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## **Children's Hospital Oakland Scientist First to Capture Complex Movements of Enzymes Targeted for Development of Anti-obesity and Anti-cancer Drugs**

February 11, 2009-Oakland, Calif.- A groundbreaking study has revealed in great detail how enzymes in the cell cooperate to make fat. These enzymes are integrated into a single molecular complex known as fatty acid synthase. This complex is regarded as a potential target for developing new anti-obesity and anti-cancer drugs.

Dr. Stuart Smith, at Children's Hospital Oakland Research Institute, collaborated with Drs. Edward Brignole and Francisco Asturias from The Scripps Research Institute in La Jolla, Calif. in a study published in the February 2009 edition of *Nature Structural and Molecular Biology* and featured on the cover of the journal.

"Fatty Acid Synthase is a remarkably complex structure. It contains all of the components needed to convert carbohydrates into fat," Dr. Smith explained. "We have suspected for some time that the enzyme complex is extremely flexible, which makes it difficult to analyze using X-ray crystallography. Last year the X-ray structure of the complex was solved by a group in Switzerland, but this structure provided only a snapshot of the complex in one of its many poses. We were able to use state-of-the-art electron microscopy to obtain images of the complex in many of its different conformations and assemble these images into a movie that displays the full range of motion of the components of the complex." The results reveal how enzymes that appear distantly located in the X-ray structure are able to make the contacts with each other needed for catalysis. The extraordinary swinging, swiveling and rolling motions of fatty acid synthase are represented on the cover of the journal in the form of a flamenco dancer.

Some pharmaceutical companies are focusing on inhibitors of fatty acid synthase because they are known to block the conversion of carbohydrates into fat and suppress appetite as well as slow the growth of cancer cells. Structural information garnered from X-ray and electron microscope images may aid in the design of more effective inhibitors that could be used therapeutically.

## **About Children's Hospital & Research Center Oakland**

Children's Hospital & Research Center Oakland is Northern California's only freestanding and independent children's hospital. Children's is the leader in many pediatric specialties including neonatology, cardiology, neurosurgery and intensive care. The hospital is a designated Level 1 pediatric trauma center and has the largest pediatric critical care facility in the region. Children's Hospital has 190 licensed beds, 201 hospital-based physicians in 30 specialties, more than 2,611 employees and an operating budget of \$312 million. Children's research arm, Children's Hospital Oakland Research Institute, has about 300 staff members and an annual budget of more than \$49 million. Primary research funding comes from the National Institutes of Health. The institute is a leader in translational blood diseases, developing new vaccines for infectious diseases and discovering new treatment protocols for previously fatal or debilitating conditions such as cancers, sickle cell disease and thalassemia, diabetes, asthma, HIV/AIDS, pediatric obesity, nutritional deficiencies, birth defects, hemophilia and cystic fibrosis.