LAY ABSTRACT

Atherosclerotic vascular disease is a major cause of morbidity and mortality in the United States and other western countries. The development of atherosclerosis involves chronic inflammatory processes, endothelial dysfunction, and lipid oxidation. Many of these processes are mediated by a complex network of intracellular signaling cascades. Modulating factors include the balance of nitric oxide in endothelial cells, circulating levels of blood lipids and lipoproteins, and the presence of additional bioactive components such as flavonoids. Thus the current view of cardiovascular disease risk is one of multifactorial etiology, but which can be partially modified through lifestyle choices, exercise and diet, including bioactive phytochemicals. Food phytochemicals such as the polyphenolic flavonoids from a wide variety of foods and beverages, such as soy foods, have been associated with cardiovascular protective effects in epidemiologic studies. Significant controversy exists regarding the efficacy and mechanisms for the cardiovascular protection of soy foods. New evidence is emerging that physiologically relevant concentrations of bioactive soy flavonoids, isoflavones, may impact cell signaling processes in vascular and other tissues, in addition to lowering blood lipids. There is a need for greater understanding of the cellular and molecular mechanisms underlying the physiologic responses to isoflavones in the vascular compartment.

Therefore, this research project proposes to examine metabolic responses to soy and bioactive soy components in a human clinical trial and in vascular cell culture experiments in order to provide insights into potential mechanisms which contribute to the cardiovascular protection of soy. Specifically, this research will investigate the effects of dietary whole soy protein foods on blood and urine metabolites which can be changed by diet and are biomarkers of cardiovascular risk, focusing on lipoproteins, lipid metabolism and inflammation in individuals with high cholesterol. This research will also investigate the cellular and molecular effects of soy isoflavones in human macrophage cells by examining changes in gene expression and cell signals. Together, the results of these studies will help scientists to understand more about the mechanisms of how soy foods can lower cardiovascular risk factors. This will lead to better and more accurate recommendations about how dietary soy can improve health.