



**CALIFORNIA STATE SCIENCE FAIR
2005 PROJECT SUMMARY**

Name(s) Lisa B. Noble	Project Number S0518
Project Title PPAR Delta Crystallography	
Abstract Objectives/Goals The peroxisome proliferator-activated receptor delta (PPAR delta) is a ligand dependent protein which regulates the transcription of genes related to lipid and cholesterol metabolism. The compound L-165,041 was developed by Merck and was found to act as a selective PPAR delta agonist. The nature of the interactions occurring between the protein and this ligand are presently unknown. Methods/Materials To gain further understanding of PPAR delta biology, the protein (PPAR delta), and the ligand, Merck compound L-165,041, were first cocrystallized and then x-ray crystallography was used to visualize the structure. The crystallography experiment commenced by diffracting microscopic protein crystals with a beam of X-ray photons that were collected on a charged coupled-device. It was necessary to use a beam of photons that was extremely powerful that can only be produced at synchrotron facilities such as the Advanced Light Source at the Lawrence Berkley National Laboratory. Various computer programs were used to refine, integrate, and scale the diffraction data and to calculate a 2.5 Å resolution electron density map of the crystal lattice Results A model of the protein-ligand structure was constructed using this information. The ligand-binding site was found to be in the center of PPAR delta. The ligand is held in this site by van der Waals forces and hydrogen bonds with the surrounding amino acids of the protein. Conclusions/Discussion This particular structure may help to design new compounds that have improved interactions with PPAR delta. The greater understanding scientists have of PPAR delta and its biology will impact how future drugs help our society with the growing issue of cholesterol metabolism.	
Summary Statement My project explores the technique of x-ray crystallography to determine the three dimensional structure of the PPAR delta protein bound to Merck compound L-165,041.	
Help Received Used lab equipment at the Lawrence Berkley National Laboratory under the supervision of Dr. Andrew Shiau.	