G. CEULENEER

Figure 1 **Rough country. The Oman ophiolite, one of the largest outcrops of ocean crust and upper mantle exposed on the continents, forms a 400-km-long part of the mountains of northern Oman.**

along present-day oceanic spreading centres. But no previous geochemical analysis of the Oman mantle rocks has been based on such a detailed field survey as that conducted by Le Mée and colleagues. Their high-resolution sampling along the 400 km of these rugged mountains took many months; Figure 1 shows the terrain they had to work in. This 'exploration geology' approach, with the ensuing analytical data firmly anchored in the context of field geology, is, alas, less and less in vogue in the academic community.

Back in the laboratory, Le Mée *et al.* found that the chemical composition of Oman mantle rocks varies considerably between samples. In particular, incompatible elements show significant variation: simple mass-balance considerations were used to calculate that the least-depleted samples correspond to a relatively low degree of partial melting (about 10%), whereas the more-depleted samples correspond to partial melting reaching 30%. This range is similar to that estimated from the composition of ocean-floor basalts[2].

Le Mée and colleagues' most notable result is related to the geographical distribution of their data. They show that the variations in composition of Oman mantle rocks are not random but have 'highs and lows', separated by tens of kilometres, allowing the authors to define a chemical segmentation of this fossil spreading centre. This pattern is reminiscent of those defined on a morphological and geochemical basis along certain segments of present-day oceanic spreading centres. Translated into mantle temperatures — not, as I've said, a straightforward exercise — these variations in chemical composition could correspond to temperature contrasts of several tens of degrees, which are high enough to drive mantle convection. In that respect, Le Mée *et al.* could have provided the missing link allowing us to relate segmentation of mid-ocean ridges to small-scale convection processes in the shallow mantle[5].

One possible confounding factor, however, is that a variable degree of partial melting is not the only way to account for the variable composition of residual mantle rocks. The shallow mantle may act as a 'reactive filter' whose composition, particularly in the concentrations of incompatible elements, may be permanently modified by complex reactions with magmas percolating to the surface[6]. Le Mée *et al.* have made every effort to sample areas apparently not affected by such mantle–melt reactions. But we cannot be entirely sure that they have avoided the cryptic effects of these reactions — effects that have changed mineral composition but not mineral proportions.

It is often the case that later studies fail to support this or that scientific model of a natural process, and such could be the fate of Le Mée and colleagues' interpretation of chemical variability at spreading centres in terms of partial melting. But the map they have patiently extracted from the barren desert rocks of Oman will endure: it will prove an invaluable document in debates about basalt composition, mantle processes and the thermal structure of the Earth. ■

*Georges Ceuleneer is at the Observatoire Midi-Pyrénées, CNRS, 14 Avenue E. Belin, 31400 Toulouse, France.*
*e-mail: georges.ceuleneer@cnes.fr*

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DNA repair

# Big engine finds small breaks

Anna Marie Pyle

When a break occurs in the DNA double helix, it must be dealt with rapidly. The structure of one of the cellular machines responsible is now revealed, offering insights into its impressive speed and flexibility.

A double-strand break in DNA is the cellular equivalent of a three-alarm fire. As any taxpaying citizen knows, most communities maintain an impressive collection of hardware for dealing with major emergencies. Cells are no different, and for bacteria, the RecBCD complex of proteins is the heavy machinery that rushes to the scene of the conflagration[1]. On page 187 of this issue, Wigley and colleagues[2] unveil the crystal structure of *Escherichia coli* RecBCD interacting with a DNA break. This remarkable structure helps us to visualize how the complex careers along the DNA, applies the brakes at a designated site, and chops up unwound DNA in its wake.

RecBCD aids in the repair of double-strand breaks that occur during normal DNA replication and as a result of damage by ionizing radiation[1]. It is a tight complex of three proteins, two of which, RecB and RecD, have the ability to unwind DNA (they are helicases). These two motors move in the same direction along a DNA double helix, but on opposite strands (hence they move with opposite polarity, RecB progressing in the so-called 3′ to 5′ direction, and RecD in the 5′ to 3′ direction). In this way, they can push together against a duplex section of DNA, opening it[3,4] (Fig. 1, overleaf). RecB also chops up the unwound DNA. RecC, meanwhile, has been implicated in the recognition of 'signal' sequences in DNA, known as Chi sequences (5′-GCTGGTGG-3′), that direct the complex to slow down[5]. Remarkable features of RecBCD include its unprecedented speed and processivity — its ability to remain associated with its substrate — together with a puzzling affinity for DNA that is terminated by a clean cut (a 'blunt end')[1].

The RecBCD structure now published by Wigley and colleagues[2] reveals an elaborate

complex of interlocked proteins that have invaded a DNA duplex, opened four base pairs of DNA and sent the separated single strands in opposite directions. The 3′-terminated strand is fed towards the RecB motor and the 5′-terminated strand is fed towards the RecD motor. RecC appears to manage this operation, holding the helicase domains of RecB and RecD in place, splitting the DNA and directing the orientation of the divided strands.

The structure is particularly significant because it provides a molecular framework for understanding the recognition of Chi DNA by RecC, a protein that has long been mysterious because it shares little sequence similarity with known protein families. Wigley and co-workers show that RecC is no orphan: it has the architecture of an SF1-type helicase that has lost key catalytic amino acids. Indeed, the 3′-terminated strand of DNA passes over a region of RecC that is typically used as a helicase–nucleic-acid interface. The structure suggests a remarkable model in which RecC has exchanged the ability to actively unwind DNA for the ability to scan it and then apply the brakes when it passes over a Chi sequence.

