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Defect in Muscle Disease Pinpointed

By HAROLD M. SCHMECK Jr.

Scientists have discovered the specific muscle defect that causes Duchenne muscular dystrophy, the most common and one of the most devastating of all inherited muscle diseases.

The cause has been identified as the total lack of a particular protein that appears to be always present in normal skeletal muscles.

The scientists named the protein dystrophin. The same research group earlier discovered the gene defect that is responsible for the disease. A gene is usually the genetic blueprint that living cells use to manufacture specific proteins. Having discovered the muscular dystrophy gene, the scientists concentrated on finding the protein produced under the gene's orders.

The identity and role of the protein were reported yesterday by a medical research team led by Dr. Louis M. Kunkel at Harvard Medical School, Children's Hospital and the Howard Hughes Medical Institute in Boston. Effort to Design Treatments

"We hope this advance will enable us to design treatments specifically aimed at replacing dystrophin or compensating for its absence," Dr. Kunkel said. He described the protein as the critical missing piece in the disease. The task of translating the discovery into practical medical use may take a long time.

The scientists found that the same protein is lacking in a breed of laboratory mice that develop some of the characteristics of muscular dystrophy. But unlike humans, the mice survive the disease, apparently because their muscles do not become infiltrated irreparably with connective tissue as happens in the human patients.

This difference is considered an important clue to possible future treatment of Duchenne muscular dystrophy. The research has established that the nonfatal muscle wasting in the mice has the same fundamental cause as the disease in humans, suggesting that mice can be used to advantage in research on the human muscle disorder.

"Possible rational therapies for boys afflicted with D.M.D. might therefore result from the ability to control the connective tissue proliferation within the muscle tissue," the scientists reported in the journal Cell. Deadliness of Disease

Duchenne muscular dystrophy is an inherited disease that occurs in about one of every 3,500 live male births. The disease first becomes apparent as muscle weakness in boys from the ages of 3 to 5 years. By the age of 12, most patients are confined to wheelchairs. Later, the progressive wasting of muscles leads to helplessness and death, usually by the early 20's.

In a report in the latest issue of Nature, to be published Thursday, Dr. Kunkel and his colleagues say dystrophin is normally present in muscle tissues in close association with minute structures called triads where electrical excitation of the muscle fiber triggers the process of contraction. In addition to Dr. Kunkel, authors of the two reports made public yesterday were Eric P. Hoffman, Robert H. Brown, C. Michael Knudson and Kevin P. Campbell.

The Muscular Dystrophy Association, which has supported the research, called the discovery "a landmark achievement."

Now that they know the identity of the critical "missing piece" in the disease, Dr. Kunkel said, scientists will begin to understand how that one protein's absence weakens and ultimately destroys muscle, a key question in study of the disease. Findings May Generate Clues

In an editorial in Nature, an expert on muscular dystrophy said the research should reveal much about how the internal environment of muscle fibers is regulated.

"Understanding why the lack of dystrophin has such different effects on boys and mice may ultimately suggest ways of treating the many boys still dying from D.M.D.," Dr. Clarke R. Slater, of Newcastle General Hospital, in Newcastle Upon Tyne, England, wrote in the editorial.

The new advances against the disease stem from the discovery less than two years ago of the gene that is defective in Duchenne muscular dystrophy. The search for genes that figure importantly in human diseases is one of the most active areas of modern biomedical research. A major purpose in searching for such genes is to find the proteins that are the genes' products.

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