

networks at day 11 exhibited expression of both NG2 (FIG. 7E-7H) and  $\alpha$ -SMA (FIG. 7I-7L) Further, a 3-D Z-stack animation was created from sections stained with vWF and  $\alpha$ -SMA individually to observe the tube architecture formed in the fibrin gels. The co-localization of these markers typically demonstrated that  $\alpha$ -SMA occupied a position on the exterior of the tube relative to vWF. This indicated that the cell populations expressing endothelial and pericyte markers are separate with the pericyte markers occupying a pericellular position within the growing network.

**[0075]** ASC Migration from chitosan Microspheres

**[0076]** As shown in FIGS. 7 and 16, cells that had been seeded onto chitosan microspheres were able to migrate through either PEGylated fibrin (FIG. 16A-C) or collagen (FIG. 16D-F). Migration was seen in both gels as early as day 2 after seeding. Migration and/or proliferation continued throughout the times monitored (day 8 for PEGylated fibrin and day 12 for collagen). ASC migrating into the PEGylated fibrin demonstrated the characteristic tubular morphology as seen in the gel matrix alone, while ASC migrating through the collagen matrix had a spindle-shaped morphology.

**[0077]** When ASC were pre-labeled with Qdot 565 nanocrystals and visualized after 6 days in culture, the labeled cells could be clearly seen as distinct from the chitosan microspheres. The fluorescent images as well as the brightfield overlay for migration into both PEGylated fibrin (FIG. 17A-C) and collagen (FIG. 17D-F) are shown. This result provides evidence that the ASC are able to migrate from the embedded microspheres and into either collagen or PEGylated fibrin.

**[0078]** Matrix-Based Morphology of ASC

**[0079]** FIG. 17 consists of a series of light microscopy images over an 11 day timecourse as ASC grow out of chitosan microspheres into either collagen or PEGylated fibrin. The cells that had been cultured on the surface of microspheres were "sandwiched" between the two different gel layers. This type of experimental setup allowed for the independent investigation of the effects that the matrix environment had on cell migration and differentiation. Cells were clearly able to leave the microsphere surface and migrate into either the collagen gel or the PEGylated fibrin. Cells in both gel layers were evident from day 3 until the end of the culture period. The morphology of the migrated ASC were dramatically different in the two gel layers. In the collagen gels, the cells exhibited a spindle-shaped morphology similar to what was seen in the collagen gel layer by itself. In the PEGylated fibrin gels, the cells demonstrated multicellular tubular networks analogous to those in the PEGylated fibrin layer alone. In a number of the figures, it can be clearly seen that the same microsphere population is shown either from the underside (PEGylated fibrin, FIGS. 18B, D and F) or the top side (collagen, FIGS. 18A, C and E). This indicates the close proximity of the two cell phenotypes as well as the fact that cells on the same bead can exhibit two distinct phenotypes. The cells in the PEGylated fibrin were able to form extended networks that spanned the dimensions of the acquired image. This result provides evidence for the purely matrix-driven differentiation of ASC in either collagen or PEGylated fibrin.

**[0080]** Therefore, the present invention is well adapted to attain the ends and advantages mentioned as well as those that are inherent therein. It should be understood, however, that the description of specific example embodiments is not intended to limit the invention to the particular forms disclosed, but on the contrary, this disclosure is to cover all modifications and equivalents as defined by the appended

claims. While numerous changes may be made by those skilled in the art, such changes are encompassed within the spirit of this invention as illustrated, in part, by the appended claims.

What is claimed is:

1. A laminar construct comprising:
  - a hydrogel matrix comprising at least a first hydrogel layer and a second hydrogel layer, and
  - a plurality of mesenchymal stem cells.
2. The construct of claim 1 wherein at least a plurality of the mesenchymal stem cells comprise adipose derived stem cells.
3. The construct of claim 1 wherein the first hydrogel layer comprises a material that causes at least one of the mesenchymal stem cells to differentiate into a blood vessel cell.
4. The construct of claim 1 wherein the first hydrogel layer comprises at least one material selected from the group consisting of fibrin, PEGylated fibrin, hyaluronic acid, any derivative thereof, and any combination thereof.
5. The construct of claim 1 wherein the first hydrogel layer comprises PEGylated fibrin.
6. The construct of claim 1 wherein the second hydrogel layer comprises a material that causes at least one of the mesenchymal stem cells to differentiate into a dermal fibroblast.
7. The construct of claim 1 wherein the second hydrogel layer comprises at least one material selected from the group consisting of collagen I, collagen II, collagen III, collagen IV, collagen V, fibronectin, tenascin, vitronectin, a glycosaminoglycans, any derivative thereof, and any combination thereof.
8. The construct of claim 1 wherein at least one of the mesenchymal stem cells are sandwiched between the first and second hydrogel layers.
9. The construct of claim 1 wherein at least one of the mesenchymal stem cells are seeded within the first and second hydrogel layers.
10. The construct of claim 1 wherein a plurality of the mesenchymal stem cells are seeded on microcarriers and sandwiched between the first and second hydrogel layers.
11. A method of creating a laminar construct comprising:
  - providing a hydrogel matrix comprising at least a first hydrogel layer and a second hydrogel layer, and
  - introducing a plurality of mesenchymal stem cells to the hydrogel matrix.
12. The method of claim 11 wherein introducing a plurality of mesenchymal stem cells to the hydrogel matrix comprises sandwiching the plurality of mesenchymal stem cells between the first and second hydrogel layers.
13. The method of claim 11 wherein introducing a plurality of mesenchymal stem cells to the hydrogel matrix comprises seeding the plurality of mesenchymal stem cells within the first and second hydrogel layers.
14. The method of claim 13 wherein the plurality of the mesenchymal stem cells are seeded on microcarriers.
15. The method of claim 11 wherein at least a plurality of the mesenchymal stem cells comprise adipose derived stem cells.
16. The method of claim 11 wherein the first hydrogel layer comprises at least one material selected from the group consisting of fibrin, PEGylated fibrin, hyaluronic acid, any derivative thereof, and any combination thereof.
17. The method of claim 11 wherein the second hydrogel layer comprises at least one material selected from the group consisting of collagen I, collagen II, collagen III, collagen IV,