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1946, 1981, & 2002 Inhibitor needed

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COVER

1973

DNA repair enzymes have been selected for this year's Molecule of the Year. They form a molecular maintenance crew that works 24 hours a day to cut out and replace damaged pieces of the double helix. Their labors prevent an overaccumulation of mutations, preserving the information in the genetic code and preventing cancer. See Editorial on page 1925, Molecule of the Year on page 1926, and Perspectives beginning on page 1954. [Illustration: R. J. Kaufman, Brookline, MA]

Trans-Acting Dosage Effects on the

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1961 Membrane routes to nanomaterials







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A Sigma-Aldrich Company Circle No. 4 on Readers' Service Card Sulfides in sediments are usually strongly depleted in ³⁴S relative to ³²S, even though most sulfur-reducing bacteria produce a smaller depletion as they produce sulfide and sulfate. The origin of this depletion bears on models for the early evolution of Earth's atmosphere and the extent of Precambrian life. Canfield and Thamdrup (p. 1973) point out that typically 90 percent of the sulfide can be inorganically reoxidized back to sulfur. They show experimentally that severe depletion can occur when bacterial reduction is repeatedly combined with such oxidation.

Old cold lakes

Because of the colder temperatures, precipitation during the last glacial period tended to have lower ¹⁸O/¹⁶O ratios than today. Direct samples of this precipitation, for example, as in ice cores, can be most simply used to infer past air temperatures and climates. However, old ice is now primarily restricted to polar regions. Remenda et al. (p. 1975) sampled Pleistocene ground water contained in pores in sediments from glacial Lake Agassiz, which formed along the North Dakota-Manitoba border. The low ¹⁸O/¹⁶O ratios of the waters imply that air temperatures in this region-and perhaps in a region to the north where ice was melting-averaged -16° C in the Pleistocene, compared with 0°C today.

In time for winter

One suggested application for fullerenes has been in the area of lubrication; theoretical studies suggest that these materials could be very rigid and with-

Piecing together the SL1 transcription factor

Proper initiation of transcription of the genes for 18S and 28S ribosomal RNA requires the SL1 transcription factor. SL1 contains the TATA binding protein (TBP) and a set of three TBP-associated factors (TAFs). Comai *et al.* (p. 1966) have cloned all of the TAFs of SL1. Because TBP is required for transcription from all three eukaryotic RNA polymerases, they have examined the ability of TBP to differentially associate with SL1 TAFs and TAFs from the RNA polymerase II transcription factor TFIID. They find that the binding of TBP to TAFs from SL1 prevents binding of TBP to TAFs from SL1 and vice versa. Zomerdijk *et al.* (p. 2015) have used the recombinant TAFs from SL1 and have reconstituted transcription. All three SL1 TAFs and TBP were required to form a transcriptionally active SL1 complex.

stand high loading forces, yet macroscopic studies of the tribological properties of C_{60} films give varying results that depend on preparation conditions. Lüthi *et al.* (p. 1979)



studied C_{60} films grown on NaCl(001) with a modified scanning tunneling microscope. They were able to move islands of C₆₀ (roughly 200 nanometers in diameter) with relatively low applied forces (2 to 10 nanonewtons), which corresponds to a very low shear strength (0.05 to 0.1 megapascals). Such collective behavior could not be observed for C_{60} films grown on graphite, where the films adsorbed more strongly. One possible application would be in the fabrication of nanomachines: Large molecules could be deposited on an island and moved on such a "nanosled" to another location.

Bacterial gene splicing

The RNA transcripts of bacterial genes do not usually undergo pre-messenger RNA (premRNA) intron splicing as commonly occurs in eukaryotes. Magrelli et al. (p. 1986) have studied Agrobacterium rhizogenes, which is involved in the pathogenesis of hairy-root disease, where it transfers some of its DNA, including the rolA gene, to the infected plant. Their analysis of rolA transcripts from infected Arabidopsis plants shows that this gene has an untranslated pre-mRNA leader sequence that is spliced in the host plant cell.

Slight of handedness

Combinatorial libraries of peptides have been useful for the rapid identification of new ligands for known receptors. Dooley et al. (p. 2019) introduced a twist into this procedure and came up with an unusual ligand for the μ class of opioid receptors. Constructing the library from amino acids of the D configuration, not the biologically predominant L forms, vielded a hexapeptide that bound with 10 to 50 nanomolar affinity to µ receptors. Furthermore, the ligand was selective for this subtype of opioid receptor, with micromolar affinity for the δ and κ subtypes. Unlike most other synthetic ligands, this peptide exhibited full agonist activity in vitro and diminished pain reception when administered intraperitoneally in mice. This peptide can cross the blood-brain barrier and can induce analgesic effects similar to those of morphine.

Tails in translation

The translational activation of maternal mRNAs responsible for pattern formation is necessary for early development in Drosophila. Sallés et al. (p. 1996) examine the mechanism responsible for translational activation. They find that three mRNAs (bicoid, Toll, and torso) involved in the regional specification of anterior, dorsoventral, and terminal pattern show an increase in polyadenylate [poly(A)] tail length coincident with translation. For bicoid mRNA, this cytoplasmic poly(A) addition was shown to be required for translation.

-

The means to the ends The ends of eukaryotic chromosomes, called telomeres, become shorter with each cell division. Sufficiently short telomeres may be a signal for cellular senescence. Kim et al. (p. 2011) developed a highly sensitive assay for measuring the activity of telomerase, the enzyme that synthesizes telomeres. Their evaluation of a large panel of human immortalized cells, normal somatic cells, tumor biopsies, and normal tissue indicate that telomerase is tightly repressed in normal somatic tissue but is reactivated in immortalized cells and in cancer.

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Scanning electron micrographs of primary rat mammary epithelial cells at 24 hours (inset) and 36 hours (background) on MATRIGEL^{*} Basement Membrane Matrix. Photo courtesy of Dr. Margaret Neville.

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