Electric healing

Wounds have electrical fields that help cells to flood into and heal them, according to Min Zhao (University of Aberdeen, UK), Josef Penninger (Institute of Molecular Biotechnology, Vienna, Austria), and colleagues.

For over a decade, Zhao has been studying how cells migrate in response to electrical fields. It has been a lonely field, however. Electricity does not fit easily into the gene–protein paradigm of cellular control, and the field’s reputation was tainted by some poorly controlled experiments conducted early in the 20th century.

Now, Zhao and colleagues have confirmed claims first made more than 150 years ago that wounds generate electrical fields. There is normally a potential difference between basal tissue layers and apical skin surface—a difference generated by transport of Cl⁻ ions outwards and Na⁺ ions inwards. But this potential difference is short circuited by a wound. The wounded basal edge becomes electrically more like an apical surface, so that now the potential difference is between this damaged basal edge and the undamaged, internal basal tissue. The result is an electrical field directed into the wound.

The researchers found that electrical fields of this magnitude could direct cell migration both in vitro and in vivo, either slowing or accelerating wound healing, depending on the field directionality. The correlation between the magnitudes of naturally occurring and experimentally effective field potentials “got us more and more excited and thinking this is a real phenomenon,” says Zhao.

The pathway required PI3Kγ and was enhanced by loss of PTEN. These proteins are well known as mediators of chemotactic signaling, but with a whole genome screen the group hopes to discover molecules unique to electrotaxis. JCB

Reference: Zhao, M., et al. 2006. Nature. 442:457–460.

Relaxing after damage

Phosphorylated KAP-1 fans out from DNA damage sites, spreading a message of chromatin relaxation, according to Yael Ziv, Yosef Shiloh (Tel Aviv University, Tel Aviv, Israel), and colleagues. The temporary relaxed state may allow proteins that detect and repair damage to gain better access to DNA.

Chromatin relaxation after DNA damage has been seen before but has been primarily a local effect at the site of damage. The Israeli group, however, documented a global effect that increased susceptibility to nuclease digestion throughout the genome.

The relaxation begins with the damage-detecting ATM kinase. The researchers found that ATM phosphorylates KAP-1, previously known as a transcription corepressor, and that this phosphorylated form spreads within minutes from the damage sites to a pan-nuclear localization. The result is a transient chromatin relaxation that lasts an hour or so. KAP-1 lacking the critical phosphorylation site does not induce relaxation.

“The phosphorylated KAP-1 “is carrying a message to the chromatin,” says Shiloh. “If we had used 10 or 11 minutes as our first timepoint [it would have spread already and] we would have lost a critical element of this story.”

“The group is now looking for proteins that interact with KAP-1 only before or only after phosphorylation, and for proteins or modifications that define the relaxed DNA state. The effect of that relaxed state is unknown; one possibility is that it helps the transcriptional apparatus to scan DNA for further damage. JCB

Reference: Ziv, Y., et al. 2006. Nat. Cell Biol. doi:10.1038/ncb1446.

Making a single centrosome

Separase cuts sister chromosomes apart at the end of mitosis. The same enzyme also, say Meng-Fu Bryan Tsou and Tim Stearns (Stanford University, Stanford, CA), releases a block to centriole and thus centrosome duplication. “It’s so simple to have separase involved in both processes, because it is so critical to not do either one prematurely,” says Stearns. “It does make perfect sense that it is arranged this way.”

Microtubules can focus to form an organizing center in several ways, but “in dividing cells, the centrosome is the main player,” says Stearns. “And if you control centriole number you’ve controlled centrosome number.”

His group found recently that there is a block to reduplication that is intrinsic to centrosomes rather than being determined by the cytoplasm surrounding them. This block is now found to be released not by mitotic exit or by G1 kinase activity but by separase activity.

The separase disengages each tightly apposed pair of centrioles—a process that is subtle in cultured cells but more obvious in frog extracts where there is no G1 phase. During the subsequent cell cycle, a new centriole then forms orthogonal to each of the two disengaged centrioles. The visible fibers that connect daughter centrioles may contain a separase substrate, but there are no obvious candidates as yet. JCB

Reference: Tsou, M.B., and T. Stearns. 2006. Nature. doi:10.1038/nature04985.