

# Scientists reveal how proteins team up to repair DNA

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Scientists have revealed an important mechanism in the repair of DNA double-strand breaks, according to new research published today in *eLife*.

The discovery will help our understanding of why DNA repair processes do not work properly in some people, causing inherited diseases and cancer.

One of the main DNA repair processes is called homologous recombination (HR). This repairs a severe form of DNA damage where both strands of DNA are broken. A [protein](#) called Rad51 orchestrates HR, and Rad51 itself is supported by several 'helper' proteins.

"We already know that a group of helper proteins can be sub-grouped into two modules, and that each [module](#) has a different role," says lead author Bilge Argunhan, a researcher in senior author Hiroshi Iwasaki's lab at the Tokyo Institute of Technology, Japan. "In this study, we aimed to understand exactly how Module 1 interacts with Rad51 and how the two modules cooperate to switch on Rad51."

The researchers started by using [yeast](#) cells to study Rad51 and its helper proteins, called Swi5-Sfr1. They genetically engineered yeast cells so that they lacked either Module 1 or Module 2 of Swi5-Sfr1 and found that this prevented DNA repair by HR. This shows that both modules are needed for Rad51 to switch on HR repair.

Next, they purified the Swi5-Sfr1 helper proteins from cells to identify the precise regions within Module 1 that attach to Rad51. Then, by mutating the [protein sequence](#), they were able to modify these regions in a way that prevents Swi5-Sfr1 from attaching to Rad51. Surprisingly, they found that although the mutated helper proteins could not switch on Rad51 in a [test tube](#), [yeast cells](#) with these mutations were still able to repair their DNA without problems. This led the team to speculate that another group of helper proteins, which are present in the cell but absent in the test tube, was rescuing the DNA repair process.

Previous genetic studies have shown that there are two HR sub-pathways in yeast—one that depends on Swi5-Sfr1 and another that relies on molecules called Rad51 paralogs. To test whether it was this other HR pathway that was rescuing DNA repair, the team used yeast that lacked the Rad51 paralogs. The results were striking: in yeast with mutant Swi5-Sfr1 and no Rad51 paralogs, the DNA damage was much more severe. This suggests that the damaging effects of mutations to the Swi5-Sfr1 helper complex are suppressed by a second group of helper proteins.

"Although these two groups of helper proteins were previously thought to function independently, our study shows that they actually work together to activate Rad51 in DNA repair," explains senior author Hiroshi Iwasaki, Professor at the Tokyo Institute of Technology. "The fundamental mechanisms of DNA repair are highly conserved from yeast to humans. Our new insight into DNA repair in yeast may serve as a template for

understanding why DNA [repair](#) processes do not function properly in human disease."

**More information:** Bilge Argunhan et al, Cooperative interactions facilitate stimulation of Rad51 by the Swi5-Sfr1 auxiliary factor complex, *eLife* (2020). [DOI: 10.7554/eLife.52566](https://doi.org/10.7554/eLife.52566)

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