**Nucleus runs ahead of centrosome**

The nucleus is not pulled by the centrosome in migrating neurons, according to a new direct imaging study by Hiroki Umeshima, Tomoo Hirano, and Mineko Kengaku (RIKEN Brain Science Institute, Wako, Japan).

Previous studies showing the centrosome leading the nucleus in migrating neurons led to the suggestion that the centrosome provides the motive force for nuclear migration. “Our results clearly argue against this accepted model,” Kengaku says.

The imaging study in mouse cerebellar slices indicates that the nucleus sometimes passes in front of the centrosome—a phenomenon not seen previously in isolated cells. While the nucleus spent part of its time behind the centrosome, it also jumped ahead. Neither the dynamic microtubules enveloping the nucleus or the stable microtubules extending from nucleus to leading edge converged at the centrosome.

Disruption or excess formation of the stable microtubules interrupted nuclear movement. One possibility is that the stable filaments form a track along which the nucleus is pulled by the dynamic microtubules.

Inhibition of LIS1, which regulates the microtubule motor dynein, prevented migration of the nucleus without interfering with the centrosome, indicating the two use different mechanisms to migrate. What, then, is the centrosome’s role in nuclear migration? “That’s the next question we have to answer,” Kengaku says. “We think the centrosome is important for microtubule organization,” perhaps in preparing microtubules during the cyclic pauses in nuclear migration for future movements, “but we haven’t proven it yet.”

Reference: Umeshima, H., et al. 2007. Proc. Natl. Acad. Sci. USA. doi:10.1073/pnas.0708047104.

**Forward walk with a random twist**

Myosin-V makes a random twist as it traverses hand over hand along its actin filament, according to a study by Yasunori Komori, Atsuko Iwane, and Toshio Yanagida (Osaka University, Osaka, Japan).

The transport molecule myosin-V, which bears two actin-binding heads each linked by an arm to a central stalk, carries cargo along the cytoskeletal network. The hydrolysis of ATP drives the lagging head off of actin, but how that head swings around the leading head to rejoin the actin was unknown.

In the new experiments, fluorescently labeled actin filaments bound to an immobilized myosin-V were seen to twist randomly clockwise or counterclockwise during each clamp-release-reclamp cycle. The finding indicates that in the cell, where actin is fixed and myosin is free to twist, the trailing myosin head can swing in either direction as it searches out its next forward binding site.

Yanagida thinks the ability to twist in either direction gives the motor better mobility. “The cell is very crowded by the many kinds of proteins within,” he says. “It’s probably not easy to transport cargo along the complex actin meshwork.” In addition, unlike a twist in a fixed direction, a random twist allows multiple myosin-V molecules on a single cargo to avoid twirling each other around as they move.

Reference: Komori, Y., et al. 2007. Nat. Struct. Mol. Biol. doi:10.1038/nsmb1298.

**Hand it to the nucleolus**

Long viewed as merely a biofactory for ribosomes, the nucleolus has recently come to be seen as a multifunctional and dynamic subnuclear organelle. New support for this view comes from a study by David Martindill, Paul Riley (UCL Institute of Child Health, London, UK), and colleagues, who show that a cell fate regulator is held inactive in the nucleolus until phosphorylation releases it to trigger differentiation.

Differentiation of mouse trophoblast stem cells into a specialized cell type called giant cells requires Hand1, a bHLH transcription factor. Hand1 interacts with a wider variety of other bHLH partners than do others of its class. The authors thus wondered whether it might also interact with unrelated partners that help it time giant cell differentiation. Using a yeast two-hybrid approach, they found that Hand1 bound to a nucleolar subunit of a protein called HIC.

While Hand1 hung out with HIC in the nucleolus, trophoblast cells did not differentiate. But Hand1 exited the nucleolus at the time of their differentiation to giant cells. This exit required the phosphorylation of Hand1.

The kinase that phosphorylated Hand1, called Polo-like kinase 4, is evolutionarily conserved. Phosphorylation-dependent release of transcription factors from the nucleolus may turn out to be a widespread mechanism to control their activity.

Reference: Martindill, D.M.J., et al. 2007. Nat. Cell Biol. doi:10.1038/ncb1633.