Mutations Not Sufficient for Carcinogenesis?

In their report "Mismatch repair deficiency in phenotypically normal human cells" (5 May, p. 738), Ramon Parsons *et al.* report a subset of patients with hereditary nonpolyposis colorectal cancer who have a profound defect in mismatch repair and a consequent high mutation frequency in all tissues examined, yet who have few tumors. Parsons *et al.* point out that one interpretation of this observation is that mutations per se may not be sufficient for a high rate of tumorigenesis. A similar conclusion has been drawn from a consideration of the evidence for sunlight-induced skin cancer (*1*). The diseases xeroderma pigmentosum (XP) and photosensitive trichothiodystrophy (TTD) can arise from mutations in the same gene. Both types of patient have photosensitive skin, and their cells are indistinguishable in that they show pronounced hypermutability and hypersensitivity when exposed to ultraviolet light. Yet only XP patients exhibit the pronounced freckling and high incidence of skin cancer expected on the basis of a simplistic view of the somatic mutation theory of cancer.

Parsons *et al.* suggest that exogenous mutagens are carcinogenic because they kill cells and thus trigger active regeneration of tissues in addition to inducing mutations. This argument does not, however, explain the XP-TTD paradox, because hypersensitivity to cell killing (at least as measured in vitro) is similar in both diseases. Perhaps the time has come to look more rigorously at the evidence that mutation induction constitutes a rate-limiting step in carcinogenesis.

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References

1. B. A. Bridges, *Carcinogenesis* **2**, 371 (1981); *Jpn. J. Cancer Res.* **81**, 105 (1990).

Corrections and Clarifications

The news article "The culture of credit" by Jon Cohen (23 June, p. 1706) described the Nobel Prize–winning work of Phillip Sharp and Richard Roberts as the discovery of "gene splicing"; it should have used the term "split genes" instead. The third sentence of the caption for the diagram on page 1706 should have read, "After a gene is 'transcribed' into RNA (2), the regions corresponding to introns are snipped out (3)." The credit for that diagram should have noted that it referred only to the top panel of the diagram.

The Research News article by Wade Roush "Cell movement tale told by bacterial tail protein" (7 July, p. 30) should have stated that in experiments on the IcsA protein by Marcia Goldberg and Julie Theriot, the protein was expressed uniformly over the surface of a mutant *Escherichia coli* organism, not concentrated at one end.

In the Book Reviews of 7 July (p. 109), the caption accompanying the photograph of the sculpture of Albert Einstein on the grounds of the National Academy of Sciences should have noted that the sculptor was Robert Berks.

In the report "Strain-dependent epithelial defects in mice lacking the EGF receptor" by M. Sibilia and E. F. Wagner (14 July, p. 234), figure 1C on page 235 was printed incorrectly. The correct figure is shown below.