

pigmentosum group B (reviewed in ref. 5), and it contains the canonical helicase motifs that typically enable proteins to unwind RNA and/or DNA duplexes in an ATP-dependent fashion. Indeed, ERCC3 allows TFIIF to unwind DNA locally in an ATP-dependent reaction⁴. Guzder *et al.* now furnish direct biochemical evidence that RAD25, the yeast equivalent to ERCC3, not only contains ATP-dependent helicase activity, like ERCC3, but also that this helicase activity is vital for RNAPII-mediated transcription².

A string of recent papers has revealed that ERCC2, the gene that corrects the DNA-repair defect in xeroderma pigmentosum group D (ref. 5), also encodes a component of human and yeast TFIIF, and that the entire TFIIF complex can function in DNA-excision repair independently of its involvement in transcription⁶⁻⁹. The yeast equivalent of ERCC2 is RAD3, and like RAD25 it encodes a DNA helicase required for DNA-excision repair. RAD3 and RAD25 are further related in that both are essential for viability in yeast.

The difference between the two proteins comes from analysis of key mutations in the nucleotide-binding domain. Such a mutation in RAD3 abolishes its ATPase/helicase activity, impairing its DNA-repair function, but not affecting cell viability, indicating that the RAD3 helicase is not required for the protein's essential function¹⁰. Indeed, this mutation does not affect the transcriptional role of yeast TFIIF (ref. 6). A similar mutation in RAD25, however, is lethal, implicating the ATPase/helicase activity of this protein as the essential component^{9,11}. Prakash and colleagues have provided compelling evidence, both *in vivo* and *in vitro*, that RAD25 (ref. 2) and RAD3 (ref. 12) are essential for viability because of their involvement in transcription by RNAPII. The observation by Guzder *et al.*², that RAD25 with a mutation in the nucleotide-binding pocket is defective in transcription, clearly shows that, unlike RAD3, the ATPase/helicase activity of RAD25 is essential for its function in transcription and cell viability.

What precisely does RAD25/ERCC3 helicase do in transcription? Open complex formation is ATP dependent¹³, as is the helicase activity of RAD25/ERCC3. So, most logically, it functions in open complex formation during transcription initiation. Interestingly, this step is not entirely specific for ATP: it appears that at high enough concentrations, any nucleotide can provide the β - γ energy bond, with ATP having the lowest K_m (J. Gralla, personal communication). Because the helicase activity of RAD25/ERCC3 is specific for ATP, it is unlikely that it catalyses open complex formation.

What else might the RAD25/ERCC3 helicase do? Studies on the composition of

the RNAPII ternary complex have excluded the involvement of RAD3/ERCC2, RAD25/ERCC3 and TFIIF in elongation, as none of these factors has been detected in the ternary complex (P. Kumar, L. Zawal and D. Reinberg, unpublished results). TFIIF and ATP may act at a stage subsequent to open complex formation yet before elongation¹⁴, a phase called promoter clearance. This phase is akin to a functional roadblock, bypass of which requires energy in the form of ATP. Once the polymerase forges through this roadblock, the TFIIF helicase activity (provided by RAD25/ERCC3) and the ATP cofactor are no longer required. Moreover, the use of a pre-melted linear template (a template already in the open conformation) that extends over the transcription start site circumvents the requirement for ATP in RNAPII transcription¹⁵. This bypass probably encompasses the open complex and promoter clearance phases of initiation and obviates the requirement for the TFIIF (RAD25/ERCC3) helicase.

This study may also shed light on the observation that superhelicity of the DNA template circumvents the requirement for TFIIF and ATP hydrolysis^{16,17}. Superhelical tension perhaps provides the energy for a stable open complex, similar to the pre-melted heteroduplex, thereby bypassing the ATPase requirements for open complex and promoter clearance.

On current understanding, it seems that open complex formation and promoter clearance are two energy-dependent steps. It is likely that the RAD25/ERCC3 subunit of TFIIF functions at the second step, but the activity involved in open complex formation remains unknown. We will have the answer, in mechanistic terms, only after nucleotide and factor requirements are biochemically correlated. It should not be long in coming. □

Ronny Drapkin and Danny Reinberg are in the Department of Biochemistry, UMDNJ-Robert Wood Johnson Medical School, 675 Hoes Lane, Piscataway, New Jersey 08854, USA.

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Lagging ahead

THE gas butadiene is an ingredient of synthetic rubber. It has a nasty tendency to polymerize prematurely. The interior of a pipe or tank of the gas often becomes coated with a mass of frothy polymeric solid. Once initiated, this 'popcorn polymer' grows at the expense of the gas. It can jam valves, block pipes and even burst containers. The higher the temperature, the more luxuriantly it grows. The infestation has to be cleared away mechanically, and the installation 'disinfected'.

Daedalus sees opportunities in this nuisance. He points out that, like foamed polystyrene, butadiene popcorn polymer is an excellent heat insulator. Imagine, he says, a boiler room or industrial plant with a wide range of complex hot vessels and pipes. Conventional lagging would be expensive to apply, and tricky to manoeuvre into all the little corners. But release butadiene into the room, and it would polymerize spontaneously to popcorn polymer on all the hot parts. It would lag the whole installation, including all the tricky and inaccessible details. Furthermore, the process would be self-optimizing. A very hot object would acquire a thicker coating before its lagged surface was cool enough not to attract further polymerization. Every part would thus receive just enough insulation for its temperature.

DREADCO's chemists are now exploring the popcorn reaction. They argue that a reaction so hard to prevent must be very easy to encourage. By adding copolymers and modifiers, they hope to perfect an autolagging vapour whose strongly temperature-dependent polymerization gives an ideal foamy or whiskery thermal insulator. Released among the steam pipes and heat exchangers of chemical works and generating stations, 'Vapourlag' will coat their most complex recesses with perfectly proportioned insulation. Blown under the floorboards of a house, it will insulate the longest and most labyrinthine central-heating and hot-water pipes. Expensive, labour-intensive lagging will be a thing of the past.

The converse problem, that of insulating cold surfaces, defeats this elegant chemistry. But Daedalus recalls that α -methylstyrene does not polymerize above 0 °C; for a long time it was thought not to polymerize at all. The DREADCO team hopes to devise an analogous Vapourlag monomer which can only polymerize on cold surfaces. The world's deepfreezes and refrigerators, and its more weather-beaten houses, could then also gain the benefits of cheap, easily renewed Vapourlagging.

David Jones