Early replication for short telomeres

Like first-class airline passengers, short telomeres get preferential treatment. They cut to the front of the line during DNA replication, according to Alessandro Bianchi and David Shore (University of Geneva, Switzerland).

The shortening of telomeres with each cell division is counteracted by telomerase, which extends these repetitive sequences that cap the ends of linear chromosomes. The squeaky telomere gets the grease, however, as shorter ends seem to recruit or activate more telomerase.

Bianchi and Shore set out to examine the basis of this inequality by comparing individual short and long telomeres. “We expected to see a quantitative difference in the binding of telomerase or Cdc13, which activates it,” says Bianchi. “But instead we noticed a shift in the replication timing.” Shorter telomeres were replicated earlier in S phase.

The early start comes from an earlier firing of replication origins. Origins near long telomeres consistently fired late, but those near short telomeres were more likely to fire early. The mechanistic basis of this difference is still unclear.

The head start on replication corresponded with the creation of longer telomeres. Longer extension may be due to the noted advanced arrival of Cdc13 to early firing origins along with DNA polymerase. Telomerase inhibitors, on the other hand, were not affected by replication timing. JCB

Reference: Bianchi, A., and D. Shore. 2007. Cell. 128:1051–1062.

The pore slides open

Structures of a nuclear pore protein, presented by Ivo Melčák, André Hoelz, and Günter Blobel (Rockefeller University, New York, NY), suggest that the pore’s central channel expands by an unusual sliding between hydrophobic residues.

The crystals reveal structures of one of the four nucleoporins that make up the main channel. The authors suggest that the pore is encircled by eight side-by-side tetramers of this nucleoporin, called Nup58/45. The tetramer came in two forms; in one, the dimer–dimer interface was laterally displaced by ~6 Å compared with the other.

Most protein interfaces depend on hydrophobic residues. But in Nup58/45, an electrostatic dimer–dimer interface permits expansion by allowing alternative hydrogen bond pairings. Hoelz describes this interaction as “the opposite of a leucine zipper.” Intermediate steps that resemble sliding-like movements are probable.

Because each structure was equally abundant in the crystals, the authors propose that little energy is required to switch between the states. Perhaps only the binding of the cargo complex is needed.

If each tetramer is at full extension, the pore diameter might widen by 30 Å, probably during the export of large cargo such as preribosomal subunits. Perhaps the other core pore proteins have similar sliding mechanisms. How accessory proteins alter the situation will be studied for years to come. “There are so many proteins involved,” says Hoelz. “I think that the nuclear pore complex will be full of surprises like [this one].” JCB

Reference: Melčák, I., et al. 2007. Science. 315:1729–1732.

Plant hormone is human cytokine

Human hormones don’t arouse plants’ desires. But plant hormones can be stimulating to humans—or at least to their immune cells—based on new work from Santina Bruzzone, Elena Zocchi (University of Genova, Genoa, Italy), and colleagues. The authors identify the plant hormone abscisic acid (ABA) as a human cytokine.

In plants, ABA triggers stress responses such as seed dormancy and stomatal closing. Zocchi previously found that very simple animals such as sponges also use ABA-driven pathways to respond to light and heat. She now finds that ABA’s reach extends to mammals.

For humans, the first cells to be exposed to environmental stresses are often immune cells. The group’s results show that phagocytosing immune cells called granulocytes synthesize ABA in response to high temperature, like that of a fever.

The ABA calls in more granulocytes, and possibly other immune cell types, by activating chemokinesis. It also stimulates phagocytosis and the production of reactive oxygen species (which help kill pathogens) and nitric oxide (another cytokine).

As in plants, the biochemical pathway that activates granulocyte ABA responses induced intracellular calcium increases via cyclic ADP–ribose. “The capacity to respond to environmental stimuli through biochemical events is really at the heart of life,” says Zocchi. It’s no surprise then that it has been so highly conserved. JCB

Reference: Bruzzone, S., et al. 2007. Proc. Natl. Acad. Sci. USA. 104:5759–5764.