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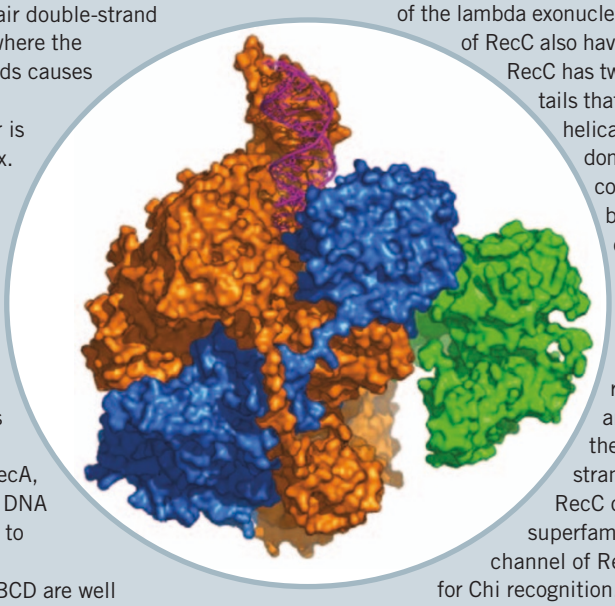
Rec-ing DNA

Double-strand DNA (dsDNA) breaks are caused most frequently by ionizing radiation. The breaks can cause cell death if not repaired, because they prevent the progression of polymerases along the DNA. The cell can repair double-strand breaks through recombination, where the reunion of the broken DNA strands causes a physical exchange of parts. In eubacteria, recombination repair is initiated by the RecBCD complex. RecBCD has a high affinity for blunt DNA ends and so is able to bind the damaged dsDNA. It also possesses helicase and nuclease activities that unwind and chew away dsDNA until the complex encounters a Chi (crossover hotspot instigator) site, a DNA sequence that favors recombination, on the 3′ strand. At the Chi site, RecBCD loads RecA, a recombinase that can catalyze DNA strand exchange, onto the 3′ tail to initiate recombination.



The multiple activities of RecBCD are well studied and can be mapped to its three components: RecB is a nuclease and 3′→ 5′ helicase, RecC recognizes the Chi site, and RecD has 5′→ 3′ helicase activity. To elucidate how RecBCD is able to perform these various tasks, Singleton *et al.* (*Nature* **432**, 187–193; 2004) have solved the structure of *Escherichia coli* RecBCD in complex with a dsDNA substrate, a 19 bp duplex with a 5 bp hairpin on one end and a blunt end on the other.

The structure of the complex shows DNA (purple) bound between RecB (orange) and RecC (blue). RecD (green) is located on the periphery of the complex and interacts with RecC. As had been anticipated, the DNA is bound to RecBCD with its blunt end lying in the complex and the last 4 bp unwound. Both RecB and RecD share structural similarity with members of the superfamily 1 group of helicases. The C-terminal portion of RecB has a fold similar to that of the lambda exonuclease core. Interestingly, two of the domains of RecC also have the same fold as superfamily 1 helicases. RecC has two channels that accommodate the ssDNA tails that run to and from the RecB and RecD helicase subunits. The third and final RecC domain interacts with RecB, makes extensive contacts with the two ssDNA strands, and bears a 'pin' that physically separates the duplex DNA before feeding the 3′ strand to RecB and the 5′ strand to RecD.

The structure of RecBCD reveals how nuclease and motor helicase activities are coupled, allowing for Chi site recognition. The helicase motors of RecB and RecD pull the DNA strands across the pin of RecC, splitting the duplex. Each strand of the DNA is passed through the RecC channels. The ssDNA-binding site in the superfamily 1 helicases corresponds to the 3′ tail channel of RecC, which the authors theorize is a site for Chi recognition. This is supported by previously identified mutations in this region that alter Chi site recognition. The 3′ tail exits from this channel and is passed directly into the nuclease domain of RecB, where it is digested processively. The 5′ tail must first be passed to RecD before reaching the nuclease domain, and is therefore cut less frequently. When a Chi site is recognized by RecC, it is able to bind tightly to the 3′ strand, preventing further digestion of this strand and allowing for more frequent cleavage of the 5′ tail. The challenge is now to understand the subsequent steps of recombination repair (which include recruitment of RecA to the 3′ tail) that allow double strand break repair to begin.

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