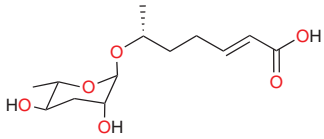
It's just a 'hop' to the left

Processivity factors are proteins that are instrumental to the physiological function of some DNA polymerases: these accessory proteins enable the polymerase to diffuse along DNA during replication and prevent it from fully dissociating from the DNA template. Like other proteins that move along DNA, processivity factors can utilize a three-dimensional diffusional mode (where the protein fully detaches from the DNA and binds to another piece of DNA that is in close proximity) or a one-dimensional diffusional mode (by 'sliding' along the DNA or by 'hopping' from one site to an adjacent region of the same piece of DNA). Komazin-Meredith *et al.* used a combination of ensemble and single-molecule experiments to study how UL42, a processivity factor associated with herpes simplex virus (HSV) DNA polymerase, moves along DNA in a one-dimensional fashion. They measured the half-lives of UL42-DNA complexes and calculated the diffusion coefficients of UL42 along DNA in the presence of varying concentrations of sodium chloride. Although the HSV DNA polymerase holoenzyme moves along its DNA template one base pair at a time *in vivo*, both sets of experiments surprisingly indicated that UL42 is able to hop along DNA *in vitro*, moving several base pairs in a single 'leap'. The underlying utility of the hopping is not entirely clear, leading the authors to propose that UL42 might have other cellular functions *in vivo*. (*Proc. Natl. Acad. Sci. USA*, published online 25 July 2008, doi:10.1073/pnas.0802676105) *JMF*

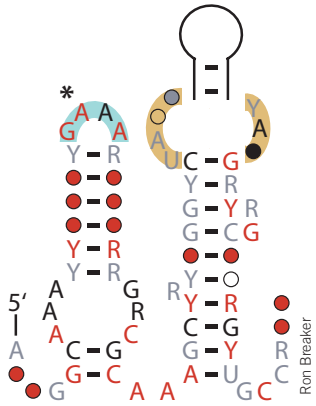
To mate or to dauer



***Caenorhabditis elegans* males are strongly attracted to hermaphrodites by an unidentified chemical mating signal. To identify the chemical cue, Srinivasan *et al.* chromatographically separated the secreted metabolites of hermaphrodite worms and identified three fractions that in combination, although not alone, attracted males. From these fractions, the authors identified three ascarosides, derivatives of the dideoxysugar ascarylose, that were strongly synergistic in a male attraction assay. The attractant response to one of the ascarosides, ascr#3, involved both general and sex-specific sensory neurons, which provides an explanation for the different responses of male and hermaphrodite worms to this signal. Ascarosides had been previously shown to induce the formation of an alternative larval stage called 'dauer' that enables *C. elegans* to persist through adverse conditions, and all three of the ascarosides identified as male attractants also induced dauer formation, although at varying levels. Looking more closely at this dual response, the authors found that ascr#3 acts as a male attractant at concentrations at least four orders of magnitude lower than those required to induce the dauer larval stage. Thus, surprisingly, different ratios and concentrations of the same mixture of chemical signals regulate worm mating behavior and dauer formation. Future characterization of ascaroside biosynthetic and signaling pathways will enable a mechanistic understanding of how these reproductive and developmental pathways intersect. (*Nature*, published online 23 July 2008, doi:10.1038/nature07168)** *JK*

Written by Amy Donner, Joshua M. Finkelstein, Joanne Kotz & Terry L. Sheppard

di-GMP hits it off with RNA



Cyclic diguanosine monophosphate (di-GMP) is a second messenger that induces a variety of physiological responses in eubacteria. The mechanisms by which di-GMP elicits cellular responses remain unclear, but some have suggested that di-GMP signaling could be mediated by riboswitches—RNA motifs that regulate gene expression in response to small-molecule ligand binding. In support of this notion, Breaker and colleagues previously identified conserved 'GEMM' RNA motifs associated with bacterial genes known to be involved in modulating cellular di-GMP levels. Sudarsan *et al.* have now demonstrated that GEMM motifs are riboswitches that sense di-GMP and regulate the expression of di-GMP–responsive genes in diverse eubacteria. Secondary structural analysis of Vc2 RNA, a GEMM element from *Vibrio cholera*, revealed that di-GMP binds to a domain composed of two conserved hairpin loops and induces an alternative RNA Vc2 conformation. Vc2 is specific for di-GMP binding, as the second messenger is bound at least 1,000 times tighter than noncyclic dinucleotide and mononucleotide analogs. Using reporter gene constructs, the authors showed that GEMM riboswitches in three bacterial species sense di-GMP and regulate the expression of genes involved in virulence and the generation of bacterial pili and flagella. Bioinformatic analysis revealed that GEMM elements are widely distributed across eubacterial genomes and, in one case, bacteriophage DNA, which suggests that these di-GMP–binding RNA elements may be the primary system by which bacteria respond to this second messenger. (*Science* **321**, 411–413, 2008) *TLS*

Superoxide in a flash

Excess production of reactive oxygen species (ROS) leads to apoptotic or necrotic cell death, while homeostasis levels regulate essential cellular processes. Leakage from the mitochondrial electron transfer chain (ETC) is believed to account for most cellular ROS, such as superoxide anions, in quiescent cells. The serendipitous discovery of the reversible fluorescent superoxide sensor circularly permuted yellow fluorescent protein (cpYFP) enabled Wang *et al.* to observe real-time ROS fluctuations in living cells. Mitochondrial-targeted expression of cpYFP resulted in transient fluorescent flashes associated with single or closely paired mitochondria in all cell types evaluated. Superoxide dismutase mimics or ROS scavengers in cells diminished both flash frequency and duration confirming that cpYFP senses superoxide anions *in vivo*. The authors hypothesized that transient mitochondrial permeability transition pore (mPTP) openings triggered the flashes. Consistent with their hypothesis, they observed that all flashes coincided with a decrease in mitochondrial membrane potential and were attenuated by chemical or siRNA-based inhibition of mPTP. Similarly, chemical or genetic inhibition of ETC activity abolished flash generation. Thus, quantized release of superoxide anions is dependent on both mPTP and ETC. The observation of localized superoxide spikes in quiescent cells suggests that microdomains of active ROS-dependent signaling might exist in normal cells while the bulk of the cell remains dormant. (*Cell* **134**, 279–290, 2008) *AD*