Biomedicine

Lens crystallins may be moonlighting

After 25 million years of blindness, why do mole rats, with their evolutionarily atrophied eyes, still have ocular lenses? A novel experiment sheds new light on alpha-crystallin — the eye lens protein that has already impressed scientists as a model of structural and functional elegance (SN: 6/27/87, p.409).

Wiljan Hendriks and his colleagues at the University of Nijmegen, the Netherlands, report that they have determined the nucleotide sequence for the gene that codes for mole rat crystallin. They compared that sequence to the crystallin code in rodents that have evolved with normal vision. Mole rat crystallin has remained remarkably unchanged, they found — despite the fact that, being blind, mole rats are under no apparent selective pressure to keep making the protein. The researchers suggest that crystallin may serve other, less obvious, selective advantages.

Crystallin seems to be involved, for example, in the embryological development of the rudimentary retina that mole rats retain. And there is good evidence, the researchers say, that the mole rat's retina, "though not able to detect light anymore, is still of vital importance for photoperiod perception, which is required for the physiological adaptations of the animal to seasonal changes." The researchers published their findings in the August Proceedings of the National Academy of Sciences (Vol.84, No.15).

Blood clot agent's genes are read

The protein responsible for triggering blood clots in the body has been cloned and its genetic code cracked, researchers report. The new information, they say, could eventually lead to the development of a new class of anticlotting drugs to combat heart attacks and strokes.

The protein, called tissue factor, is one of eight major proteins involved in coagulation. But unlike the other clotting proteins, which circulate in the blood, tissue factor is bound to cell membranes within blood vessel linings. Because of the difficulties in working with such membrane-bound proteins, and because the protein is present in extremely minute quantities, tissue factor did not succumb easily to genetic analysis.

"It took a long time to convince people that it even existed," Ronald Bach, one of the researchers, told Science News. "This is not just an accelerator, but the initiator" of the clotting process, he says. And not surprisingly, he notes, the amino acid sequence of tissue factor is remarkably different from other clotting factors — evidence that tissue factor has separate evolutionary roots. Whereas other clotting factors rely upon proteolytic activation by blood-borne enzymes, tissue factor triggers coagulation in response to tissue damage. It is the last of the blood clotting proteins to have its genetic sequence completely deduced.

The research, published in the August Proceedings of the National Academy of Sciences (Vol.84, No.15), was a collaborative effort by scientists at Yale University in New Haven, Conn., and the Mount Sinai School of Medicine in New York City. According to Bach, who was part of the Mount Sinai team, the work could lead to the development of antibodies or assays to measure tissue factor availability. Such tests might detect early signs of thrombosis — the blocking of blood vessels due to unwanted clots — so as to allow early intervention with clot-dissolving drugs. The research could also facilitate the discovery of natural clot inhibitors capable of blocking coagulation before it even begins.

Such inhibitory mechanisms are sure to exist, Bach says. "A microgram of this protein — one-millionth of a gram — is enough to clot all the blood in your body in about 25 seconds. This tells you that it must be very tightly controlled."

Chemistry

Making a meal of iron

While Popeye can count on spinach for his source of energy, researchers now report that certain methane-producing microorganisms are able to extract their supply directly from iron in its elemental form. "To our knowledge this is the first demonstration of [metallic iron] as an energy source for growth of any organism and thus represents a novel type of chemolithotrophic energy metabolism," microbiologist Lacy Daniels and his colleagues at the University of Iowa in Iowa City report in the July 31 Science.

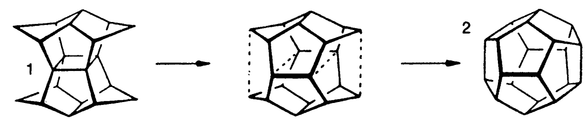
Methane-generating bacteria, which thrive in an oxygen-free environment, normally produce methane and water by combining hydrogen gas and carbon dioxide. Working with pure cultures of various methane-generating bacteria, Daniels and his group showed that these organisms can also grow and produce methane in the presence of iron. In this case, iron reacts with hydrogen ions to produce iron ions and hydrogen gas. Although thermodynamic calculations show that this reaction is energetically unfavorable, the continual removal of hydrogen by the bacteria keeps the iron reaction going. One result is that the iron is oxidized.

"Our work suggests that methanogens could contribute significantly to metal corrosion in anaerobic areas," the researchers conclude. These organisms can be found in sediment at the bottom of almost any lake, pond or stream from the Arctic to the equator, says Daniels. Metal objects buried in soil or sediment, submerged in water or inside containers such as anaerobic digestors would be vulnerable. "In these systems," he says, "[hydrogen gas] is often present in only low levels and [carbon dioxide] is abundant, so that [elemental iron] could serve as a significant electron donor."

The finding is important because researchers interested in biocorrosion have in the past concentrated their efforts almost exclusively on sulfate-reducing bacteria (SN:7/20/85, p.42). Now a second family of bacteria capable of corroding metal has entered the picture.

Crafting a miniature pagoda

When the structural formula of a remarkable, newly synthesized molecule resembles the shape of an oriental temple, the molecule's informal name can be nothing other than "pagodane." That was the name coined by a team of German chemists at the University of Freiburg who recently synthesized this "highly complex, esthetically appealing $C_{20}H_{20}$ polyquinane" (shown in diagram 1). Their report appears in the July 22 Journal of the American Chemical Society.



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The synthesis of pagodane starts with the insecticide isodrin, a compound with 12 carbon atoms already arranged in four five-membered rings. This compound goes through about 45 structural and functional changes before the molecule appears in its final form. Despite the large number of steps needed, the overall process is surprisingly efficient with a yield of 24 percent.

Wolf-Dieter Fessner and his colleagues are interested in pagodane because of its close relationship with the molecular sphere dodecahedrane (shown in diagram 2). Changing only a few bonds converts one into the other. By constructing pagodanes with various molecular groups attached to certain corners, the researchers hope to develop a convenient, efficient path for assembling substituted derivatives of dodecahedranes. These highly symmetric molecules are likely to have interesting chemical properties.