Biomimetic nanomatrix for tissue engineered atherosclerosis model and arteriovenous fistula maturation

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Atherosclerosis is the main cause of cardiovascular disease. To evaluate therapeutics for treating atherosclerosis, *in vivo* and *in vitro* atherosclerosis models are developed. However, those atherosclerosis models have their own limitations. *In vivo* models, like pig and non-human primates, can develop lesions in coronary arteries, however, inducing atherosclerosis in them requires high cholesterol intake, long induction time, gene knock-out, and high expense. Although mouse models are the predominant models used in the labs, however, most of the currently mouse models show different plaque structure and genome from that of human. *In vitro* models are also used for evaluation due to their low cost; however, most of the those models are not generated following the pathogenesis of human atherosclerosis and are two-dimensional (2D) models which are limited to static culture in tissue culture plate and unable to provide three-dimensional (3D) tissue structures with proper functions. Thus, the main goal of this study is to develop an innovative biologically inspired 3D in *vitro* platform – tissue engineered atherosclerosis model (TEAM), featured with endothelial dysfunction, macrophages, and foam cells, following the pathogenesis of human atherosclerosis with low cost.

About 600,000 patients in the US suffer from end-stage renal disease (ESRD), and more than 75% of ESRD patients undergo dialysis. Vascular access dysfunction is a major cause of morbidity and hospitalization in dialysis patients. Ateriovenous fistulas (AVFs) are considered the gold standard of vascular access for dialysis. However, up to 60% of AVFs fail to mature sufficiently to allow dialysis because of early venous neointimal development, inadequate vasodilation, and adverse vascular wall remodeling. Therefore, to promote proper AVF maturation, we propose the application of nitric oxide (NO) releasing nanomatrix gel on the created AVF. The NO releasing nanomatrix is composed of a self-assembled peptide amphiphile (PA), which contains an endothelial cell adhesive ligand (YIGSR) and a polylysine (KKKKK) group to form NO donating residues. This nanomatrix gel releases NO over a one month period, which promotes recruitment of endothelial progenitor cells in blood and endothelial cells from surrounding tissues, vasodilation of the AVF during maturation, and inhibition of smooth muscle cell proliferation. In this study, we test our hypothesis that the NO releasing nanomatrix gel applied at the time of AVF creation can stimulate AVF maturation by decreasing neointimal hyperplasia, enhancing vasodilation, and improving local endothelial function.