SOUTHWESTERN NEWS

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UT SOUTHWESTERN RESEARCHERS DECODE FILAMENT STRUCTURES THAT HELP ORGANIZE SIGNALING MOLECULES IN CELLS

DALLAS – Aug. 20, 2002 – Scientists at UT Southwestern Medical Center at Dallas have found the blueprint for how filaments assemble during the development of caveolae, a membrane system that organizes signaling molecules used by cells to communicate with each other.

The findings, appearing in today's edition of the *Proceedings of the National Academy of Sciences*, show that a protein called caveolin, in conjunction with cholesterol, forms filaments found on the inside surface of caveolae. Caveolae are structures that function as containers for signaling molecules in cells. The findings shed new light on how cell behavior is regulated.

Dr. Richard G.W. Anderson, chairman of cell biology at UT Southwestern and the study's principal investigator, said caveolae are vital for communications within a cell and between cells. They help ensure that signaling molecules are in the right location in the cell to do their job.

"We believe that signal transduction is not an interaction that can take place just anywhere in the cell," said Anderson. "Caveolae contain a whole array of signaling molecules, and their job is to spatially organize signal transduction at the cell surface."

The study also sheds light on the defect in limb-girdle muscular dystrophy, one of nine forms of the disease of which Duchenne is the most common. It is known that many limb-girdle patients have mutations in muscle-cell caveolin. The new study shows that these mutations cause defective filament assembly.

The researchers set out to deconstruct intact caveolin filaments, which are surrounded by cholesterol. Introduction of cholesterol-attracting drugs into cells disrupted the cholesterol sheath surrounding caveolin, and the filaments crumbled into individual subunits. The researchers were then able to determine that each subunit was composed of seven caveolin molecules. In limb-girdle dystrophy patients, whose disease is characterized by weakness and wasting of pelvic-girdle muscles and/or shoulder-girdle muscles, the defective caveolin can assemble into subunits,

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but these subunits are unable to form filaments.

Other contributors to the study were Dr. Imma Fernandez, a former postdoctoral researcher in Anderson's lab; Dr. Yunshu Ying, instructor of cell biology; and Dr. Joseph Albanesi, associate professor of pharmacology.

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