

# Single-DNA images give clues to breast cancer

**For the first time, researchers at the University of California, Davis, have watched single strands of DNA being prepped for repair. The research, published this week in the journal *Nature*, has implications for understanding the origins of breast cancer.**

"It's clear that in cells, DNA breaks all the time, and there's machinery to repair those breaks and retain genetic integrity," said Stephen Kowalczykowski, distinguished professor of microbiology and of molecular and cellular biology at UC Davis. Kowalczykowski is senior author of the paper.

To repair a break in the DNA double helix, a single strand has to seek out and find its matching sequence on the opposite strand—a task that Kowalczykowski compares to finding a needle in a haystack. To do that, the single strand first has to be coated with a protein called RecA.

"The RecA/DNA filament is the machine that looks for that needle," he said.

In the new study, graduate student Jason Bell used technology developed in Kowalczykowski's lab over the past decade to image individual strands of bacterial DNA as they were coated with a protein called RecA. Studying how this process works gives insights into the "mediator" proteins responsible that facilitate it, Kowalczykowski said. In humans, one of those mediators is the protein BRCA2, which is strongly associated with breast cancer.

RecA, called Rad51 in humans, helps the single strand of DNA find its complementary, matching strand elsewhere in the chromosome. The RecA protein has to displace another protein, imaginatively named single-strand DNA-binding protein, to get to the DNA.

The researchers were able to watch in real time as the RecA units displaced single-strand DNA-binding proteins and then spread in both directions until the whole strand was covered.

They found that the process has to start with two molecules of RecA attaching to the DNA. Then single molecules of RecA can be added at either end, similar to adding beads on a string.

One surprise was that in the absence of mediators, the process was relatively slow, Kowalczykowski said. It took about 30 minutes to coat a strand—longer than the time *E. coli* takes to go through a cell division cycle.

The mediator proteins are crucial for controlling the speed at which RecA assembles on the single strand of DNA, Kowalczykowski said. Too slow, and DNA breaks would not be repaired properly; too fast, and it would capture and coat the short pieces of single-stranded DNA briefly produced during normal DNA replication. Instead, the process only works on DNA that persists because it is actually damaged or broken.

"I'm sure that BRCA2 works in the same way," he said.

Provided by UC Davis

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