



Award ID:  
RP110486-P5

Project Title:  
P5: The Coronary Microvasculature as a Target for Cardioprotection for  
Cancer-Therapy Induced Heart Failure

Award Mechanism:  
Multi-Investigator

Principal Investigator:  
Jay W Schneider

Entity:  
The University of Texas Southwestern Medical Center at Dallas

#### Lay Summary:

The heart is often inadvertently caught in the crossfire of cancer chemotherapy. The mechanisms through which chemotherapy injures the heart remain poorly understood. Heart damage associated with cancer chemotherapy is called cardiotoxicity. Cardiotoxicity can occur immediately with cancer chemotherapy or it can appear in a cancer survivor many years after successful cancer treatment. Cardiotoxicity often leads to the development of heart failure, a devastating disease condition with very high morbidity and mortality. The goal of this CPRIT Multi-Investigator Research Award application is to assemble the leading heart failure scientists in the state of Texas studying cancer chemotherapy cardiotoxicity. Forging a scientific alliance between world-class investigators at UT Southwestern and MD Anderson, two major heart and cancer research centers, we have assembled the most powerful research team possible for tackling this crucial problem. Together, our team has scientific and clinical synergy that makes the whole far greater than the sum of its individual parts. Our research will focus on discovering the mechanisms by which chemotherapy injures the heart. We will define the precise molecular and cellular targets of chemotherapy drugs in the heart and elucidate how targeting these molecules and cells leads to heart failure. Our preliminary studies have set the stage for this work. At the molecular level, we will study key enzymes and biochemical reactions involved in cardiotoxicity; moreover, we will study microRNAs, a newly discovered class of regulatory molecules. In addition to heart muscle cells, we will study how chemotherapy damages heart progenitors (or stem cells) and blood vessel cells. Most importantly, we will focus on developing new mechanism-based therapies to prevent, alleviate or reverse cardiac damage due to chemotherapy. Successfully achieving the 15 aims of this research proposal will make chemotherapy safer for the hearts of cancer patients.