

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.)*

Ruthenium-based metal complexes containing phosphine ligands (RAPTAs) have shown great potential recently as an alternative to the current platinum-based anticancer drugs on the market. Their appeal stems from the fact that their higher aqueous stability makes them less toxic in the body and hence, they display fewer of the unwanted side effects that are associated with their platinum counterparts. The downfall of this reduced cytotoxicity, however, is that in order to be effective a higher relative dose must be given. This limits the efficacy of those compounds which have lower solubilities than required to achieve the concentration necessary to be an effective treatment. It is our intention to construct ruthenium complexes that are structurally similar to the RAPTAs with a new series of phosphorus ligands that will allow for greater aqueous solubility and stability. This will allow us to overcome the concentration limitations of the first generation RAPTA type ruthenium drugs. Our synthetic strategy also allows for greater ligand variability that could eventually be used to impart cell specific targeting moieties directly into our drug design. The advantages to a successful ruthenium based anticancer drug would be far reaching and many. These drugs could either be used as a first offensive against newly discovered tumor growths or they could be used as a follow up treatment to the many instances where cancerous relapses display an acquired resistance to the initial (usually platinum based) treatment.