primordial protein structures may be best preserved in organisms of presumably early evolutionary origin like the anaerobic, sulfate-reducing bacteria. In fortuitous cases, such structures may suggest plausible pathways for the evolution of enzyme function[2].

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TBP held hostage by cisplatin

How certain anti-cancer drugs affect the cell is still somewhat mysterious. One such drug — cisplatin — binds to DNA and distorts the helix in a manner similar to a UV-induced pyrimidine dimer. Although the exact mechanism of cisplatin anti-cancer action is unclear, the recruitment of proteins involved in nucleotide excision DNA repair to cisplatin–DNA adducts is thought to play a role. A number of chromatin proteins of the high mobility group protein class have been shown to bind to cisplatin–DNA lesions, but a direct connection to DNA repair has so far not been demonstrated.

Interestingly, nucleotide excision repair occurs preferentially in actively transcribed genes, perhaps because the RNA polymerase complex, stalled on the damaged DNA, recruits the repair machinery. In fact, the basal transcription factor TFIIH was recently shown to be involved in nucleotide excision repair. Thus, it seemed reasonable to ask if TFIIH or other components of the basal transcription machinery could interact directly with cisplatin–DNA. In a recent paper, a group of researchers find that TBP, the TATA box binding protein, binds strongly to DNA damaged by either cisplatin or UV radiation (Vichi, P. *et al. EMBO J.* **16**, 7444–7456). Furthermore, their *in vivo* experiments suggest that sequestration of TBP to the damaged sites could possibly help explain a long-standing observation that overall RNA synthesis is reduced in cells after treatment with DNA damaging agents. Thus, the connections between DNA repair and transcription keep getting stronger.

In searching for a structural explanation for their interesting biochemical observation, this group noted a strong similarity (previously unreported) between two structures that had been determined by different groups. Both the cisplatin–DNA structure and the TATA DNA structure in the TBP–TATA complex have similar overall shapes that are quite different from canonical B-DNA, with bends toward the major groove, B- to A-form transitions near the bent portions with flattening of the minor grooves and partially unwound helices. This similarity is intriguing, but is it really significant and responsible for TBP's affinity for cisplatin–DNA? Future experiments should elaborate on the extent of these similarities in an attempt to answer this question and to define TBP's direct role, if any, in cisplatin action and nucleotide excision repair. TLS