Martian meteorite redux: New evidence for ancient life

The famous martian meteorite that may or may not contain relics of biological activity is back in the news. Scientists have published new evidence that they say shows the magnetic crystals found in the meteorite known as ALH84001 were produced by microorganisms. One paper compares single crystals of magnetite in ALH84001 with crystals found in earthly magnetotactic bacteria and concludes that they’re very similar [Proc. Natl. Acad. Sci. USA, 98, 2164 (2001)]. Another study published in PNAS (98, 2176 (2001)) focuses on chains of these crystals found in the meteorite. The authors say the chain formation, along with other features such as flexibility, also suggest a microbial origin. In the top micrograph shown here, a chain of magnetite crystals is clearly visible in modern magnetotactic bacteria; in the lower image, arrows mark a chain of such crystals in ALH84001. Evidence for past microbial life in the meteorite has been hotly debated since it was first reported in Science in 1996, and the latest reports aren’t likely to end the controversy.

Chemokines guide migrating cancer cells

Metastasizing breast cancer cells identify the specific tissues where they will set up new colonies of malignant cells using the same molecular signaling system as white blood cells (leukocytes) [Nature, 410, 50 (2001)]. Anja Müller and Albert Zlotnik of DNAX Research Institute, Palo Alto, Calif., and their colleagues find that human breast cancer cells have elevated levels of a receptor for a specific attractant chemical that leukocytes use to find their way to sites in the body where they are needed. Cells lining the blood vessels in the liver, lungs, and bone marrow release large amounts of an attractant chemical, known as a chemokine, that is recognized by the receptor. These are the tissues where breast cancer preferentially spreads. Other organs—including the kidneys, skin, and the brain—that are not usually sites for metastasis from breast cancer don’t release the chemokine, the researchers find. In the test tube, at least, the chemokine stimulates breast cancer cells to carry out the first steps needed to invade new tissue. And treating the cancer cells with an antibody that blocks their chemokine receptors reduces their ability to invade lymph nodes and lungs. “Our findings are probably not unique to breast cancer,” the researchers write. They propose that small-molecule antagonists of chemokine receptors may be useful in treating cancer.

CO binding mechanism reviewed

Simple heme compounds prefer binding CO over O₂ by a factor of about 20,000, but in the heme proteins myoglobin and hemoglobin CO binding is much less strongly favored. This discrimination mechanism is essential to life, as it prevents CO from disabling the proteins’ essential O₂ storage and transport functions. One group of researchers has hypothesized that the effect is due to the protein’s crowding of CO; another camp has contended that hydrogen bonding and electrostatic interactions are responsible (C&EN, Dec. 6, 1999, page 31). Chemistry professor Thomas G. Spiro of Princeton University and assistant professor of chemistry Pawel M. Kozlowski of the University of Louisville are now attempting to resolve the controversy [Acc. Chem. Res., 34, 137 (2001)]. Their analysis of recent density functional and mutagenesis studies reveals that both sides are right, to a degree: Steric hindrance accounts for about 15% of the discrimination effect, and hydrogen bonding and electrostatics account for the remaining 85%.

Another way to bioactivate an anticancer drug

A hydrolysis reaction that unmask the latent DNA-damaging ability of an anticancer compound has been identified as a new type of bioactivation process. The natural product leinamycin is a DNA-cleaving agent that is being developed by Kyowa Hakko Kogyo Co., Tokyo, as an antitumor drug. It has been known that leinamycin can’t cleave DNA until it is chemically activated in a reaction with cellular thiols. But associate professor of chemistry Kent S. Gates and coworkers at the University of Missouri, Columbia, now find that leinamycin can also be unleashed via a previously unknown thiold-independent bioactivation process [J. Am. Chem. Soc., 123, 2060 (2001)]. The researchers believe that an initial attack of water or hydroxide on a key carbonyl group of the antitumor drug produces a sulfenic acid intermediate, which reacts with a neighboring carboxylate to form the exact same activated oxathiolanone generated by conventional thiol activation.

E. coli churns out polyketides

The macrocycl core of polyketide antibiotics such as erythromycin is ordinarily made by a soil bacterium that is slow-growing and hard to work with. It doesn’t take well to genetic modifications designed to produce variants of the natural products that might be promising candidates for new drug development, and the complexity of the products makes laboratory synthesis difficult. Stanford University chemistry and chemical engineering professor Chaitan Khosla and his colleagues propose to get around all these problems by producing the macrocyclic core in the laboratory workhorse bacterium Escherichia coli [Science, 291, 1790 (2001)]. Coaxing E. coli to make polyketides involved inserting four genes and their regulatory elements from other bacteria into E. coli as well as turning off one of E. coli’s own enzymes. All the switches were successful, and the engineered bacterium produces the erythromycin macrocycle at levels that compare well with bacterial strains used industrially. Furthermore, the researchers can modify the E. coli to produce a novel variant of the macrocycle. Under an agreement with Stanford, the patent for the process is held by Kosan Biosciences of Hayward, Calif., a company Khosla cofounded.