

James & Esther King Biomedical Research Program

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*2008 Program
New Investigator (3-year project)*

Project Title: Mechanisms of MCP-1/CCR2 Axis-Regulated Vein Graft Neointimal Hyperplasia

Project Summary: Vein bypass surgery remains the only option for a large set of patients suffering from occlusive arterial disease. However, nearly 50 percent of the vein grafts fail within two years, and the risk of graft occlusion for tobacco users is 3.1-fold that of non-tobacco users. Vein grafts occlude largely as the result of neointimal hyperplasia (NIH). Recent studies have established a stimulatory role for the CC chemokine monocyte chemoattractant protein (MCP) -1 and its receptor CCR2 in this process. The deleterious impact of the MCP-1/CCR2 axis on vein graft performance is more pronounced in tobacco users due to the elevated levels of serum MCP-1 in this population. Emerging evidence suggests that MCP-1/CCR2 promote vein graft NIH via monocyte independent mechanisms. However, neither have the exact cellular producers and functional performers been identified, nor has the impact of the MCP-1/CCR2 axis on neointimal cell biologies been defined. While the existing data suggest that MCP-1/CCR2 intrinsic to the graft wall promotes NIH, direct evidence remains lacking. Therefore, the grant's research goals are to define the impact of MCP-1 and CCR2 signaling both intrinsic and extrinsic to the graft wall on NIH during vein graft adaptations. Genetic and molecular approaches will be employed in these studies. Completion of this research will lead to the identification of therapeutic targets and lay the foundation for the development of effective therapeutic strategies.