Abstract to accompany the talk by Joseph Hill

Heart failure (HF) with preserved ejection fraction (HFpEF) accounts for ≈50% of all HF and is associated with significant morbidity, mortality and healthcare expenditures. Sadly, there are no evidence-based therapies with demonstrated efficacy in HFpEF. None. We have no therapies to treat these tens of millions of individuals worldwide; rather, we are relegated to treating symptoms and comorbidities. It has been said that <u>HFpEF is the single greatest unmet need in cardiovascular medicine</u>.

Comorbidity-driven systemic inflammation has been suggested to play a major role in the pathogenesis of myocardial alterations in HFpEF. This notion derives largely from observations of increased levels of circulating inflammatory biomarkers in HFpEF epidemiological studies.

Mechanistic research in HFpEF has been hampered by a dearth of reliable preclinical models that recapitulate the multiple dimensions of clinical HFpEF as seen in patients. Indeed, much of what is called HFpEF in the preclinical literature falls well short of mirroring the clinical realities realized by patients. This is a huge shortcoming and, at the same time, a huge opportunity to do a better job.

In this presentation, I will discuss a recently developed and validated mouse model that faithfully mirrors most of the clinical features of human HFpEF. I will go on to outline novel mechanisms, never reported previously in cardiovascular disease, that we have uncovered.