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**Project Summary:** Tobacco smoking is one of the major contributing factors to atherosclerotic cardiovascular disease that plagues millions of Americans. Bypass grafting, the mainstay of treatment for the disease, was performed for over half a million patients in 1999. To perform these cardiovascular surgeries, large numbers of grafts are needed. Currently, most of these grafts are obtained from patients' own blood vessels (i.e., autologous) or through use synthetic materials. However, both autologous and synthetic grafts are associated with various problems ranging from limited availability to proneness to thrombotic occlusion. The long-term clinical objective is to fully restore the functions of diseased or injured blood vessels by implantation of the grafts grown in vitro. To achieve this goal, new materials that support cell growth and function and novel culturing technologies and strategies must be developed. The successful accomplishment of the research goals in the proposed study will not only enhance understanding of the vascular development under a physiological environment but also establish a novel strategy for functional blood vessel regeneration. The knowledge obtained and technology developed in this study will have important impact on the treatment of atherosclerotic cardiovascular diseases.