## Genetic Chimerism

A report by Ramon Parsons *et al.* (5 May, p. 738) establishes that, in some patients with hereditary nonpolyposis colorectal cancer (HNPCC), inheritance of a single mutant allele of a gene involved in DNA mismatch repair can decrease repair efficiency to a level which generates a high rate of mutations in phenotypically normal cells. Parsons *et al.* state that they assume the same defect was penetrant during embryogenesis and that this elevated mutation rate is compatible with normal development. This has an important implication. Such elevated mutation rates during embryogenesis would undoubtedly generate altered DNA sequences in stem cells or progenitor cells, which would then give rise to genetic chimerism in tissues of the individual. Mutant alleles of the HNPCC genes may be present at a frequency greater than 0.2% of individuals in Western populations, so there is the potential that the cell types and organs outside the immune system in many millions of individuals are genetic chimeras. This number would expand if additional genes involved in complex repair systems also failed to act efficiently during development. Such chimerism among cells within normal tissues may explain why we and other investigators occasionally observe two alleles of a microsatellite in normal tissues which are not present at equal frequency. More important, the fundamental precept that all cells of an individual are genetically identical may require revision.


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## Inventions

Daniel E. Koshland Jr., in his editorial "The crystal ball and the trumpet call" (17 Mar., p. 1575), relates an anecdote about Abraham Lincoln's commissioner of patents recommending that the Patent Office be closed in a few years because the rate of discovery had become so great that there would be nothing left to discover. In actuality, the anecdote is a variant of an urban legend. Curtis D. MacDougall, in his book *Hoaxes* (*1*), states that the story was invented by a newspaper feature writer. MacDougall quotes from a "letter of resignation" supposedly written in 1837 by an employee of the Patent Office (*1*, p. 287).

> I am now moved to resign, since all the great fundamental inventions have been made, and I am not willing to endure the drudgery of dealing with unimportant matters.

Samuel Sass discusses the origin of the legend in *Skeptical Inquirer* (*2*), saying that it may have started in a 1843 report to Congress by Henry L. Ellsworth, Patent Commissioner. In that report, Ellsworth commented that

> The advancement of the arts, from year to year, taxes our credulity and seems to presage the arrival of that period when human improvement must end.

Sass states that Ellsworth was merely using hyperbole to illustrate the greatest number of inventions occurring and did not mean that patentable discoveries would cease anytime soon.

L. Sprague de Camp has even traced the notion that "all has been invented" back to ancient times. He quotes Sextus Julius Frontius, Roman engineer, as writing

> Laying aside also all considerations of works and engines of war, the invention of which has long since reached its limit, and for the improvement of which I see no further hope in the applied arts. . . .

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**References**

1. C. D. MacDougall, *Hoaxes* (Dover, New York, 1958).
2. S. Sass, *Skeptical Inquirer* (Spring 1989), pp. 310–312.
3. L. S. de Camp, *ibid.* (Fall 1989), pp. 104–105.

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## Quantitative Trait Locus for Reading Disability: Correction

We recently reported evidence for a possible quantitative trait locus (QTL) for reading disability on chromosome 6 in two independent samples of sibling pairs (Reports, 14 Oct., p. 276) (*1*). In a sample of 126 sibling pairs from 19 extended families, four markers located on the short arm of chromosome 6 in bands 6p21.31-p21.1 were genotyped. Subsequently, polymerase chain reaction was used to obtain more informative DNA markers in the same region for a subset (114 pairs) of the kindred sibships and for an independent sample of 50 twin pairs, in which at least one member of each pair was reading disabled.

Results obtained from interval mapping of reading performance data by using the four original markers localized a possible QTL to the short arm of chromosome 6 ($P$ = 0.0027). Results of corresponding analyses of data from sibling pairs genotyped for five DNA markers localized the quantitative trait locus (QTL) to 6p21.3 ($P$ = 0.0417). Analyses of reading performance data from the independent sample of twin pairs provided evidence for linkage in the same region ($P$ = 0.0003). Interval mapping analyses of reading performance data from individuals with more extreme deficits yielded somewhat stronger evidence for linkage in the sibling pairs genotyped for the original markers ($P$ = 0.0003) and the twin sample ($P$ = 0.0001), but not in the sibling sample genotyped for the DNA markers ($P$ = 0.0667).

Recent reanalyses of the twin data revealed that four identical twin pairs had been inadvertently included in the sample. After these twin pairs were deleted from the sample, results of interval mapping analyses of data from the fraternal twin pairs also provided evidence for a QTL in the same region. Although results obtained from the more extreme sample of fraternal twins are less significant ($P$ = 0.0369), those from the unselected sample of twin pairs are significant ($P$ = 0.0094). In order to confirm this evidence for a possible QTL for reading disability on chromosome 6, analyses of data from additional twin pairs will be required.

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1. L. R. Cardon *et al.*, *Science* **266**, 276 (1994).

### Corrections and Clarifications

In the news article "Can risky mergers save hospital-based research?" by Wade Roush (19 May, p. 968), the statement that University Hospitals of Cleveland rose from 20th in the rankings of teaching hospitals funded by the National Institutes of Health (NIH) in 1991 to 12th at present was incorrect. In fact, it was Case Western Reserve University (CWRU), with which University Hospitals of Cleveland is affiliated, that received $69 million in NIH grants in 1993, making it the 20th largest recipient of such grants among medical centers; the university then received $97 million in 1994, raising its rank to 12th. About $15 million of the increase, or 53%, was attributable to CWRU's 1992 affiliation with Henry Ford Hospital in Detroit. Other hospitals affiliated with Case Western include MetroHealth Medical Center, Mount Sinai Medical Center, St. Luke's Medical Center, and Cleveland Veterans' Affairs Medical Center.