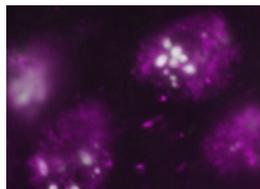


## Paraspeckles may provide stress relief



Paraspeckles stand out in the nuclei of stomach epithelial cells.

The enigmatic nuclear structures known as paraspeckles may only be necessary during times of stress, Nakagawa et al. report.

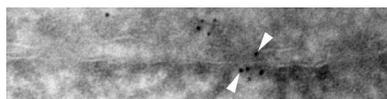
Discovered in 2002, paraspeckles stick close to the larger and better-known splicing speckles that help edit mRNA. Paraspeckles harbor RNA and protein, but researchers aren't sure what they do.

To help pin down their function, Nakagawa et al. analyzed gene expression in different mouse tissues. The noncoding RNA NEAT1\_2, a component of

paraspeckles, was abundant only in a few cell types, such as the epithelial cells in the linings of the stomach and colon. By contrast, paraspeckles show up in almost all kinds of cultured cells.

The researchers eliminated paraspeckles from mice by deleting the NEAT1 gene. The animals were apparently healthy, suggesting that the loss of paraspeckles was no handicap, at least for life in cushy laboratory conditions. However, paraspeckles may help cells cope with stress. One pressure that could induce formation, the researchers suggest, is infection—previous studies have found that pathogens such as the rabies virus activate the NEAT1 gene. Nakagawa et al. say that future work should determine whether NEAT1-lacking animals can fend off infections and whether abnormalities appear in specific tissues or as the mice age. Nakagawa, S., et al. 2011. *J. Cell Biol.* doi:10.1083/jcb.201011110.

## Multiple routes to the inner nuclear membrane



Gold particles mark the location of the INM protein NET39 in the ONM (downward arrowhead) and in the INM (upward arrowhead).

At least four mechanisms can usher inner nuclear membrane (INM) proteins to their proper location, Zuleger et al. show.

A freshly made membrane protein can diffuse through the ER to the outer nuclear membrane (ONM), but reaching the INM is trickier. Researchers think that proteins cross from the ONM to the INM via nuclear pore complexes. However, instead of using the pore's front door, the central channel, they use peripheral channels as side entrances. How proteins traverse these small-bore structures has remained mysterious. Some previous studies suggested that proteins diffuse between the ONM and INM, whereas other work indicated that this movement requires ATP or the nuclear transport factor Ran.

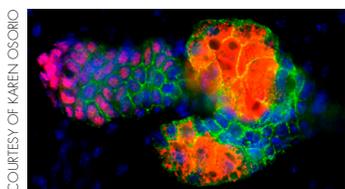
Zuleger et al. performed photobleaching experiments to test the different proposed mechanisms for six INM proteins. Two proteins required ATP but not Ran to reach their destination. Another protein needed Ran but not ATP. The remaining three proteins apparently traveled by diffusion.

When helping to ship proteins through the central nuclear pore channel, Ran separates a soluble cargo molecule from its transport receptor after the pair have crossed the channel. But the combination of Ran, a transport receptor, and an INM protein is too hefty to fit through the narrow peripheral channels. Thus Ran might function differently during peripheral channel transport.

A fourth mechanism also could give certain INM proteins a helping hand. The researchers found that proteins moved faster when they carried stretches of phenylalanine-glycine repeats, and this effect disappeared when a peripheral channel nucleoporin that also sports the repeats was absent. Interactions between these repeats might allow INM proteins to function as their own transport receptors.

Zuleger, N., et al. 2011. *J. Cell Biol.* doi:10.1083/jcb.201009068.

## Wnt sends mixed signals in the skin



A hair follicle from a mouse lacking Runx1 in the dermis is aglow with the Wnt activator Lef1 (red).

Osorio et al. reveal that Runx1 has opposing effects on the Wnt pathway in the two layers of the embryonic skin, thus ensuring that hair follicles have plenty of stem cells.

A hair follicle goes through cycles of growth, regression, and inactivity. Hair follicle stem cells (HFSCs)

provide fresh cells for the follicle's resurgence. The researchers previously showed that, in adult mice, Runx1 helps activate HFSCs and spurs them to divide. During embryonic development, Runx1 helps determine which cells will become hematopoietic stem cells that spawn new blood cells. Whether the protein performs a similar function for HFSCs during development was unknown.

Osorio et al. deleted Runx1 from either the epithelial or mesenchymal skin layers in embryonic mice. Loss of the protein from the skin's epithelium only delayed the appearance of hair follicles and progenitors of adult HFSCs, suggesting that Runx1 in this layer isn't essential for their development. Losing Runx1 from the mesenchyme, on the other hand, caused hair follicles to gradually degenerate and form oily cysts, indicating that the HFSCs adopted a sebaceous gland fate and failed to self-renew.

The Wnt signaling pathway orchestrates hair development. The team found that epithelial Runx1 revs up this pathway by boosting expression of Lef1, an activator of several Wnt-regulated genes. But in the mesenchyme, Runx1 quashed Wnt signaling. The researchers think that these opposing effects of Runx1 promote the origin and maintenance of HFSCs by controlling communication between the two skin layers.

Osorio, K.M., et al. 2011. *J. Cell Biol.* doi:10.1083/jcb.201006068.