

Ping pong in the pore

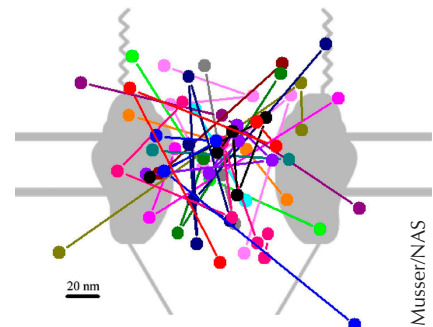
Proteins traversing the nuclear pore complex (NPC) bounce back and forth within the central pore until they are finally expelled, according to Weidong Yang, Jeff Gelles, and Siegfried Musser (Texas A&M University System Health Science Center, College Station, TX).

The group imaged single import complexes (ICs)—importin(s) and cargo—interacting with NPCs. Trajectories of the ICs within the pore indicate rapid, random movement forward and backward.

One transport model proposes an affinity gradient across the pore between ICs and pore components, but the back and forth movements do not support

this model. Rather, the data suggest that molecules move randomly within the pore and exit either side. “If the IC enters the pore and reexits the same side,” says Musser, “no net energy went in, so you’ve lost nothing. But if the IC gets out the other side, it can be dissociated by RanGTP, and you’ve [achieved] transport.”

The distribution of the time an IC resides within a pore suggests there is only one rate-limiting step during import. When RanGTP was depleted, ICs lingered longer in the pore, so RanGTP-mediated dissociation is probably this limiting step. Since dissociation is expected to occur on the nucleoplasmic side, the IC may need to land close enough to the pore’s edge to encounter RanGTP and exit. ■



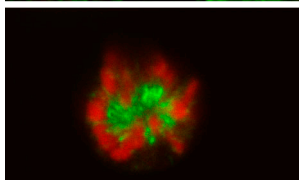
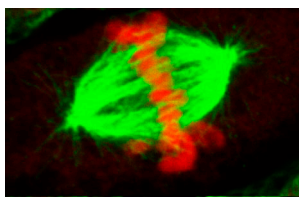
ICs move randomly within the central nuclear pore.

plasmic side, the IC may need to land close enough to the pore’s edge to encounter RanGTP and exit. ■

Reference: Yang, W., et al. 2004. *Proc. Natl. Acad. Sci. USA*. doi:10.1073/pnas.0403675101.

Division at right angles

A misoriented mitotic spindle may be a short cut to metastasis, based on results from Jurii Vasiliev (Moscow State University, Russia), Edward Bonder (Rutgers University, Newark, NJ), and colleagues.



Bonder/NAS

A spindle turned perpendicular (bottom) to the surface leaves only one daughter on the matrix.

Cells in an epithelial layer normally divide perpendicular to their surface; each daughter cell thus remains in contact with the matrix and surrounding cells. The new results show that cells with too much RhoA activity, as found in several cancer cell lines, lost the spindle orientation needed for this perpendicular division. Many of the cells thus made a spindle that left only one daughter on the matrix.

The other cell, atop its matrix-bound sister, lacked the spread phenotype of matrix-attached cells. Due to inadequate cell–cell adhesions, these rounded cells occasionally detached

from the epithelium, floated off in the medium, and settled at new sites.

Cells with overactive RhoA were more contracted and had altered actin networks suggestive of hyperactive myosin II. Blocking myosin II activity reversed the RhoA effects. Bonder now wonders, “does myosin II activity alter the movement of the formed spindle relative to the cell itself, or is the process of forming the spindle aberrant from the very start?”

The results suggest that cancerous cells may not have to acquire the ability to migrate to metastasize. “[Unregulated] cell division would lead not only to increased tumor mass,” says Bonder, “but could also be squirting out cells.” Circulatory flow could then sweep off some of these cells and deposit them elsewhere. ■

Reference: Vasiliev, J.M., et al. 2004. *Proc. Natl. Acad. Sci. USA*. doi:10.1073/pnas.0404723101.

Getting to the inner circle

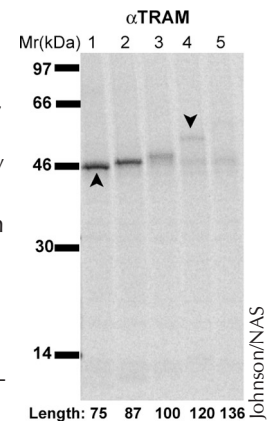
Contiguity between the ER and the nuclear envelope means nuclear membrane proteins have a direct shot to their target. In fact, inner nuclear membrane (INM) proteins were thought to need only to diffuse to the nucleus, pass through the nuclear pore, and then be retained by nuclear-localized binding partners. But new results suggest a more active process.

Suraj Saksena, Arthur Johnson, and colleagues (Texas A&M University, College Station, TX) now show that INM-bound proteins are sorted as they enter the ER through the translocon. They find that transmembrane sequences of both viral and mammalian INM proteins cross-link to Sec61 α and TRAM, which are fundamental translocon proteins. Association with TRAM continues even though the growing peptide is long enough to release the transmembrane segment into the bilayer.

Only two native non-INM proteins have been found to be adjacent to TRAM. “This sent us a signal that TRAM might act as a recognition component,” says Johnson. “This goes along with my belief that the cell doesn’t let anything happen randomly.”

After leaving the translocon, the viral INM proteins were handed off to other viral proteins that are known to be needed for INM targeting. Now, the authors are seeking the endogenous nontranslocon components that take care of this job. ■

Reference: Saksena, S., et al. 2004. *Proc. Natl. Acad. Sci. USA*. doi:10.1073/pnas.0404934101.



Lasting proximity to TRAM indicates active sorting to the INM.