside a Living Cell

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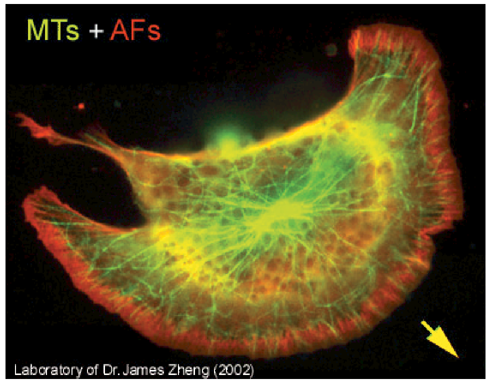

A living cell is like a city in its infrastructure. It has workers (proteins), a power plant (mitochondria), roads (actin fibers and microtubules), trucks (kinesin and dynein) whose cargo are containers (vesicles), factories (ribosomes that make proteins), a library (genome), post office (golgi apparatus sorts, packages and modifies macromolecules for secretion or for delivery to other organelles), and police (chaperones). Wayward or malformed proteins get a ticket (ubiquitin) and then get shipped off for degradation. Cells are also involved in exporting and importing. Communications and regulation occurs through complex signalling pathways that help keep everything running smoothly.

Inside a cell things can be transported in two ways. The first is by diffusion in which small molecules are released and just wander around. This is usually used for small molecules like ATP which is the fuel that is used to power molecular motors. The second way is through active transport that works like container shipping. Container shipping revolutionized the shipping industry. Rather than stacking sacks of sugar on ships, the sacks are placed in metal containers that can be stacked on the decks of ships and then later transferred from the ship onto 18-wheeler trucks. Similarly cells pack cargo into small bags called vesicles. These vesicles have motor proteins attached to their outside. There motor proteins have 2 legs and can walk just like a person, putting one foot in front of another. They walk along roads that are thin filaments of polymers. As they walk along these roads, they haul the cargo vesicles. These cargos can be a wide variety of things. For example, vesicles can contain pigment which, when spread out, will change the color of a skin cell. Or the cargo can be a mitochondria which is a power plant (organelle) that makes ATP. Sometimes viruses co-opt the transportation machinery and use motors to carry them along the roads.

The roads are of two types (see figure): microtubules (MT) are like interstate highways; they spread radially outward from the nucleus of the cell. Actin filaments (AF) are like local surface streets that are randomly placed. Cargos can go transfer from microtubules to actin filaments and vice-versa, just as we exit from interstate highways onto local streets.

My research is focused on understanding how this transportation system is regulated. For example, we studied pigment cells in frogs [1]. When frogs get scared by a predator, they change color. We have found that when the pigment granules are spreading out from the nucleus, they will go straight through actin filament intersections until they get to the end of the filament. When the granules need to return to the nucleus, cargos will often switch at actin filament intersections as if to find the nearest on-ramp to a microtubule.

In other research we made a simple model to understand one of the molecular motors called dynein [2]. As noted earlier, molecular motors have 2 legs and take one step at a time. The motor called kinesin walks outwards along microtubules towards the periphery of the cell and takes 8 nanometer steps. The motor called dynein walks along microtubules inwards toward the nucleus. Dr. Roop Mallik in Prof. Steven Gross' group (UC Irvine) has found that dynein effectively has a transmission or gear shift [3]. It can take steps of varying sizes: 8, 16, 24, or 32 nanometer steps depending on the load it is hauling or on the amount of ATP (fuel) that is available. Under a heavy load it takes small steps. Under no load and with lots of ATP available, it takes large steps.

The transportation system is very important to cells, especially to neurons where the cell body can be up to a meter away from the periphery. (Nerve cells extend about a meter from your spine to your toes.) Active transport is needed to move things from the cell body to the outer reaches of the cell. Neurodegenerative diseases such as Alzheimers and Parkinson's disease are marked by a breakdown of this transportation system, so understanding how active transport is important.

References

[1] Snider, J., Lin, F., Zahedi, N., Rodionov, V., Yu, C. C., & Gross, S. P. (2004) *Proc. Natl Acad. Sci. USA* **101**, 13204–13209.

[2] Singh, M. P., Mallik, R., Gross, S. P., & Yu, C. C. (2005) *Proc. Natl Acad. Sci. USA* **102**, 12059–12064.

[3] Mallik, R., Carter, B. C., Lex, S. A., King, S. J., & Gross, S. P. (2004) *Nature* **427**, 649–652.