Waltz of the chromosomes

During interphase, chromosomes are supposed to be as immobile as a sailboat on a windless day. But according to a new study, chromosomes are more active than anyone thought, hustling around the nucleus at a speed of up to three microns a minute. The nonrandom movements require energy and may prepare DNA for transcription, the researchers believe.

To track these movements, Susan Gasser of the University of Geneva (Geneva, Switzerland) and colleagues used GFP to tag four positions on two yeast chromosomes. Although the centromeres and telomeres are tethered to the edge of the nucleus and move little, the chromosomal arms are mobile and may traverse one third the diameter of the nucleus in as little as 10 s. Previous workers may not have noticed the movements because they are less obvious in the much larger mammalian nucleus, says Gasser. She showed that adding carbonyl cyanide chlorophenyl hydrazone, which drains the cell’s ATP, hampered mobility, thus eliminating the possibility that chromosomes were simply drifting like seaweed in the tide. Movements also became smaller once DNA replication began.

“Replication complexes sit like a dead weight on the chromosome and slow it down,” says Gasser.

What does the cell accomplish by expending energy to tug its chromosomes around? According to Gasser, experiments on mutants suggest that movements may be a prelude for transcription, allowing the chromosome to hook up to nucleosome remodeling factors that give transcription factors access to genes. Or they may allow homologous chromosomes to sidle up next to each other and swap snippets of DNA.

Reference: Heun, P., et al. 2001. Science. 294:2181–2186.

Grow-your-own synapses

Many neuroscientists are convinced that learning and experience rewire the brain, but they have never been able to observe the process. For the first time, a team of researchers has seen the formation of new synapses by using a novel technique for exciting individual neurons in culture.

To show that learning changes brain circuitry, scientists have relied on indirect evidence—before and after counts of the number of synapses in particular regions. To nab direct evidence of neural remodeling, Yukiko Goda (University of California, San Diego, CA) and colleagues used light to trigger a current through coupled neurons resting on a silicon chip. Then they observed the response of the actin cytoskeleton of the presynaptic and postsynaptic terminals, and were able to detect changes in individual synapses.

Repeated stimulation triggered action on both sides of the synapse. On the presynaptic side, actin networks changed shape to form projections, or puncta, some of which developed into functional presynaptic terminals with vesicles for recycling neurotransmitters. The postsynaptic side also sent out extensions that cozied up to the puncta that formed on the presynaptic side, thus completing the new synapses. This is the first direct demonstration of neural remodeling of brain synapses at the cellular level, says Goda. “We have a very conclusive demonstration of activity-induced remodeling,” she says. “We were able to capture it as it happened.” One of the key mysteries left to solve, she says, is how the electrical signal gets translated into morphological change.

Reference: Colicos, M.A., et al. 2001. Cell. 107:605–616.

The good side of a maligned protein

Scientists have discovered a new function for amyloid precursor protein (APP), a protein linked to Alzheimer’s disease. The finding may reveal how APP gets mixed up with the enzymes that make it go bad.

APP has an evil reputation. The β and γ secretases transform it into amyloid-β peptide, a component of the plaques that riddle the brain in Alzheimer’s disease. Previous work by Larry Goldstein (University of California, San Diego, CA) and coworkers suggested that APP normally links to kinesin, a protein that tows vesicles and organelles around the cell. Now Goldstein and colleagues have bolstered this hypothesis by examining neurons from APP-deficient mice. They found that the protein cargoes usually transported by kinesin couldn’t travel along the axon, whereas proteins not hauled by kinesin could. The researchers conclude that APP serves as a trailer hitch, coupling the membrane of a vesicle or organelle to kinesin.

It turns out that two of the proteins moved by kinesin are the β-secretase and APP, which colocalize in mouse sciatic nerve.

“The results may give us some clues as to why neurons die in the disease,” says Goldstein. One possibility is that increased cleavage of APP, perhaps triggered by an injury, may foul up transport along the axons—in effect creating a fatal intracellular traffic jam.

Reference: Kamal, A., et al. 2001. Nature. 414:643–648.