CMMRF Funding for Indiana Center for Vascular Biology and Medicine
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Peripheral Vascular Disease

Michael Murphy, M.D.

More than 100,000 patients in the US each year undergo amputation due to advanced atherosclerotic vascular disease in the leg. Ten to fifteen million more with this disease have crippling pain that limits their walking. More than half of these patients have this disease as a complication of diabetes. There is accumulating evidence that this PAD may be effectively treated with stem cells that stimulate new blood vessel development.

Dr. Michael Murphy has completed the first Phase I trial of stem cells (derived from one's own bone marrow) that was FDA-approved in the USA to treat vascular disease in legs for patients who have been told their only hope is amputation. Thus far, only three patients of 32 treated have required amputation. The autologous bone marrow mononuclear cells "SAVE" study is now being extended to a Phase III randomized study between patients receiving cells or no cells, to compare outcomes directly. The study has received conditional FDA approval and will be conducted at 10 centers throughout the US, with the ICVBM being the lead center for the study. Duke University in North Carolina and the University of Alabama in Birmingham are among those participating. This study forms a key platform to move into treatments of heart disease; developing new therapies in legs allows testing safety in leg muscle before moving into heart muscle.

Dr. Murphy's team also launched a new trial that evaluates a new source of stem cells; **A Laboratory Analysis of Endometrial Regenerative Cells (ERC).** This study collects menstrual blood. The goal is to develop a sterile laboratory technique for expanding ERCs from a single donor to reach a target population of 1 x108 cells with a normal karyotype. ERC appear to possess numerous advantages compared to other stem cell sources that make them attractive to further investigation. Firstly, the ease of collection of ERC allows for the creation of patient-specific cell banking (holding them back until needed). If the cells behave as expected, they may be expanded (multiplied) and may possess the ability to change into various tissues.

Isolation and Characterization of Endothelial Colony Forming Cells (ECFCs) from Human Adult Blood Vessels.

Michael Murphy, M.D.

Highly proliferative endothelial stem cells were isolated from human arteries and leg veins by Dr. Murphy, using colony forming assays developed by David Ingram, MD and Merv Yoder, MD (collaborators in Pediatrics). The significance of this study is that (1) we have developed the ability to isolate these cells from vessel endothelium, a critical step in the analysis of ECFCs in the pathogenesis of disease; and (2) we have shown that autologous vein, potentially available by minimally invasive harvesting methods, can provide a practical source of ECFCs that are available for

autologous use in cell therapies. We are also studying how diabetes and aging affect these cells and may cause blood vessel disease by making them unable to fulfill their repair functions.

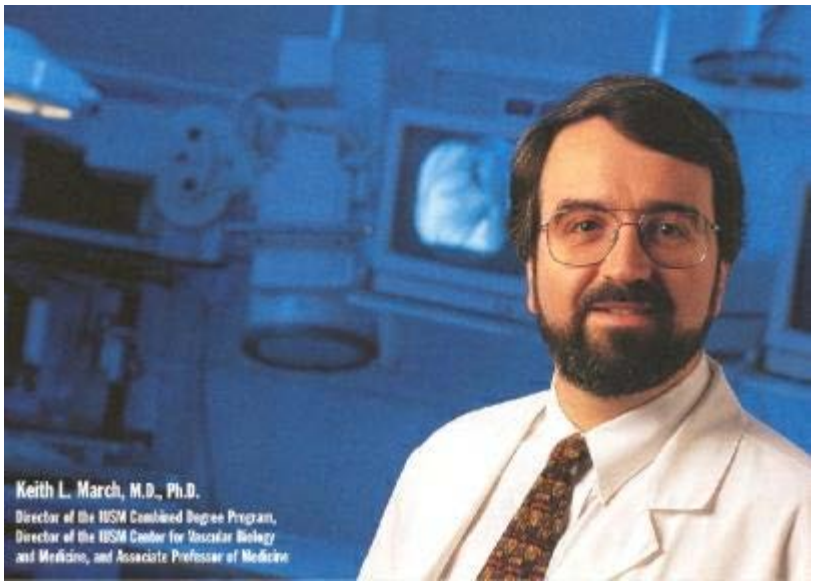
Adipose Stem Cells for Peripheral Arterial Disease.
We are working with the FDA as well as a corporate partner, Tissue Genesis, to test the feasibility and safety of providing adipose (fat) stem cells (ASCs) in patients with severe peripheral vascular disease. Animal trials that we have conducted have suggested that ASCs are very potent in this regard; multiple other labs have also corroborated these data. We would like to be the first to complete testing of this concept in a human Phase I critical limb ischemia trial essentially identical in design to the ABMNC “SAVE” study.

Diabetes: working towards a cure
Carmella Evans-Molina, M.D., Ph.D.

Nearly 24 million people in the United States are affected by diabetes. Type 2 diabetes is the most common form of diabetes. In type 2 diabetes, either the body does not produce enough insulin or the cells ignore the insulin. Insulin is necessary for the body to be able to use glucose for energy. When you eat food, the body breaks down all of the sugars and starches into glucose, which is the basic fuel for the cells in the body. Insulin takes the sugar from the blood into the cells. When glucose builds up in the blood, the body cannot make efficient use of its main source of fuel, and over time, high blood glucose levels may hurt your eyes, kidneys, nerves or heart.

"Our researchers are working today to develop the medicine of tomorrow."

- Keith March, M.D., Ph.D.
Director, IU School of Medicine ICVBM



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