SOUTHWESTERN NEWS

EMBARGOED FOR 4 P.M. EDT, THURSDAY, JULY 3, 1997

Contact: Susan A. Steeves
(214) 648-3404
or E-mail: ssteev@mednet.swmed.edu

X-RAY CRYSTALLOGRAPHY ELUCIDATES STRUCTURE OF MOLECULE BASIC TO LIFE

DALLAS — July 4, 1997 — Scientists are one step closer to understanding the life-sustaining cellular process that produces energy for such functions as heartbeats and breathing. Using X-ray crystallography, researchers at UT Southwestern Medical Center at Dallas and at Oklahoma State University have been able to study the structure of a molecule basic to the production of cellular energy.

The bc_1 complex, also called Complex III, performs an intermediate step in cellular respiration — a series of chemical reactions that frees energy from food for use in cellular metabolism. Investigation of bc_1, which sits in the membrane of the cell's power plant, the mitochondria, revealed some unexpected properties of the large protein molecule.

The research, published in today's issue of *Science,* was led by 1988 Nobel laureate Dr. Johann Deisenhofer, a professor of biochemistry and an investigator in the Howard Hughes Medical Institute (HHMI) at UT Southwestern, and Dr. Chang-An Yu of OSU.

"We had an idea of what happens during cell respiration," Deisenhofer said. "When the energy stored in nutrients such as sugar is finally used to fuel cell processes, it involves many steps of metabolism. What is produced is a compound that stores high-energy electrons."

The main function of bc_1 is to provide energy to make the cell's "energy currency" called ATP (adenosine 5'-triphosphate). Cells must extract and transfer this energy in a controlled way along a metabolic pathway so that it can be used by other cellular processes.

"If the bc_1 complex is not functioning, then the cell can't live," said Deisenhofer, holder of the Virginia and Edward Linthicum Distinguished Chair in Biomolecular Science. "Every cell of the body needs to have its energy source in the mitochondria. If this doesn't function then there is no life."

By first crystallizing the bc_1 molecule and then using X-ray diffraction, the

(MORE)

researchers were able to see the protein's structure and discover how its atoms are positioned and interact. In the study, the scientists used mitochondria from a bovine heart. Mitochondria are more abundant in organs that require a high level of energy, such as a heart or a liver. They picked a cow's organ because its bc_1 complex can be easily crystallized.

"Essentially we get a more comprehensive understanding of the function of bc_1," Deisenhofer said. "What we found is pretty much in agreement with most previously accepted theories except that we were not aware that the bc_1 complex forms such a tight dimer — the molecule always appears in two identical copies. I'm convinced that the dimerization must enhance the function of the molecule."

The scientists also were surprised to discover how electrons are passed to the next step in the electron transfer chain of cellular respiration. That step is from bc_1 to cytochrome C oxidase — iron- and copper-containing protein molecules that are essential in the energy-producing process.

"Electron transfer in the bc_1 complex appears to be the first known case in which the electron is transferred to a protein domain, which then changes its orientation in the bc_1 complex," Deisenhofer said. "The transfer seems to involve the physical movement of a whole protein chain from one place to another. We certainly would like to know why nature has not used a more usual method to conduct electrons.

"Understanding this basic science brings us a step closer to understanding organisms and what drives them. It also will help us understand mutations in the molecules involved in cellular respiration so that we can study some genetic diseases."

Other UT Southwestern researchers involved in the study were Dr. Di Xia, assistant instructor of biochemistry, and Dr. Hoeon Kim, an HHMI research associate. Other OSU scientists involved were Drs. Jia-Zhi Xia, Anatoly M. Kachurin and Linda Yu, all of the Department of Biochemistry and Molecular Biology.

The research was supported by grants from the National Institutes of Health and the Welch Foundation.

###