Stem cell biology has made cell-based therapies promising. While the use of human embryonic stem cells is ethically controversial, adult stem cells attracts more and more attention from clinicians and scientists. Adult mesenchymal stem cells (MSC) are derived from various tissues, including bone marrow, subcutaneous adipose tissue, cruciate ligament, muscle, and synovium, which are potential donors for stem cell therapy. Adipose tissue is composed of lipid-filled mature adipocytes and a heterogeneous stromal vascular cells. Similarly, the bone marrow is composed of multiple cell types including adipocytes, hematopoietic, osteoprogenitor, and stromal cells necessary to support hematopoiesis. Both adipose and bone marrow contain a population of MSC with the potential to differentiate into multiple cell lineages, including adipogenic, chondrogenic, vascular, and osteogenic cells, depending on the culture conditions. Although bone marrow-derived MSC (BM-MSC) are being widely used in cell-based therapy and tissue engineering, adipose-derived MSC (ASC) serve as an alternative source of MSC. Subcutaneous adipose depots are accessible, abundant, and replenishable, thereby providing a potential adult stem cell reservoir for each individual.

ASC and BM-MSC have the similar potential to differentiate into multiple cell lineages. However, growing evidence from patients show that ASC are more active in terms of their proliferation compared with BM-MSC. Chen et al found that this discrepancy might be a result of the low expression of p21 gene and senescence-associated $\beta$-galactosidase activity in ASC. ASC showed positive $\beta$-galactosidase staining after 70 population doublings, whereas BM-MSC were stained positively only for 30 population doublings, suggesting that BM-MSC appear to senesce much earlier than ASC. Additionally, ASC and BM-MSC show their own distinctions on the secretion of chemokines or cytokines. ASC showed greater production of vascular endothelial cell growth factor and hepatocyte growth factor than BM-MSC, which is important for angiogenesis after ischemia. As expected, ASC administration remarkably attenuated brain ischemic damage in mouse stroke model. It has also been reported that the expression level of 5 chemokine receptor (CCR1, CXCR4, CCR7, CXCR6, and CXCR3) is higher in ASC than BDSC, which

**Figure.** A combination of drug eluting stents (DES) and cell-based therapy. Bone marrow mesenchymal stem cells (BM-MSC) and adipose tissue derived stem cells (ASC) can be used as cell sources for local cell delivery or engineered artificial vessel in coronary artery bypass graft (CABG). DES contain Fab fragment of antibody against inflammatory cytokines, antagonist to inflammatory gene expression etc for ASC, or growth factors (GF) to increase proliferation, antagonist to senescence, etc for BM-MSC. Specific DES is used together with local delivery of specific MSC or with MSC-based engineered vessels in CABG.
indicated ASC might show a better migration and homing capacity following transplantation. These distinct characteristics will determine the strategy for cell-based therapy.

To understand the mechanisms underlying the different characteristics between ASC and BM-MSC, Nakashita et al has made an important progress. They confirmed that ASC possessed vast proliferation capability, which amplified 200 times in 2 weeks compared to 30 times for BM-MSC. Microarray analysis revealed that both ASC and BM-MSC possessed specific gene expression profiles. ASC feature with upregulation of genes involved in inflammation, whereas BM-MSC feature with genes involved in organ formation. Accordingly, ASC secreted higher levels of inflammatory chemokines or cytokines compared to BM-MSC. These findings will provide therapeutic guidance on the implication of these 2 MSC as cell source for cell-base therapy.

Clinical Perspective
Coronary artery disease is the main cause of impaired quality of life, morbidity, and death throughout the world, especially in diabetic patients. Although off-pump coronary artery bypass grafting (CABG) has shown some particular benefits including shorter operating time, rapid recovery, and lower rate of revascularization, the occurrence of major adverse cardiac and cerebrovascular events is similar as drug (sirolimus)-eluting stent (DES). As a result of diabetic peripheral angiopathy, the available vessel for CABG from the patient is also limited. Therefore, patient-derived MSC show great potential in future applications. They can not only contribute vascular lineages to construct tissue engineered vessel but also to induce angiogenesis or cardiogenesis in paracrine manner when applied with DES or CABG. However, it is essential to find out the specific adult stem cell with great potential for tissue engineering and transplantation, which require good survival rates and stable hemodynamic behavior. In addition, the differences between gene and protein expressions in different adult stem cells have to be clarified first.

The success of stem cell-based therapy will depend on cell availability, the potential to differentiate into specific cell lineage, inflammation response after transplantation, etc. With the vast capability of proliferation and secretion of angiogenic growth factors such as vascular endothelial cell growth factor and hepatocyte growth factor, ASC seems to be more attractive cell source for cell-based therapy in vascular disease treatment as compared to BM-MSC. However, the high level expression of inflammatory genes in ASC and secretion of inflammatory cytokines by ASC will limit their implications. Based on Nakashita and coworkers’ findings, one can postulate a combination strategy of DES with local delivery of stem cells or CABG with stem cell-engineered artificial vessels. For example, if BM-SMC are used as a cell source, a stent containing growth factors for proliferation and differentiation toward endothelial cells and antagonist to senescence can be used. However, if ASC will be used, a stent containing Fab fragment of antibody against inflammatory cytokines and antagonist for inflammatory gene expression is used instead (Figure). Importantlly, a delicate combination of different MSC with DES or CABG should be considered carefully. Then a long term improvement of life quality could be expected after establishments of more elaborate experimental and clinical trials.

References
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