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Office of Medical Information
The University of Texas Southwestern Medical Center at Dallas
5323 Harry Hines Boulevard Dallas, Texas 75235-9060 214/688-3404

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CONTACT: Mike West
OFFICE: 214/688-3404
HOME: 214/321-0550

****Sophisticated biophysical tools help scientists unravel protein-folding mystery

DALLAS--A scientific presentation Jan. 18 by Dr. Lila Gierasch, professor of pharmacology and biochemistry at The University of Texas Southwestern Medical Center at Dallas, will focus on state-of-the-art biophysical methods scientists use to investigate proteins. Gierasch's presentation in San Francisco, in a symposium titled, "New Visions of Proteins: NMR and Computer Graphics," is part of the annual meeting of the American Association for the Advancement of Science.

Some of the tools Gierasch and her research team use include nuclear magnetic resonance, infrared and fluorescence spectroscopies, circular dichroism, and computer simulations. These spectroscopic methods help the scientists understand protein conformation and how "signal sequences" of amino acids target the protein-forming chains.

The discovery of the double-helix structure of DNA was the major breakthrough in beginning to understand the genetic code, which is the key to life. Now, scientists are attempting to unravel the "second half of the genetic code" -- how the sequences of amino acids specified by the DNA base sequence lead to the critical three-dimensional structures of functional proteins, which are essential for growth and repair of tissue. Proteins are constructed inside a cell using "building block" amino acids according to the unique genetic code contained in the cell's DNA.

In many cases the information in a linear sequence of amino acids is sufficient to direct the formation of a very complex three-dimensional structure. Gierasch and her colleagues are also investigating how certain sequences, called signal sequences, function in the cell to localize and target developing protein chains correctly, thus enabling their folding to occur in the appropriate cellular compartment.

AT UT Southwestern, part of Gierasch's research involves studying "pieces" of genes that are thought to determine the structure of a final protein. One example of a project is the LDL receptor: how this protein achieves its structure and assumes its role as a receptor on the cell's surface. This knowledge could give scientists a better understanding of how the LDL receptor traps and absorbs a certain type of cholesterol (low-density lipoprotein) from the bloodstream. Deficiencies in LDL receptors can lead to cardiovascular disease as cholesterol plaques build up in arteries, restricting blood flow.

The LDL receptor was discovered by Drs. Joseph Goldstein and Michael Brown at UT Southwestern -- a discovery that won them the Nobel Prize in Physiology or Medicine in 1985.

While Gierasch's research is at a basic scientific level, long-term clinical implications of such research could include earlier diagnosis of genetic disorders, better explanation of disease processes, and possible therapies to correct either the genetic defect itself or the defective product. Better medications could be developed to treat medical problems including diabetes, cardiovascular disease, blood disorders, viral infections, and hormone regulation of many body functions.

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NOTE: The University of Texas Southwestern Medical Center at Dallas comprises Southwestern Medical School, Southwestern Graduate School of Biomedical Sciences and Southwestern Allied Health Sciences School.