Meanwhile, the structural features of RecB help to explain why its 'nuclease' domain occasionally interrupts its continuous chewing of the 3′-terminated strand of the DNA (its exonuclease activity) in order to take a bite out of the other strand (endonuclease activity), particularly when the complex has paused at a Chi site. RecB's helicase and nuclease domains are connected by a long tether that provides sufficient freedom for the nuclease to take occasional swipes at the 5′-terminated strand.

Although this work provides ample insight into the molecular mechanisms for repairing DNA, it also contains rewards for simple 'motorheads' such as myself who want to understand how proteins move along, and work on, DNA and RNA. For example, it goes a long way towards answering a basic question: how can a helicase move so fast? RecBCD unwinds DNA at around 1,000 base pairs per second, which is the fastest machinery yet discovered for unwinding nucleic-acid duplexes. And yet the structure shows that the RecB and RecD motors look like generic SF1 helicases, which typically mosey along their substrates with comparatively unexceptional velocities[6,7]. Indeed, RecB and RecD unwind DNA slowly in isolation.

Although there is probably synergy in the coupled motion of RecB and RecD, a key to the speed of the complex may lie with the component that is not a motor: RecC. By surrounding and splitting the DNA strands before feeding them to the motors, RecC might reduce the tendency of the divided strands to clamp shut, allowing RecB and RecD to move faster. RecC is also likely to enhance processivity by effectively tying

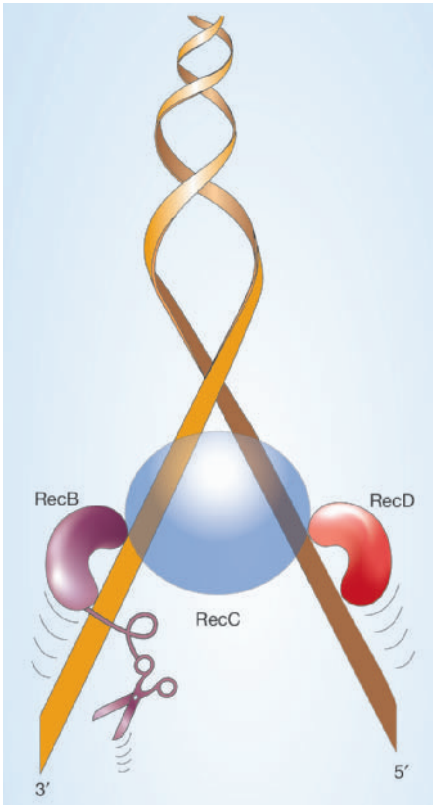


Figure 1 **Heavy machinery for dealing with DNA breaks. The RecBCD complex of proteins helps to repair DNA by unwinding the DNA double helix in the region of a double-stranded break, and chopping up the unwound strands. RecB and RecD are helicases that push on the DNA duplex together to unwind it. RecB also has 'nuclease' activity, which snips up the unwound DNA. RecC has been implicated in recognizing DNA sequences that direct the complex to slow down. Wigley and colleagues[2] have now presented the crystal structure of RecBCD bound to DNA, revealing details such as how the complex binds DNA at the site of a break and how the actions of the three proteins are coordinated.**

RecB and RecD to the substrate. Whatever its mechanism of action, RecC clearly engages the DNA before delivering it to the motors, thereby turbo-charging two otherwise unexceptional engines.

The structure also helps us understand how a helicase can move backwards. Most SF1 and SF2 helicases move along single strands of DNA or RNA in a 3′ to 5′ manner. However, single-molecule studies have detected apparent backward motion by helicases[8], and there are examples of closely related helicases (such as Dda and, of course, RecD) that move in the opposite direction[3,4,9]. The new structure shows that RecD does not do this by turning around — that is, the helicase domains are not arranged in an opposite orientation relative to the polarity of the DNA strand. Rather, RecD simply drives in reverse, much like variants of the cytoskeletal motors myosin and kinesin[10]. This structural evidence for forward and reverse gears in a helicase opens the door to structure–function studies aimed at understanding directionality of motion.

Insights into how helicases and substrates recognize each other are also provided. Most helicases require a single-stranded launch pad attached to the duplex before they can initiate unwinding[11]. But RecBCD can load directly onto a DNA blunt end, and the structure shows how: it creates its own single-stranded tails by melting the first four base pairs of the duplex in the absence of adenosine triphosphate (ATP, the fuel for biological motors such as helicases). So the intrinsic binding energy of the motor makes major contributions to unwinding events prior to any conformational changes that are induced by ATP hydrolysis.

Despite the appealing mechanical concepts suggested by the new structure, however, it should be emphasized that it represents a snapshot of an initiation complex that has not undergone forward motion in the presence of ATP. The actively translocating complex may, in fact, contain features that differ markedly from those seen here. For example, a compelling feature of the complex is the 'pin' provided by RecC that appears to split the DNA strands before they are delivered to RecB and RecD. However, the pin substructure may be subjected to substantial force during forward motion. It will be interesting to see whether it persists during unwinding, and to understand its mechanical role in RecBCD complexes that are actively moving.

Similarly, it will be essential to explore the existence of the proposed binding site between RecC and the Chi sequence, and to test the suggested model by which the Chi–RecC interaction regulates the nuclease activity of RecB. Like any significant crystal structure, that of RecBCD poses intriguing new questions. In this case, it also provides a valuable roadmap for mutational and mechanistic analyses. ■

*Anna Marie Pyle is in the Department of Molecular Biophysics and Biochemistry, and the Howard Hughes Medical Institute, Yale University, 266 Whitney Avenue, New Haven, Connecticut 06520, USA.*
*e-mail: anna.pyle@yale.edu*

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