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COVER Photomicrograph of Anabaena species strain DW12-2.2 filaments containing a mutant xisA gene that was inactivated by site-directed insertion of an antibiotic gene cassette. The mutant strain forms heterocysts when transferred to a medium lacking a source of combined nitrogen, but the heterocysts are unable to excise an 11-kilobase DNA element from the chromosome and do not fix nitrogen. See page 1421. [James W. Golden, Texas A&M University, College Station, TX 77843]

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#### Superconductivity at two

ow well matched are theoretical explanations of the structure and behavior of high transition temperature superconducting materials and experimental findings of the past 2 years? In reviewing the accumulating data and evaluating this question, Little finds that the Bardeen-Cooper-Schrieffer theory that describes conventional superconducting materials can also account for many features of copper-oxide superconductors (page 1390). Experiments show that the carriers of electric currents are electron pairs existing in the same spin state as in conventional superconductors; pairs form flat pancake-like structures in the copper-oxide planes. A weak association having energy several times that of a photon holds the members of the pair together. Although the exact coupling mechanism remains unidentified, a number of experiments appear to rule out magnetic interactions and others favor electronic effects.

#### **South Pole dinosaurs**

IVERSE flora and fauna inhabited southern Australia during the Early Cretaceous (105 to 120 million years ago), a time when this part of Australia was well within the Antarctic circle and shrouded in darkness for a month or two each year. The mean annual temperature, calculated from oxygen isotopes in calcite, was between 5°C and -6°C, and the region was humid (page 1403). Rich et al. describe the diverse indigenous wildlife that lived in habitats ranging from open moorlands to deciduous and evergreen forests-6 to 8 species of dinosaurs, turtles, and other vertebrates, and 80 species of invertebrates (mostly insects), and a variety of plants. Separated physically (by climate or geographic barriers) from more northern animals, some distinctive dinosaur species appear to have evolved in the region. The ability of polar dinosaurs to withstand conditions of extreme cold and darkness may constrain hypotheses explaining their extinction.

### Liver disease in transgenic mice

RANSGENIC mice carrying a mutant gene for human  $\alpha_1$ -antitrypsin develop signs of a disease that resembles the human deficiency disease α<sub>1</sub>-Pi (page 1409). About 100,000 people in the United States have symptoms of this genetic disease; 15% of affected newborns develop hepatitis and grow slowly for the first couple months of life, and 25% of them die by age 8 with obstructive jaundice and cirrhosis. Pathology centers around production of mutant  $\alpha_1$ -antitrypsin molecules: this protein normally inhibits other enzymes, but, because mutant molecules cannot get out of cells, other enzymes remain active; unchecked enzyme activity destroys lung alveolae and produces emphysema in adults. Dycaico et al. characterized transgenic mice carrying human genes encoding normal or mutant  $\alpha_1$ -antitrypsin. Animals with a mutant gene were smaller than normal for several months after birth; livers were abnormal, serum levels of  $\alpha_1$ -antitrypsin were low, and intracellular levels were high. These and other parallels with human disease suggest that the transgenic mice are apt models of neonatal and possibly also adult  $\alpha_1$ -Pi.

#### **Homologous enzymes**

OMPLEMENTARY DNA for a human gene that encodes an insulin-degrading enzyme has been cloned and sequenced (page 1415). This enzyme, a proteinase that is thought to play a central role in the intracellular processing of insulin, was purified from human red blood cells. The deduced protein sequence showed closest homology with the sequence of Escherichia coli protease III, which also degrades insulin. The two enzymes share several properties that distinguish them from other proteinases. Affholter et al. point out that, with this cloned material, it should be possible to learn more about the enzyme, including determining if the enzyme is overproduced in insulin-resistant patients in whom insulin is readily degraded.

### Site-directed gene inactivation

**EVERSE-GENETICS** experiments illustrate structure-function relations in the Anabaena chromosome (page 1421). Anabaena are filamentous blue-green photosynthetic bacteria (cover). In the absence of a source of combined nitrogen, 10% of photosynthetic cells terminally differentiate; they become nondividing cells that can fix nitrogen. As these heterocysts form, two DNA rearrangements occur: a 55-kilobase element and an 11kilobase element are removed from the chromosome. The smaller element is situated within a nitrogen-fixation gene and contains the xisA gene that is thought to encode the enzyme needed for excision. Golden and Wiest report that when a mutant xisA gene is substituted for the normal gene, the 11kilobase element does not get excised and nitrogen fixation does not occur. The 55-kilobase element is excised and heterocytes form and develop correctly. Concurrent excision of these two elements under normal circumstances may therefore be merely coincidental.

