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LAY ABSTRACT

Type 2 diabetes is correlated with oxidative stress and heart disease. Eating fruits and vegetables may reduce diseases, including heart disease. Natural antioxidants, such as Vitamin C, may contribute to the healthy effects of eating fruits and vegetables. However, effectiveness of Vitamin C consumption for treating type 2 diabetes remains uncertain. We propose experiments to identify the basic mechanisms by which vitamin C can regulate oxidative stress through a mitochondrial protein named uncoupling protein-2 (UCP2). UCP2 influences the oxidative stress produced by mitochondria. Existing peer-reviewed literature indicates that natural variants of UCP2 influence type 2 diabetes in people. Other data demonstrate clear effects of UCP2 on both insulin secretion by pancreatic beta cells and effects on glucose sensing neurons in the hypothalamus. Our preliminary data in mice show that absence of UCP2 from mice leads to increased levels of the oxidative products of vitamin C. Thus, we will test the effects of injected vitamin C in mice lacking UCP2 on levels of these metabolites. All mammals except primates, guinea pigs and fruit eating bats make vitamin C. We will also determine the diabetes and serum cholesterol phenotypes of mice genetically engineered to be deficient in production of vitamin C and UCP2. The overall results of our work will be to determine if there is indeed a connection between UCP2 and vitamin C. Since variants of UCP2 are common in all human populations, then the results may provide a rational explanation for differences in response of humans to supplemental vitamin C.