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Rad51: Watching Single Strands Of DNA Being Prepped For Repair Could Help Fight Breast Cancer

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Watching single strands of DNA being prepped for repair may help researchers understand the origins of breast cancer.

In a new study, graduate student Jason Bell imaged 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. 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.

Proteins assembling on single-strand DNA . Videography by Jason Bell and Steve Kowalczykowski

"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 at UC Davis and 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.

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.

Published in *Nature*. Co-authors are postdoctoral researchers Jody Plank and Christopher Dombrowski.

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