#### Leber's neuropathy

EBER's hereditary optic neuropathy (LHON) causes optic nerve degeneration, blindness in both eyes, and an uneven heart rhythm. It is transmitted from mother to offspring. Wallace et al. have identified a change in one nucleotide in mitochondrial DNAwhich is also maternally inherited-that is associated with LHON (page 1427). The altered DNA encodes a histidine instead of an arginine in a respiratory protein. The mutation is necessary but not sufficient for disease symptoms; the identification of other factors that induce the disease phenotype may point to approaches for preventing disease in at-risk but unaffected individuals. A fortuitous consequence of the change is that it prevents the restriction enzyme Sfa NI from cutting this piece of DNA: a simple diagnostic test for the individuals with the LHON mutation is, therefore, now available.



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#### **Isotopes in Earth Science**

mprovements in instrumentation have increasingly affected the ways in which research in the earth sciences is conducted. An example is a proliferation of equipment capable of providing accurate data concerning isotopes of beryllium, carbon, nitrogen, sulfur, rubidium, strontium, neodymium, samarium, rhenium, osmium, lead, and uranium. Measurements of isotopes of these elements provide crucial data concerning earth history, heterogeneities in the earth's mantle, subduction of tectonic plates, paleotemperatures and atmospheres, and biogeochemistry.

Stable and radioactive isotopes have been used for many years to provide information relevant to earth science. But during the past 5 years, precision and sensitivity of measurements have greatly improved. The desirability and practicality of employing <sup>10</sup>Be (with a half-life of 1.5 million years) and <sup>187</sup>Re (half-life 43 billion years) have been demonstrated.

More than one radioactive clock is used in dating old rocks. A favorite and perhaps most trustworthy one is uranium-lead preserved in zircons. The rubidium-strontium and samarium-neodymium clocks are also commonly employed. The rhenium-osmium chronometer is being developed. Its attractive features guarantee that it will become important, particularly in dating ultramafic rocks.

Some of the earth history of the last 570 million years was deciphered employing paleontological evidence. However, events occurring between 4500 and 570 million years before the present were only partially known. Earth tectonic processes occurring then may have differed from those now prevalent. In those earlier times the heat emanating from the interior of the earth was substantially greater than that flowing at present.

In Canada there are large areas where Precambrian rocks are exposed, and the Canadians are world leaders in studying ancient events. They have perfected radioactive dating techniques and are able to detect differences of age of 2 million years in rocks that are 2700 million years old. Their work has practical applications in the discovery of ore deposits.

Scientists at the Australian National University have developed and have at present the sole copy of a Super-High Resolution Ion Microprobe (SHRIMP), which has enabled them to date a series of spots on a polished section of zircon at 4100 years before the present.

Samples of the mantle are obtained when xenoliths are violently propelled from depths. Slabs of the mantle have been brought to the surface. Magma (partially contaminated with crust) can also be studied. Isotopic measurements conducted on such samples testify to the heterogeneity of the mantle. In these studies the strontium isotopes are particularly useful.

Small amounts of <sup>10</sup>Be are formed by the action of cosmic rays on atmospheric oxygen. The radioactive isotope falls to the surface and is incorporated in sediments (about  $10^{-17}$  g/ g) at the top of tectonic plates. When the plates are subducted, the <sup>10</sup>Be is carried along down and, ultimately, when magma is formed at about 150-km depth, the <sup>10</sup>Be accompanies it upward. Half-gram samples of the rock are processed, together with a known amount of <sup>9</sup>Be. The abundance of the <sup>10</sup>Be is determined by accelerator mass spectrometry; highenergy ions of <sup>10</sup>Be are individually counted.

This type of equipment has also been applied to determinations of <sup>14</sup>C ages. The measurements can be conducted comparatively rapidly and require smaller samples than the older beta-counting procedure. An important application for the method relevant to possible greenhouse phenomena will be a determination of the rate at which <sup>14</sup>CO<sub>2</sub> from earlier atmospheric bomb tests moves downward in the ocean.

Chemical compositions of phytoplankton membranes change in response to sea-surface temperatures. Organic compounds associated with these changes can be recovered from sedimentary rocks as old as 200 million years. The variations in abundance correlate with the oxygen isotopic temperature scale.

Evidence concerning food sources for humans and ecological webs can be obtained by measuring carbon and nitrogen isotope ratios of organic matter recovered from fossil bones.—PHILIP H. ABELSON

Under the chairmanship of Peter Wyllie of Caltech, a National Research Council report delineating opportunities in the earth sciences is being prepared. It will cover in detail phenomena studied by applications of isotopes as well as many other phenomena, some of which are highly relevant to present-day societal concerns.

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