

Research Roundup

Greater risk from radiation?

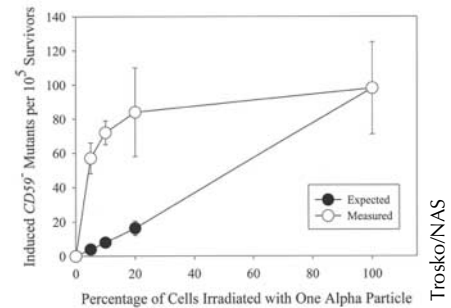
Radiation can harm cells even if they don't take a direct hit, according to a new study. Injured cells apparently pass on damage to neighboring cells through gap junctions. The report has raised a ruckus because it suggests that current safety standards may underestimate the hazards from low-level radiation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



Many mutations occur at low dosages.

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

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



Less Myc makes smaller mice.

Numbers game

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.