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THE CHALLENGE

The presence or absence of just a few letters of DNA on the end of a chromosome can mean the difference between a young cell and a cell at the end of its life span. The length of these telomeres—the physical ends of chromosomes—is controlled by an intricate balancing act: A protein complex called telomerase elongates these ends, but other proteins nibble away at them. If telomeres are too eroded, particularly in stem cells that replenish tissues later in life, this contributes to age-related diseases; but in cells where telomerase prevails, cancer can result. If they could control this balancing act, researchers might be able to treat conditions on both ends of the spectrum. But scientists don't yet fully understand these molecular processes and how cells maintain a healthy equilibrium.

THE APPROACH

Vicki Lundblad employs a single-cell genetic system to study the interplay between the activities that lengthen and shorten telomeres. Her group tweaks specific genes in baker's yeast (the same organism used to make bread and wine), and observes how chromosome ends respond. Using this strategy, her laboratory pioneered the discovery of the protein subunits of telomerase and uncovered mechanisms that control telomere shortening. Lundblad's group also developed a high-resolution assay that detects very small changes at each telomere as a cell divides. Using this assay, her group has identified a protein complex that inhibits telomere shortening while it promotes telomerase action. Since these telomere-related proteins are present in mammals, her research also holds lessons about human telomere length control.

THE INNOVATIONS AND DISCOVERIES

- Lundblad has shown that telomerase is switched on just as a cell has finished copying its genetic material, and then rapidly switched off, through assembly and disassembly of its protein subunits. Learning how to control these switches could allow researchers to turn telomerase activity up in aging cells or down in cancer cells.
- Her lab also discovered a hidden regulatory landscape on the surfaces of cellular proteins, which act as traffic cops for telomerase. For example, one such surface on a protein ensures that telomerase can find its way to the physical ends of chromosomes.
- Lundblad's group has engineered yeast cells that lack telomerase, to study how cells respond to eroding telomeres when telomerase is not present to counter-balance. By watching progressive cell divisions, they have identified new mechanisms that can either accelerate or slow down the process by which cells age.

For more information, please visit:
WWW.SALK.EDU/SCIENTIST/VICKI-LUNDBLAD

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