

**EXECUTIVE SUMMARY:** (State in layman's terms the application's broad, long-term objectives and specific aims, making reference to the potential public benefits of the project for California.)

In this project we propose to study the enzyme serine hydroxymethyltransferase (SHMT) which is involved in the biosynthesis of the nucleotides needed for the rapid growth of cancer cells. Serine hydroxymethyltransferase (SHMT) is a member of the thymidylate synthase cycle. This important cycle produces the pyrimidine nucleotides which are needed in rapidly dividing cells, including cancer cells. Clinically useful anticancer drugs have targeted other enzymes in the thymidylate synthase cycle suggesting that inhibitors of SHMT may also have anticancer properties. For this project human SHMT will be overexpressed and purified from *E. coli* and assays for the activity of SHMT will be developed. Computational studies, performed in collaboration with Dr. M. Ashley Spies of the University of Illinois at Urbana-Champaign, will be used to identify potential tight binding inhibitors against SHMT which may have promise as anticancer pharmaceuticals. The potential inhibitors identified computationally will then be tested for their ability to bind to SHMT. It is hoped that the project will lead to new lead to a deeper understanding of the chemistry catalyzed by hSHMT and to compounds with anticancer properties.