Blood Vessel Formation by Microtissue Implantation is Enhanced by the Addition of MSC

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Introduction

We have previously shown that blood vessels can be formed by the implantation of collagen cylinders (modules) that are coated with endothelial cells into allogeneic rats 1. The objective of this study is to determine if the addition of bone marrow derived MSC to the modules improves vessel formation. Previous reports have indicated that MSC can act as pericytes and are needed to form vessels in SCID mice 2. MSC are also known to modulate the immune system 3.

Materials and Methods

MSC were isolated from male SD rats. Modules were formed from by drawing type 1 bovine collagen embedded with or without MSC (1x10^6 cells/mL) into sterile 0.71mm polyethylene tubing and gelled at 37°C. The tubing was cut into 1 mm pieces and the collagen cylinders were seeded with rat aortic endothelial cells (EC). The modules (400) were implanted into an omental pouch of female SD rats that were treated (or not) with tacrolimus (0.3–0.2 mg/kg) and atorvastatin (0.5 mg/kg).

Results

In vitro studies of the interaction between MSC and EC show that the MSC improve the proliferation of the EC and their ability to form tubes in a tube forming assay.

Initial data shows changes to the remodeling of the implanted microtissue with the addition of MSC. There is a decrease in macrophage infiltration 14 days after implantation (Fig. 1) and an increase in the percentage of M2 macrophages. The MSC develop SMA staining and support the newly formed vessels by acting as pericytes. With the addition of MSC the number of vessels is stable for 21 days whereas EC implanted alone have an increase in the number of vessels at day 14 that then decreases with time (Fig. 2). The vessel architecture and leakiness is being determined by microCT.

Discussion and Conclusions

The addition of MSC to the implanted modules enhances the remodeling of microtissue. There appears to be stabilization of the vessels due to the ability of the MSC to decrease inflammation and act as pericytes. This is expected to improve the survival and function of the microtissue.

References


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Disclosures

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