Dr. Emily Tsai

This proposal describes a 2-year research project that will help propel mentored clinician-scientist Dr. Emily Tsai (a K08 awardee) towards full scientific independence as she develops her first Research Project Grant Program proposal (R01). The PI's long-term career goals are to gain original insight in the pathophysiology of heart failure, to identify novel targets for drug development, and to ultimately bring innovative therapies to clinical care. Now an Assistant Professor of Medicine at Columbia University College of Physicians and Surgeons, the applicant is actively expanding the scope of her research so as to build the foundation for a competitive R01 proposal in the near future. Hence, this 2-year R03 research project outlines experiments that will generate preliminary data and establish relevant animal models vital to the R01 proposal. Profoundly influenced by her clinical experience as an advanced heart failure and transplant cardiology, the PI aims to elucidate the molecular pathophysiology of right ventricular dysfunction (RVD). RVD is the strongest predictor of poor outcomes in heart failure (HF), independent of left ventricular ejection fraction. Yet the pathobiology of RVD remains poorly understood and RVD-specific medical therapy does not exist. The PI has formulated a research strategy to elucidate interventricular differences in myocardial soluble guanylyl cyclase/cyclic guanosine monophosphate (sGC/cGMP) signaling and to provide mechanistic data supporting the therapeutic potential of enhancing sGC/cGMP signaling in HF with RVD. To optimize the translational significance of her studies, the PI proposes *in vivo* studies that mimic guideline directed medical therapy (GDMT) of HF. The primary goals of the proposed research plan are to: 1) define interventricular differences in sGC/cGMP stimulation on cardiac function and remodeling; and 2) determine the effect of GDMT on myocardial sGC/cGMP signaling in the pathologically remodeled heart. Research findings of this R03 are expected to provide new insights into the differences and similarities between the right and left ventricles with regards to their pressure-overload stress response. Moreover, study results will offer evidence of optimal way(s) to enhance sGC/cGMP signaling in RVD HF. By the end of the R03 award period, the PI will be well poised to launch a career as an independent, R01-funded clinician scientist, focused on understanding the molecular pathophysiology of RVD in HF and developing novel strategies for preventing and treating it.