Heart cells alter their metabolism in response to changes in their environment, especially in the setting of heart failure and heart attack. In this proposal, Ardehali’s team will determine whether a novel protein called sucrose non-fermenting-1 related kinase (SNRK) plays a role in regulating heart metabolism and its progression to heart failure in response to injury. They will study whether this protein makes the heart more metabolically efficient and will determine the mechanism for this process.

The central hypothesis of this proposal is that SNRK affects cardiac metabolism by reducing substrate utilization and increasing mitochondrial coupling, and that SNRK overexpression protects against the development of heart failure and ischemic injury. Ardehali’s team will assess whether deletion of SNRK will result in the opposite phenotype of its overexpression, i.e., increased glucose and fatty acid metabolism with similar cardiac force.

His team has generated global SNRK+/− mice and cardiac-specific SNRK knockout mice and will measure cardiac metabolic parameters in these animals. They will also assess the role of Trib3, UCP3 and PPARα in this process. In aim two of the proposal, the team will test if the reduced glucose and fatty acid metabolism still occurs in the hearts of SNRK TG mice mediated through Tribbles homolog 3 (Trib3).

They have generated SNRK TG/Trib3 knockout mice and will measure glucose and fatty acid metabolism in their hearts. They also plan to investigate the mechanism of Trib3 regulation by SNRK, and PPARα regulation by Trib3. In aim three, they will determine whether SNRK is protective against the development of heart failure and ischemic damage and will study the mechanism for this protective effect.

Their studies showing that SNRK reduces fatty acid and glucose metabolism and improves mitochondrial coupling promise to advance the knowledge of the role of cardiac metabolism in heart failure and may lead to the development of novel therapies for this disorder.

Every year, thousands of men are diagnosed with prostate cancer, many of whom have very low-risk disease that doesn’t require invasive surgery or radiation. Instead, these men are placed onto “active surveillance,” which is the ongoing tracking and monitoring of their tumor status by their urologist.

At the first sign of tumor progression, if it should progress, more conventional treatments are deployed. A benefit of this approach is that it prevents a growing trend of the overtreatment of prostate cancer, as well as the associated urinary, bowel, sexual and emotional side effects that can persist from having the prostate removed or radiated. A challenge has been that upwards of 25 to 50 percent of men on active surveillance will eventually drop out to receive more invasive treatments when it isn’t always medically warranted.

Victorson plans to use training in mindfulness meditation to for men diagnosed with prostate cancer on active surveillance and their spouses. His team wants study if mindfulness training can help men and their partners be better able to “sit with” and tolerate some of the uncertainties and stressors that this diagnosis and treatment approach can bring. He hopes this can result in fewer men dropping out of active surveillance prematurely to receive surgery in order to get greater “peace of mind.”

Victorson and his team are partnering with other academic medical institutions to conduct a five-year multi-site randomized controlled trial where men and their spouses will either be randomized to eight-weeks of intensive mindfulness meditation training or an eight-week control group that teaches important health promotion skills.

Prior to this study, Victorson was principal investigator of a smaller pilot study of the same intervention with men on active surveillance, which showed that those randomized to the mindfulness arm endorsed significantly greater self-reported resilience over time compared to controls.