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Uncovering New Secrets in a DNA Helper

The protein RecA performs some profoundly important functions in bacteria. Two independent papers shed light on how the bacterial protein helps (1) identify and (2) replace damaged DNA while making few mistakes. Error-correction mechanisms keep DNA fidelity during replication to within an average of one error per billion "letters" or base pairs. This research may provide insight on how damage to existing DNA from processes such as UV radiation can be detected and repaired efficiently in living organisms, including humans, who carry evolutionary cousins of RecA. By polymerizing (bonding) onto damaged DNA, RecA is able to detect DNA damage and send out an "SOS" message to the rest of the cell. When the double-helix DNA is seriously damaged, single-stranded DNA is exposed and RecA polymerizes onto it, activating a biochemical SOS signal.

To do this, Tsvi Tlusty and his colleagues at the Weizmann Institute and Rockefeller University (Tsvi.Tlusty@weizmann.ac.il) suggest that RecA performs "kinetic proofreading" in which RecA can precisely identify a damaged strand and its length by using ATP (the energy-delivering molecule in cells) to inspect (proofread) the DNA's binding energy and to detach after a certain time delay (the "kinetic" part) if the DNA has the "wrong" binding energy. (For more on kinetic proofreading, see American Scientist, March-April 1978).

The researchers argue that the RecA performs the precise binding and unbinding actions that are necessary for kinetic proofreading through "assembly fluctuations," a protein's structural changes brought about by constant bonding and dissociation of RecA from its target. According to the authors, this is the first known biological process in which kinetic proofreading and assembly fluctuations are combined (Tlusty *et al.*, Physical Review Letters, 17 December 2004). Meanwhile, researchers at L'Institut Curie in France (Kevin Dorfman, Kevin.Dorfman@curie.fr and Jean-Louis Viovy, Jean-Louis.Viovy@curie.fr) have studied how RecA exchanges a damaged strand with a similar copy.

In bacteria, RecA protein catalyzes this process by binding to a healthy single DNA strand to form a filament that "searches" for damaged double-stranded DNA (dsDNA). At odds with the conventional view, they propose that the dsDNA which needs to be repaired is the more active partner in this mutual search. Unbound, it first diffuses towards the more rigid and thus less mobile filament. In a second step, local fluctuations in the structure of the dsDNA, caused only by thermal motion, allow the base

pairs of the filament to align and pair with the strand of replacement DNA. (Dorfman *et al*, Phys. Rev. Lett., 31 December 2004)