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.