Biology

Muscular dystrophy: Defective inhibitor?

A recent description of the gene that causes Duchenne muscular dystrophy (DMD) has intensified the search for a protein for which that gene codes—possibly a muscle protein absent or defective in the muscle-wasting disease (SN: 10/25/86, p.261). Identifying the gene product could lead to replacement therapy and a halt to muscle loss. A report in the October BIOCHEMISTRY AND CELL BIOLOGY from scientists at the University of Windsor in Ontario suggests the sought-after gene product may indeed be a defective protein—more specifically, an inhibitor that fails to inhibit tissue destruction by enzymes called proteases.

Increased protease activity in skeletal muscle, along with loss of muscle proteins and mass, is characteristic of muscular dystrophy in both humans and animals. From mice with a non-DMD form of dystrophy, the researchers have purified an abnormal protease inhibitor that is unable to stop muscle destruction by some classes of proteases. Theoretically, if a defective inhibitor is pinpointed as the cause of the disease, researchers could replace it with a specific, normal inhibitor.

Some experts, however, say it is unlikely that the similarities between the mouse model used in the Ontario study and DMD are adequate to consider the abnormal inhibitor an insight into the human disease. For example, the mouse model does not carry the disease on the X chromosome, unlike the sex-linked DMD. According to Anthony P. Monaco, a member of the Harvard Medical School group that described the DMD gene last year, "it is likely that we are talking about different genes, different diseases," and that the human form may result from something other than a protease inhibitor problem.

In experiments this month that may answer some of these questions, the Ontario group is cloning the mouse MD gene, as well as assaying for abnormal inhibitor in tissue from humans with a non-Duchenne, slow-onset type of muscular dystrophy. As pointed out by Donald Wood of the New York-based Muscular Dystrophy Association of America, the inhibitor concept is "novel," because it is the *regulation* of the proteases, not the proteases themselves, that is abnormal.

Spotted vaccine to follow?

Using cloning and recombinant DNA techniques, microbiologists at the National Institute of Allergy and Infectious Diseases' Rocky Mountain Laboratories in Hamilton, Mont., have produced a possible vaccine against Rocky Mountain spotted fever. Caused by the bacterium *Rickettsia rickettsii*, the tick-borne disease destroys cells of the vascular system, leading to low blood volume and fluid-swollen tissues.

Members of the Hamilton team recently described protection against the disease in mice, using antibodies against two surface antigens of *R. rickettsii*. Those antigens, however, are difficult to purify, and the bacteria are difficult to grow in culture. To optimize the system, DNA coding for the antigens has been introduced into *Escherichia coli* to create a recombinant *E. coli* capable of producing large quantities of the antigens, they report in the Jan. 2 SCIENCE. Preparations of the *E. coli* successfully protect mice against lethal doses of *R. rickettsii*, and experiments are being expanded to include guinea pigs. Preliminary results suggest that the cloned vaccine may also be effective in other species.

Between 700 and 800 cases of Rocky Mountain spotted fever are reported each year, with most of those (despite the disease's name) in the Southeast, according to the Centers for Disease Control in Atlanta. But it is likely the disease is more prevalent than these figures indicate, since spotted fever can mimic a wide variety of other disorders, such as pneumonia and measles. There is no satisfactory diagnostic test, yet early diagnosis and antibiotic treatment can save lives. The fatality rate is 4 percent with treatment, 7 percent without.

Paleontology

Landing the earliest plants and animals

Traditionally, scientists have thought of the oceans as a sort of womb from which fairly advanced plants and animals emerged to colonize the land. But could land-based life have taken root early on from simple creatures that lived in well-drained soils? The fossil record of early land life is too sparse to answer this question, but a new discovery should keep the idea germinating in more than a few scientists' heads.

In the Jan. 2 SCIENCE, Gregory J. Retallack at the University of Oregon in Eugene and Carolyn R. Feakes at Harvard describe what they believe are the oldest known traces of land animals: a network of tubular burrows ranging in diameter from 2 to 21 millimeters, which are embedded in a 488-million-year-old formation in Potters Mill, Pa. While trace fossils from this formation were known before, Retallack and Feakes say they are the first to recognize that the burrows were made not by marine or lake-dwelling animals, but by organisms living on land.

Their most important evidence is that the chemical makeup and microstructure of the burrow strata are typical of fossil soils and not of lake or river sediments, according to Retallack. Moreover, the researchers believe the burrows were a permanent feature of these soils, rather than being created long after the soil formed, because some burrows are encrusted with dolomite nodules, which normally take thousands of years to grow. They conclude that the burrows were made in a semiarid to arid environment.

Retallack and Feakes found that the burrow diameters come in specific sizes, suggesting that the animals that made them grew in spurts. From the patterns of dirt the animals threw back into the tunnels as they dug, the researchers also conclude that the animals were bilaterally symmetric. Their best candidate is an arthropod, possibly a millipede. But since the oldest millipede fossil is 436 million years old and may well be a marine organism, the researchers suggest that their burrower may be a completely unknown and extinct animal.

According to Retallack, the oldest uncontested evidence of a land-based ecosystem is 414 million years old. "Our burrows show that there were functioning ecosystems on land, with some sort of plant food and fairly large animals, 34 million years earlier," he says. As such, this find lends support to some controversial suggestions, based on fossils of spores, that land colonization began at least 458 million years ago. One implication of all these finds, says Retallack, is that "by looking in aquatic assemblages, we may be hunting in the wrong places for the ancestors of land organisms."

A new horned dinosaur

Last century, paleontologists described the first American dinosaurs from fossil teeth found in Montana's Judith River Formation. Now, this 75-million-year-old formation has yielded another important dinosaur discovery.

Peter Dodson at the University of Pennsylvania in Philadelphia reports in the Dec. 28 PROCEEDINGS OF THE ACADEMY OF NATURAL SCIENCES OF PHILADELPHIA on a new kind of ceratopsid, or horned dinosaur—the first new North American ceratopsid to be named in 35 years.

According to Dodson, the plant-eating *Avaceratops lammersi* was about the size of a boar, weighing about 400 pounds and measuring 7.5 feet long and 3 feet high—dimensions that are relatively small for a dinosaur. Unlike other, much larger ceratopsids of the time, *Avaceratops* had a frill—a bone that projected back from the skull—that was solid and fan-shaped. The frills of other ceratopsids were pierced by two large openings and curved toward the front of the skull along the midline.

The *Avaceratops* remains from Judith River include two-thirds of the skull, all of the limbs, half of the foot bones and a quarter of the vertebrae and ribs.