explain why mutations that abrogate antitermination mediated by the HK022 *put* RNA structure occur in the β′ zinc finger (*9*) and why the β half-clamp in eukaryotes contains a second zinc finger that (genetically) interacts with the β′ zinc finger (*16*): to stabilize megabase transcription.

The results of Nudler *et al.* do not explain how polymerase rotates about the DNA helix. Does the clamp rotate (and lock) in the DNA major groove, and how much flexibility exists between it and other parts of polymerase? They also do not resolve whether an RNA:DNA hybrid exists; RNA:DNA disruption could be required for termination (for example, by inducing clamp opening), but it is clear that an RNA:DNA hybrid is not sufficient for stability. The ability of DNA polymerase to pass through a transcription complex from either direction appears to require that neither the clamp nor a hybrid is the sole determinant of stability under all conditions; each must be disrupted at different points to allow DNA polymerase passage. How four known or postulated interactions—the downstream DNA duplex clamp, the RNA:DNA hybrid, single-stranded RNA in the exit channel, and RNA hairpin–polymerase contact—conspire to modulate the switches between rapid and stable elongation, pausing, and dissociation remains a challenge for clever experimentalists.

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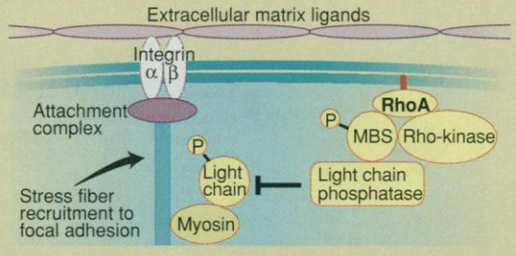
UPDATE

Rho Returns: Its Targets in Focal Adhesions

Howard Bussey

Two recent papers in *Science* (*1*) revealed why a yeast looks like a yeast. A small Ras-like guanosine nucleotide–binding protein, Rho1p, acts as a morphogenetic coordinator to activate β(1→3)glucan synthase, which makes the glucans of cell walls. A Rho1p homolog in humans, RhoA, also has a morphogenetic role—the regulation of actin stress fibers, which emanate from small patches of the membrane called focal adhesions and allow the cytoskeleton to pull against the extracellular matrix and alter cell morphology. A report in this issue (*2*) reveals the detailed biochemistry of how mammalian RhoA controls stress fibers.



RhoA recruits actin stress fibers at focal adhesions.

When activated (by growth factors or phospholipids, for example), RhoA is in its guanosine triphosphate–bound form and can bind to and activate protein kinases, including Rho-kinase. The new results show that an additional role of RhoA is to activate myosin, albeit indirectly. The direct Rho target is a regulatory subunit of a phosphatase that inactivates myosin by light chain dephosphorylation. This phosphatase regulatory subunit, called myosin-binding subunit (MBS), is inactive when phosphorylated. RhoA binds to MBS and also activates Rho-kinase to phosphorylate MBS. The result of this flurry of interactions is to inhibit myosin phosphatase activity, leading to activation of myosin through a net increase in myosin light chain phosphorylation by other protein kinases. Such activated myosin polarizes actin-myosin bundles, allowing the formation of stress fibers.

In yeast, does Rho1p also mobilize actin-myosin at the bud tip, thereby orchestrating both glucan synthesis and the underlying cytoskeleton? There are strong hints that Rho1p does just that. Cortical actin is highly organized at the bud tip; Rho1p colocalizes with it in yeast cells, as does an unconventional yeast myosin, Myo2p (*3*). Myo2p also binds yeast calmodulin as a light chain, an interaction required for polarized growth (*4*). Rho1p may activate Myo2p, much as RhoA activates human myosin, through the inhibition of a myosin phosphatase that acts on phosphorylated calmodulin, the Myo2p light chain. Yeast Rho1p interfaces between protein kinase regulation of polarized glucan synthesis and (possibly) activation of the cytoskeleton, whereas its human homolog RhoA polarizes regions of the actin cytoskeleton to plasma membrane adhesion sites. Thus, this versatile multifunctional switch is an important, conserved component in determining cellular architecture in both yeast and mammals.

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