NORTHWESTERN UNIVERSITY

Office for RESEARCH

AMERICAN RECOVERY AND REINVESTMENT ACT

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NIH Award from the National Institute on Aging

Principal investigator: Karen A. Lapidos, biomedical engineering McCormick School of Engineering and Applied Science

- **Project:** Endothelial Progenitor Cells in Diabetes and Renal Failure
- **Start Date:** May 1, 2009
- **Total Award Amount:** $137,250

How the results of this project will benefit society:
Current pharmacologic and surgical treatments have limited potential for improving the quality of life for patients in need of small diameter blood vessel replacements, repair of damaged blood vessels or heart, or the formation of new blood vessels. In contrast, the use of endothelial progenitor cells (EPCs) isolated from blood may significantly improve the clinical outcome of these patients by providing a living component of native blood vessels. In the current investigation, EPCs from patients with diabetes and kidney failure will be examined to determine their suitability for such cell-based therapies.

The problem the project is trying to solve:
Hyperglycemia in diabetes leads to kidney damage that may ultimately culminate in end stage renal disease (ESRD), the most severe stage of chronic kidney disease. ESRD patients must rely on frequent hemodialysis treatments to extend life. Some ESRD patients require surgical insertion of a synthetic arteriovenous graft into a vein for vascular access. However, eventual thrombosis in the graft leads to increased morbidity and hospitalization for patients along with a need for graft replacement. A novel therapeutic strategy to improve the longevity of an arteriovenous graft is the development of a bioengineered graft that includes a functional endothelium to naturally retard thrombosis. Circulating endothelial progenitor cells (EPCs) are a recently identified population of cells that are being investigated for the development of cell-based therapeutics to improve cardiovascular health. Autologous EPCs, those derived from the individual's body, may be an ideal source by which to obtain endothelial cells for a bioengineered arteriovenous graft.

How this project will work:
To determine the suitability of autologous EPC-based therapies for diabetic, ESRD patients, the vascular functions of EPCs from patients and age-matched controls will be investigated. Peripheral blood will be obtained from human volunteers and will be cultured in vitro to obtain endothelial cells (pbECs). Flow cytometry and immunofluorescence will be used to confirm the pbEC phenotype. To assess the vascular functionality of pbECs, the anti-thrombogenic, anticoagulant, and inflammatory activities of pbECs derived from patient and control groups will be quantified and compared on a novel biomaterial. Finally, the retention of pbECs seeded onto a novel bioengineered graft will be compared between patient and control groups. These experiments are designed to provide preliminary data to determine the suitability of autologous pbECs in the development of a novel, bioengineered arteriovenous graft for hemodialysis access.

This award is funded under the American Recovery and Reinvestment Act of 2009, NIH Award number: 1R03AG033337-01A1.