Radiation can harm cells even if they don’t take a direct hit, according to a new study. Injured cells apparently pass on damage to neighboring cells through gap junctions. The report has raised a ruckus because it suggests that current safety standards may underestimate the hazards from low-level radiation exposure.

Although some scientists suspected that radiation damage might spread from cell to cell—the so-called bystander effect—only the development of a technique for targeting individual cells allowed them to confirm the idea. The researchers were able to fire a single particle at individual cells, so they knew exactly how many cells had absorbed hits. They used the absence of the CD59 antigen on the cell surface as an indicator of mutation. Zapping only 10% of the cells in a solution caused the same number of mutations as hitting 100% of the cells, the researchers found. “We had just assumed that, when you irradiated a population of cells, the damage was due to a direct hit by the particles,” says James Trosko of Michigan State University (East Lansing, MI).

The next step was to test the idea that some kind of damage signal spreads from the targeted cell to its neighbors through gap junctions, which chemically and electrically couple cells. When the authors doused the cells with octanol, which jams gap junctions, they found that the number of mutations fell by nearly 80%. Trosko says they have no idea what is spreading through the gap junctions to the bystanders, except that it must be smaller than 1,000 D to fit through the channel.

The study could force regulators to rethink radiation safety standards, says Trosko. Guidelines for low-level exposure are based mainly on extrapolations from studies of atomic bomb survivors and assume that risk declines linearly with dose. By revealing that small doses can have disproportionately large effects, the work suggests that current standards may not be formulated correctly, he says. But he cautions that further studies using additional markers for genetic damage are necessary, and that no one knows whether other sorts of radiation have similar effects.

Reference: Zhou, H., et al. 2001. Proc. Natl. Acad. Sci. USA. 98: 14410–14415.

**Numbers game**

Although gigantic basketball player Shaquille O’Neal may dwarf us mortals, his cells are no bigger than yours or mine. He just has more of them. But how vertebrates regulate their cell number has been as puzzling as Shaq’s inability to shoot free throws. Now, a team of researchers has pinpointed a gene that helps determine body size in vertebrates by controlling cell division. The findings support the notion that vertebrates govern body size by regulating cell number, whereas insects vary both cell size and cell number.

Andreas Trumpp (Swiss Institute for Experimental Cancer Research, Epalinges, Switzerland) and colleagues focused on c-myc, a proto-oncogene that is mutated or overexpressed in 20% of human cancers and was suspected to be a cell division regulator. Recent fly studies had challenged this view, says Trumpp. Reducing the levels of dmyc, the fly homologue of c-myc, produced smaller animals that also sported smaller cells, providing strong evidence that the gene’s function was to govern cell growth.

To check this surprising result, Trumpp and colleagues created transgenic mice with reduced levels of c-Myc. The rodents were smaller than normal, but had normal-sized cells. Studies with T cells were consistent with this function of c-Myc in controlling cell number rather than cell size. Activated T cells balloon before beginning to proliferate, and the authors found that T cells carrying mutant forms of c-myc still underwent this growth spurt but rarely entered the cell cycle. Thus, c-Myc regulates proliferation, ushering cells into the cell cycle and keeping them on the path to division.

Dmyc can stimulate division in mouse cells lacking c-myc. According to Trumpp, this argues that the differences between vertebrates and insects lie in the downstream pathways, although the identities of the target genes remain unknown.

Reference: Trumpp, A., et al. 2001. Nature. 414:768–773.
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 movements 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 cozed 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.

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