The saga of transcription

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Transcription plays a key role in life processes since the products of transcription like enzymes, hormones and other proteins are the stuff a living cell needs for its vital functions. It is also involved in ailments such as cancer, where transcription goes awry.

RNA polymerase is the enzyme which transcribes information from DNA. Landick *et al.* (*Chem. Engg. News*, 12 August 1991, p. 27) have obtained the first close-up view of RNA polymerase in action by attaching molecules of this enzyme on a glass slide. Then, using a sophisticated light microscope connected to a video camera, they recorded the movements of a 40-nm gold particle attached to the end of a DNA molecule which was being transcribed by RNA polymerase. As the DNA molecule ratchetted through the RNA polymerase, the length of the gold particle's DNA tether increased, allowing the particle a greater range of Brownian motion. By analysing the Brownian motion of the particle, the authors were able to measure the rate at which the polymerase molecule moved along the DNA strand. This technique has great potential to a better understanding of how RNA polymerase starts and stops transcription, that is, the regulation of transcriptional process which has a central role in diseases like cancer.

From the point of view of RNA polymerase, however, little is still known about how this regulation is accomplished. In a prokaryote like *Escherichia coli*, the RNA polymerase is composed of four types of subunits, designated α, β, β' and σ. The σ subunit is involved in specific recognition of promoter sequences of DNA from which transcription is initiated. It has been generally assumed that β and β' compose the actual transcription machinery, possessing the enzymatic activities required for regulation of initiation and for transcriptional elongation. The α subunit has hitherto been assigned a role mainly in the assembly of the multisubunit complex, serving as a scaffold upon which the rest of the molecule is built, but recent studies discussed below show that it plays a central role in the control of polymerase activity.

Prokaryotes possess only a single RNA polymerase, while eukaryotes have three different types of the enzyme. Because of the relative simplicity of the prokaryotic enzyme, it is still the RNA polymerase of choice by many investigators for studying transcriptional regulation. It also appears to evoke the poetic instinct of scientists. 'Dances with sigmas' by Stragier (*EMBO J*, 1991, **10**, 3559) and 'Alpha: The Cindrella subunit of RNA polymerase' by Russo and Silhavy (*J. Biol. Chem.*, 1992, **267**, 14515) are good illustrations of this thesis and give a wealth of information on the current advances in transcriptional regulation.

The σ subunit of RNA polymerase varies in molecular weight from one type of bacteria to another, e.g. *Escherichia coli* and *Bacillus subtilis* or even in the same bacterium under different environmental conditions, e.g. heat shock transcription factor σ 32 of *E. coli*. (The molecular weight of σ factor from normal *E. coli* is 90,000 compared to 32,000 under heat shock conditions.) With regard to different bacteria, certain regions of σ are conserved, and it is possible to trace their evolution from one another from these conserved sequences. For instance, there are three regions of conservation in *B. subtilis* σ. One binds to core RNA polymerase and another to DNA sequences located 35 base pairs upstream of the promoter.

Russo and Silhavy have now shown that α subunit is, in addition to its role in the assembly of RNA polymerase from its subunits, also involved in interactions with transcriptional regulators like cAMP receptor protein and activators of certain operons. These regulatory proteins interact with RNA polymerase through the C-terminal domain of the subunit, changing the geometry of transcriptional factors, DNA sites and RNA polymerase that is observed in promoters *in vivo*. The situation is anomalous to the binding of eukaryotic RNA polymerases to accessory factors before they become active, and hence the study of the α-factor of *E. coli* polymerase may ultimately give clues to transcriptional regulation in eukaryotes.

The α subunit thus plays a central role in the control of RNA polymerase activity. In the words of Russo and Silhavy, 'It is time to invite α to the ball'.

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