One of These Things Is Not Like the Others...♦

♦ See referenced article, J. Biol. Chem. 2011, 286, 18701–18707

Evolution of Two Modes of Intrinsic RNA Polymerase Transcript Cleavage

The eukaryotic RNA polymerases Pol I, II, and III share a highly conserved active center that catalyzes DNA-dependent RNA synthesis during gene transcription. The same active center also catalyzes cleavage of the nascent transcript during proofreading and recovery from transcription arrest. Despite the similarity in their active centers, Pol I and III have very strong intrinsic cleavage activity whereas Pol II has only weak cleavage activity. In this Paper of the Week, Wenjie Ruan and colleagues use a clever combination of mutagenesis and cleavage assays along with x-ray crystallography to unravel the molecular basis of this difference in cleavage activities and suggest how these activities arose during evolution. Ruan et al. found that replacing the C-terminal zinc ribbon domain of subunit Rpb9 (C-ribbon) from Pol II with its counterpart from Pol III significantly increased Pol II’s cleavage activity. The authors propose that the Pol III C-ribbon directly binds the Pol II pore and complements the active center, similar to a mechanism used by elongation factor TFIIS to enhance cleavage in Pol II. Their work reveals two modes for intrinsic RNA cleavage: an allosteric mechanism that results in weak cleavage activity and a direct binding mechanism that significantly enhances cleavage activity. The fundamental importance of these results for understanding transcription elongation led the paper’s reviewing editor to note that this work will likely “be part of future textbooks on the biochemistry of gene expression.”

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