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# EDITORIAL

## Molecule of the Year: The DNA Repair Enzyme

This year's Molecule of the Year is the DNA repair enzyme that serves in a system of like molecules that preserve our health, maintain our species, make evolution possible, and contribute to a sound scientific policy on environmental hazards.

The area of DNA repair has long been an important and respectable field in scientific exploration. Recently it has flourished, not only because of important breakthroughs in the field, but also because its importance in determining public policy is being increasingly understood.

The DNA in the human genome provides the blueprint for about 60,000 proteins that keep us alive and healthy. If the DNA were copied badly, we would have diseases such as cancer at a much higher frequency, and we would not get a faithful copy of our parental inheritance. Our species would not be preserved, and we would not live long. If the DNA were copied perfectly, there would be no room for evolution, and the basis for creation of new species with better environmental adaptation would have vanished long ago. The DNA repair system allows a happy medium.

The estimated error rate for a DNA replication in the human with a well functioning repair system is about $10^{-10}$ mutations per base pair per cell generation. This system copes with a human who has $10^{14}$ cells with $4 \times 10^9$ bases per cell, who goes through $10^{16}$ division cycles in a normal life span. The spontaneous errors resulting from intrinsic DNA chemistry in the human body are usually many times more dangerous than chance injuries from environmental causes.

There are great similarities and important differences in the DNA repair system as one goes from species to species. These differences explain why a chemical found to be carcinogenic for one species can have a smaller or greater effect on another species. Aspirin, for example, causes birth defects in rabbits, but is harmless in the human. A thorough understanding of the action of DNA repair and other enzymes will allow us to establish environmental policies that are more efficient and more accurate. For example, if we delineate the differences in the metabolism and repair systems of mouse, rat, and human, we should be able to explain the discrepancies in tests for carcinogenic potency and perhaps construct a system that accurately mimics the human system. That would not only help environmental efficiency, but also avert catastrophes such as the experience with thalidomide, which is explained by different metabolic pathways in different species. Moreover, the new understanding of repair systems may bring about a reexamination of the postulated linear extrapolation for pesticides and radiation and allow more realistic assessments of environmental risk. Evaluation based on such knowledge would not depend on the opinions of partisan protagonists, but on good, solid scientific evidence.

The repair system in biology is like the fire department in a small town. Such a fire department has the equipment and facilities to be completely adequate for the frequency and extent of fires in a small town. To predict the fire danger in a city of 5 million, no one would suggest setting 1000 simultaneous fires in a town of 5000, measuring the damage, and extrapolating to the larger city. By exceeding the repair capacity of the small town the extrapolation is meaningless, but that is exactly what has to be done in carcinogenicity tests. To make up for their short life expectancy, rodents are subjected to doses of carcinogen that far exceed the repair system, and the results are extrapolated to a much larger and longer-lived species, humans. With new knowledge of biochemical repair and detoxification systems, money could be spent on effective measures instead of being wasted on fruitless ones, and the accuracy of past data could be more wisely evaluated.

The DNA repair system is fantastically interesting in itself [see *Molecule of the Year,* page 1926; Perspectives on pages 1954, 1957, and 1959; and Research News report by Jean Marx in *Science,* page 728 (4 November 1994)]. It allows the human copying system to make on the average only three base pair mistakes when copying the 3 billion base pairs in the human genome. Any highly efficient typist would be proud of a record like that. The human species can be proud that it is beginning to understand the system that delivers such a low error rate in the key biological code.

**Daniel E. Koshland Jr.**