

M-I (2) Non-technical abstract. Cardiovascular disease is the single leading cause of mortality in the United States, responsible for the deaths of two out of every five Americans, with total of nearly one million deaths annually. Coronary artery disease describes a broad spectrum of ischemic syndromes that may evolve from atherosclerosis, thrombosis, and/or vasospasm. Current therapies include pharmacologic interventions and surgical therapy by mechanical revascularization using percutaneous transluminal coronary angioplasty, coronary artery bypass grafting or transmyocardial laser revascularization. The identification of specific biologic mediators of angiogenesis make it possible to consider "therapeutic angiogenesis," where angiogenic molecules can be employed to develop new vascular networks to circumvent the ischemic consequences of atherosclerosis occluding the arterial system. The focus of this protocol is the delivery of VEGF cDNA directly into the myocardium of individuals with life threatening coronary artery disease via a non-surgical catheter-based approach. The rationale behind this study is that by injecting the VEGF expression cassette directly into the heart we can improve myocardial blood flow/function as assessed by using positron emission tomography (PET) scan. The protocol will include 10 individuals, each with clinically significant coronary artery disease. At the conclusion of the study, the following objective will be met: (1) to determine the safety/toxicity of direct administration of the vector Ad_{CU}VEGF.1 to the ischemic myocardium; (2) to assess whether direct administration of Ad_{CU}VEGF.1 to the myocardium will induce growth of collateral blood vessels, improve coronary blood flow and improve cardiac function in the region of ischemia.