

Non-technical Abstract

The purpose of this clinical investigation is to determine if gene therapy can be used to cause the development of new blood vessels in legs with blocked arteries, and to further determine if the additional blood flow which is provided by such new blood vessels will be sufficient to eliminate leg pain present at rest ("rest pain") and/or heal ulcers in the feet and legs.

While angioplasty techniques and/or surgery may often increase blood flow in patients with blocked arteries sufficient to relieve rest pain and/or heal ulcers, the blockages may in some cases be too extensive to permit either of these therapies. No medications are currently available that are likely to accomplish relief from rest pain or heal ulcers. Accordingly, we are investigating a new strategy, gene therapy, which has not been used previously for the treatment of lower extremity arterial insufficiency. This therapy has been tested thus far in laboratory animals; the experiments suggest that if one performs surgery on the animal (rabbit) to create blockages in the leg arteries, one can use gene therapy to grow new blood vessels around the blockages; this treatment is termed "therapeutic angiogenesis."

The treatment will involve using a catheter - similar to catheters which are used to perform balloon angioplasty - to deliver DNA, or genetic material, to one of the arteries which is still open in the diseased leg. The DNA is delivered to the wall of the artery from the balloon of the catheter when the balloon is inflated. Once in the arterial wall, the DNA then directs the cells of the artery wall to make a certain protein, in this case a protein called vascular endothelial growth factor (VEGF). VEGF is a protein which has been shown to cause new blood vessels to grow under a variety of conditions, including the above-described rabbit experiments in which both the protein and the gene for the protein caused new blood vessels to develop in the leg with arterial blockages.

We are thus investigating the possibility that by using a catheter to transfer the gene for VEGF to the arterial circulation of a leg with blocked arteries, new blood vessels will develop that will reduce pain in the leg and/or heal an ulcer.