

# COMPOSITIONS AND METHODS FOR TREATING PERIPHERAL VASCULAR DISEASES

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1. Meng, Guoliang, and Derrick Rancourt. "Methods and Materials for Culturing Murine Embryonic Stem Cells." Abstract. *Methods and Materials for Culturing Murine Embryonic Cells* (2009).

2. Rogers, Ian, Robert Casper, and Ryszard Bielecki. "COMPOSITIONS AND METHODS FOR TREATING PERIPHERAL VASCULAR DISEASES." (2008). Abstract.

**Abstract:** The invention relates to methods for producing endothelial cells, pericytes and/or muscle cells (in particular smooth muscle cells), cell preparations and pharmaceutical compositions comprising the cells or preparations, and the use of the cells, preparations and compositions in research or commercial applications. In aspects, the invention provides a method of treating a patient with a condition involving endothelial cells, endothelial precursor cells, pericytes and/or muscle cells, such as a peripheral vascular disease, comprising administering to the patient endothelial precursor cells, endothelial cells, pericytes and/or muscle cells obtained from multipotent CD45<sup>+</sup>HLA-ABC<sup>+</sup>Lin<sup>-</sup> cells.

**TITLE:** Compositions and Methods for Treating Peripheral Vascular Diseases FIELD OF THE INVENTION

The invention relates to methods for producing endothelial cells, endothelial precursor cells (EPCs), pericytes and/or muscle cells, cell preparations and pharmaceutical compositions comprising the cells or preparations, and the use of the cells, preparations and compositions in research or commercial applications. BACKGROUND OF THE INVENTION: Peripheral vascular disease (PVD) is due to an organic or functional blockage of the blood vessels similar in mechanism to coronary heart disease. PVD can cause intermittent claudication leading to tissue ischemia of the lower limbs. The prevalence is expected to increase due to the aging population. The unmet medical need for the treatment of intermittent claudication (IC) and critical limb ischemia (CLI) is ~31 million patients with IC in the US, Europe and Japan; -7.8 million require medical treatment and ~1 - 5% of IC patients progress to CLI. These patients are at high risk for limb loss and cardiovascular and cerebrovascular complications. The estimated cumulative economic burden is over \$30 billion per year in the US alone. Partial repair of the ischemic tissue can occur due to new vessel formation by (i) angiogenesis and (ii) vasculogenesis or (iii) arteriogenesis. Ischemia acts as a stimulus that causes circulating endothelial precursor cells (EPCs) to home to the site of injury where they proliferate and differentiate into new blood vessels. Standard treatments for PVD are targeted atherosclerotic risk-factor reduction, which generally does not improve tissue perfusion. Therapies to improve tissue perfusion (surgery or angioplasty) target larger vessels and are not generally successful for smaller (peripheral) vessels and limb amputation usually results. Correction of small vessel occlusions and the healing of wounds and skin ulcers require novel therapies. Two significant forays into the therapeutic arena are the use of growth factors to stimulate endogenous cells to undergo vasculogenesis or the transplantation of donor cells. However, pure recombinant growth factors have a short half-life in the body, therefore, the addition of cells capable of secreting factors has the advantage of delivering growth factors in a controlled and sustainable manner. The citation of any reference herein is not an admission that such reference is available as prior art to the instant invention.

These conditions include the use of suitable differentiation media. A differentiation medium generally comprises a minimum essential medium plus optional agents such as growth factors, non-essential amino acids, and other agents known in the art. A differentiation medium may contain serum (FCS) or be serum free. Differentiation media are known to persons skilled in the art and are commercially available from companies such as **Celprogen (San Pedro, CA)** and StemCell Technologies (Vancouver, Canada). A differentiation medium can comprise a differentiation factor which induces multipotent cells to endothelial cells or muscle cells as the case may be. For example, a differentiation factor which induces formation of endothelial cells is vascular VEGF.