Molecular mechanisms by which citrus flavonoids regulate cholesterol transport processes in the liver
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The American Heart Association estimates that cardiovascular disease will claim the lives of nearly two and a half million Americans in 2006. To combat high cholesterol, one of the most common causes of cardiovascular disease, researchers have been searching for new and innovative ways to lower cholesterol. Recently, flavonoids isolated from citrus fruits have been identified for their keen ability to reduce low-density lipoprotein (LDL) levels in plasma. This observation raises the question of how flavonoids interact with cholesterol metabolism in the liver to produce these effects. It is known that LDL is taken into liver cells via the low-density lipoprotein receptor (LDLR) and is subsequently broken down into cellular cholesterol and triglycerides. The cholesterol can then be reutilized within the cell, excreted as bile, or processed by the microsomal triglyceride transport protein (MTTP) to be returned to the plasma as very-low density lipoprotein. LDLR and MTTP work together to regulate cholesterol levels in hepatocytes. Since both of these genes are controlled by the transcription factor, sterol regulatory element-binding protein (SREBP), we have begun to explore the possibility that flavonoids actually operate through SREBP. To address this hypothesis, we will obtain more accurate measures of LDLR and MTTP mRNA levels through mRNA hybridization and quantitative polymerase chain reaction (PCR) methods. While the hybridizations verify the quality of our PCR products, the quantification using real-time PCR provides a more efficient way to evaluate the changes in mRNA expression. These data will permit further investigation of the specific role of SREBP in the transcriptional regulation of MTTP and LDLR by citrus flavonoids. Ultimately, we will gain invaluable information on decreasing the risk of cardiovascular disease through cholesterol reduction.