Severe ischemic diseases are often caused by atherosclerotic occlusion of arteries supplying blood to the myocardium or limbs. In such cases, transluminal angioplasty or bypass surgery is the most effective strategy for restoring blood supply in the affected arteries. However, in patients with severe ischemic heart disease or peripheral artery disease who cannot undergo bypass surgery or angioplasty, therapeutic angiogenesis is an effective means of preserving the integrity of tissues. Therapeutic angiogenesis is mediated by either injection of angiogenic cytokines, such as vascular endothelial growth factor, basic fibroblast growth factor, and hepatocyte growth factor; or implantation of angiogenic cells, including bone marrow mononuclear cells, peripheral blood mononuclear cells, and endothelial progenitor cells.

The same research group previously demonstrated that such engineered capillary networks function in vitro and improve blood perfusion in a mouse model of subcutaneous punch lesion. The novel technique used in that study was engineered capillary structure, because human umbilical vein ECs cannot be used as an autologous cell source at present. However, they overcame this issue using sphingosine 1-phosphate, which facilitated the capillary structure formation via the sphingosine 1-phosphate 2 receptor–Rho kinase–ROCK pathway. Tissue engineering techniques are emerging because coordinated cell and scaffold structure is sometimes more effective than single-cell injection. For example, mesenchymal stem cell or skeletal myoblast cell sheet implantation has been shown to improve cardiac function in severe ischemic cardiomyopathy, but such efficacies were not confirmed in the case of the single-cell injection technique. Currently, an important tissue engineering strategy for the vascular and cardiac regeneration may be cell sheet technology, using either a temperature-responsive polymer or magnetic cell arrangement methods.

Clearly, the tissue printing method demonstrated herein by Yoshida et al is an additional strategy for tissue engineering. For future clinical application, there may be several issues to...
be further studied. First, how can capillary structures composed on decellularized human amniotic membranes be implanted? It may still be difficult to place the composed capillary structures on the ischemic tissue without disturbing capillary luminal function. Second, are HOMECs the best cell source for capillary composition? Isolating HOMECs may be an invasive procedure, and additional cell sources, such as subcutaneous adipose tissue–derived ECs, would be explored.

References

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