Implantation of autologous urine-derived stem cells expressing VEGF for cell therapy in the correction of vesicoureteric reflux

Shaofeng Wu¹, Zhan Wang¹, Shantaram Bharadwaj¹, Steve Hoagie¹, Anthony Atala¹, and Yuanyuan Zhang¹

Corresponding Author: Yuanyuan Zhang¹

¹Wake Forest Institute for Regenerative Medicine, Winston Salem, North Carolina-27157, USA

Introduction

The goal of this study was to evaluate effects of vascular endothelial growth factor (VEGF) over-expression on urine-derived stem cell (USC) survival, growth and myogenic differentiation and to determine whether this technique could improve injection therapy for the correction of vesicoureteral reflux (VUR).

Materials and Methods

USC were obtained from 9 urine samples (5 healthy individual donors; ages from 3 to 27). USC were infected with adenovirus containing human VEGF gene (USC/Ad-VEGF). VEGF secreted by infected USC were measured in the culture medium. USC/Ad-VEGF plus endothelial cells (in total 5x10⁶ cells) in 500 μl collagen-I gel and other six controls were subcutaneously implanted into 20 athymic mice. The grafts were assessed grossly, with histology and immunocytochemistry on smooth muscle markers (alpha-smooth muscle action, desmin and myosin) and endothelial markers (CD 31 and von Willeband factor) up to 28 days after injection.

Results

VEGF levels in the culture medium reached a peak at 12 days after USC were infected. The grafts with USC/Ad-VEGF plus endothelial cells were larger and had better vascularization compared to the non-VEGF controls. Additionally, the total number of implanted cells expressing human nuclear markers was significantly higher. More cells expressed CD 31 and von Willebrand proteins, smooth muscle cell markers, and more nerve fibers in the USC/Ad-VEGF plus endothelial cells group than the other controls in vivo.

Discussion and Conclusions

VEGF over-expression in grafted USC enhanced the in vivo survival of these cells and increased neovascularization, myogenic differentiation of USC, and nerve regeneration within the grafts. This approach might have important clinical implications for urological cell therapy for the treatment of VUR.

Disclosures

The authors have nothing to disclose.