news THE UNIVERSITY OF TEXAS HEALTH SCIENCE CENTER AT DALLAS
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******Scientists Use Advanced Instruments To Probe Hereditary Disease*

DALLAS--Researchers at The University of Texas Health Science Center here are using some of the most sophisticated machines ever constructed in a three-pronged attack on the mysteries of hereditary diseases such as muscular distrophy.

Powerful magnetic analyzers, laser devices and electrical probes have been brought into play in an effort to gain information about differences between normal and abnormal conditions.

"Without basic knowledge, the problem of the doctor in trying to treat cystic fibrosis, muscular distrophy and similar ills is simply enormous," said Dr. Robert M. Dowben, who leads a group of scientists trying to learn the disease mechanisms.

"It's like bringing a person from another planet to Earth and having him stand beside a super highway. He's never seen a freeway or a car before. Then one of the cars breaks down and stops and you say, 'Go fix it'."

The group of scientists in the Biophysics Program at the Health Science Center believes that answers to genetically-based ills and some other problems as well may lie in the size, shape, surface or other properties of protein molecules.

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The idea is that hereditary diseases arise when defects in the genetic material pass along code errors which result in the building of abnormal protein molecules.

But how does one "see" or "feel" or measure an object as tiny as a protein when there may be several hundred thousand different kinds in one individual cell.

One way is with a very advanced instrument called a nuclear magnetic resonance spectrometer. Basically, the machine creates a very powerful magnetic field and when the samples of protein are placed in the field, the individual atoms line up with the field as if they were tiny compasses. The sample then is subjected to very high frequency radio waves, causing various atoms on the molecules to resonate or "ring" according to their individual properties and location.

The information is quite difficult to interpret--a group of partial differential equations bearing the data is fed into an IBM 370/155 computer and it takes two, three and sometimes four hours for it to deliver even partial answers.

But, as the information builds up, the scientists can begin to build models of the individual proteins.

Proteins, which are combinations of 20 amino acids in seemingly endless array of sequences, have two important functions--they serve as catalysts or expediters of chemical reactions in the body and they form the structure of living tissue, such as "myosin" in the muscle.

Not only are the biophysics researchers interested in the group of diseases characterised by muscular dystrophy, they also cast an experimental eye towards hypertension, heart failure and some kidney ailments.

The question is very much the same: Are errors in the genetic sequencing of the protein's amino acid units causing either errors in the chemical reactions it mediates or in the structure it forms?

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Another powerful probe into possible abnormalities of the protein is called the "photon counting fluoresence spectrometer." The one being constructed at the UT Health Science Center is probably only the third of its kind in the world.

Beginning with a strong argon laser, the workers direct its beam to excite a dye laser into emitting its own beam of very pure light. The advantage of the latter device is that, with the proper electronics, the light can be "tuned" from far ultraviolet to orange.

The researchers know that proteins are like some rocks--shine a particular wavelength of light on them and they themselves fluoresce or give off light. With the protein there are fluorescent groups chemically attached to specific locations on the surface.

"Very precise measurement of various fluorescent properties reveal an enormous amount of information about the size and shape of protein molecules, the location of important reactive sites and subtle structural changes between normal and diseased proteins," said Dr. Dowben.

The third unusual research instrument used in the study is called an electrical birefringence apparatus.

This device yields a great deal of information about the size, shape, flexibility and charges on protein molecules by measuring the effects of very intense electrical pulses which last only a thousandth part of a second. "The electrical field makes the protein molecules line up like soldiers on parade and this process is followed by optical means," added Dr. Dowben.

In addition, the Biophysics Group is investigating the mechanism by which skeletal muscle and heart muscle utilize the energy made available by metabolism.

Again proteins are studied with about one third of muscle and heart protein directly involved in contraction.

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"These contractile proteins are extraordinarily complex," says Dr. Dowben. While they are assembled into very specific patterns to form muscle fibers, the exact structure of the proteins and details of assembly are poorly understood.

The group also is collaborating on relationships of certain kidney cells to blood pressure and on exact mechanisms of drug action on heart muscle.

Besides Dr. Dowben, the Biophysics Group includes Dr. James Bunting, Dr. Millard Judy, Dr. Wayne Hoffman and Dr. Clark Gedney.

Most of the specialized equipment for the research was obtained with funds provided by the National Institutes of Health, Texas Heart Association, Noble Foundation, Sid W. Richardson Foundation and the Lester Levy Fund of the Dallas Community Chest. Additional funding has come from the Muscular Distrophy Association.

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