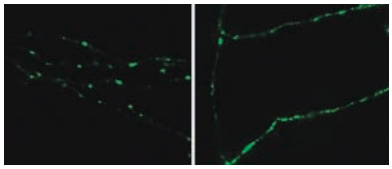
TEXT BY WILLIAM A. WELLS
WELLSW@ROCKEFELLER.EDU

Catenin keeps vesicles close

Synapse creation and maintenance takes more than the transport of proteins to the correct site, according to Shernaz Bamji, Louis Reichardt (University of California, San Francisco, CA), and colleagues. They find that synaptic vesicles are kept localized, ready for action on the presynaptic side, thanks to a PDZ-binding domain on β-catenin. The β-catenin is localized by cadherin adhesion proteins, thus linking axon–dendrite adhesion to the localization of presynaptic vesicles.

Loss of β-catenin is not exactly disastrous. Mice with β-catenin deleted from hippocampal neurons after synapse formation showed normal levels of docked neurotransmitter vesicles, and broadly similar short-term responses to stimulation. But, in the mutants, nondocked vesicles were not as well localized at the site of action, so prolonged stimulation led to a faster drop-off in transmission. Similar results were seen in vitro after expression of a β-catenin lacking its PDZ-binding domain.



Reichardt/Elsevier

Without β-catenin (right), synaptic vesicles (green) wander away from synapses.

With β-catenin functioning as a scaffold, "it's not clear to me how much adhesion you need as opposed to signaling," says Reichardt. "Cadherins do nucleate this diversity of signaling pathways. Whether you need contact [between axon and dendrite] because that nucleates something or contact because that puts you into position [for signaling] is not known." ■

Reference: Bamji, S.X., et al. 2003. *Neuron.* 40:719–731.

S is for sticky

A kinase better known for triggering DNA replication also helps create the sticky heterochromatin at centromeres of fission yeast, according to Julie Bailis, Susan Forsburg (Salk Institute, La Jolla, CA), and colleagues.

Forsburg/Macmillan

Centromeres fall apart (right) without Hsk1 action in S phase.

The dual action makes sense, as chromosomes must be stuck together as soon as they are replicated. The responsible kinase activity, Hsk1 (CDC7)–Dfp1, is restricted to S phase, when DNA replication takes place.

Dfp1 turned up in a two-hybrid screen with Swi6, the fission yeast equivalent of heterochromatin protein 1 (HP1). Cells with a mutant Dfp1 that no longer binds Swi6 can replicate their DNA but suffer segregation errors when their defective centromeres fall apart. Swi6 localization is normal in these cells but, based on in vitro results, Swi6 phosphorylation may be reduced. This is the first indication that Swi6 localization is not sufficient to define heterochromatin function.

An interesting parallel is known in budding yeast, where establishment of silent heterochromatin at the mating type locus requires passage through S phase, though not DNA replication. Budding yeast lacks an HP1 homologue, but perhaps other proteins serve an equivalent heterochromatic function. ■

Reference: Bailis, J.M., et al. 2003. *Nat. Cell Biol.* 10.1038/ncb1069.

Worms delay in deep sleep

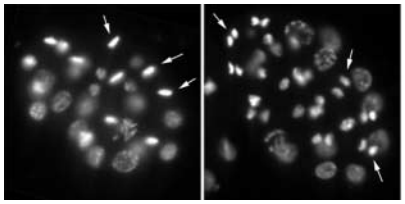
Worms deprived of all oxygen can pause, take a deep breath, and enter a suspended animation from which they can emerge unscathed several days later. Now, Mark Roth (Fred Hutchinson Cancer Research Center, Seattle, WA) and colleagues show that these worms use the spindle checkpoint to prevent passage through mitosis during anoxia. This arrest is essential for the worms' survival.

The Seattle group knew that the anoxic response was not just an exaggerated version of the hypoxic (low oxygen) response, because hypoxia-inducible factor 1 (HIF-1) was not needed for survival in anoxia. They conducted an RNAi screen, and found that two genes are uniquely required for survival in anoxia: *san-1* (suspended animation 1, which is similar to the spindle checkpoint gene *mad3*) and *mdf-2* (similar to *mad2*). Worm embryos lacking either protein die after their cells fail to arrest in metaphase during anoxia.

Anoxic worm cells arrest at several points in the cell cycle, presumably using a variety of proteins to mediate these arrests. And the cell cycle is not an anoxic worm's only concern. "There are some pretty profound things it has to think about to do with bioenergetics," says Roth. Entropy must be fought, and in particular ion gradients need to be maintained. "If you don't do that," says Roth, "you're dead."

The details of how that is achieved remain a mystery, but Roth has ideas about the general goal. For an anoxic worm, he says, "you may not have the furnace, but you better not blow out the pilot light. We think glycolysis is the pilot light."

Anoxic survival capabilities extend up to larger animals—pigs can have all their blood replaced by salt solutions for up to two hours, then recover and show normal memory retention and learning. These pigs, and humans who suffer massive blood loss, are helped by treatments that lower core body temperatures. Roth hopes that lessons from worms will enable more directed treatments so that humans can perhaps match worms in their feats of reanimatology.



Roth/AAAS

In anoxic worms, metaphase arrest (left, arrows) slips into anaphase (right) when *san-1* is defective.

Reference: Nystul, T.G., et al. 2003. *Science.* 302:1038–1041.