Molecular mechanism of RNA helicases

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Abstract

RNA helicases are often compared to a nanoscale motor that can translocate along the RNA, dissociating bound RNA and/or proteins to allow structural rearrangements in protein-RNA complexes. In the DEAH-box RNA helicase family, Prp43 is a remarquable bifunctional enzyme, required both for ribosome biogenesis and splicing, and activated by G-patch domain-containing proteins. The molecular mechanisms governing how Prp43 is activated by its G-patch protein partners remain poorly understood, as is the function of all helicases of the other DEAH box helicase family involved in splicing and ribosome biogenesis. We have investigated if the G-patch protein activation was linked to the unique nucleotide binding mode of this helicase family. Using magnetic tweezers on a model system, we have for the first time observed the activity of yeast DEAH proteins at the single molecular level. We show that given a G-patch protein co-factor, all the helicases are able to processivily unwind short stretches of nucleic acid duplexes in repetitive unwinding and reannealing cycles. We propose a unifying structural and functional model for DEAH helicase mechanism, activation and function in large macromolecular complexes. In this model, DEAH box helicases appear as motors in neutral gear, and interaction with G-patch domain proteins engages different gears to provide the helicase different speeds and/or processivity. Our understanding of the molecular mechanism governing DEAH helicase function and activation remains limited.

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