tion. We found that implanted cells survived in the implanted area and altered myocardial matrix metabolism both within and remote from the region of implantation. Matrix metalloproteinase activity decreased in the transplanted group as compared with control group. The matrix structure was maintained and ventricular dilatation was prevented. These data suggest that implanted cells prevented ventricular dilatation through the alteration of matrix metabolism, which is a possible mechanism for implanted cells to improve heart function.

Key Words: Cell transplantation, myocardial infarction, extracellular matrix, myocardial regeneration, heart function

Autologous Bone Marrow Cell Transplantation Combined with Off-Pump Coronary Artery Bypass Grafting in Human Ischemic Myocardium

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Recently, autologous bone marrow cell transplantation (CTx) for angiogenesis and myogenesis in ischemic myocardium has been extensively investigated to improve heart function. This study was designed to evaluate the effects of CTx with off-pump coronary artery bypass grafting (OPCAB) in patients who were not feasible for complete revascularization. Seven male patients underwent CTx combined with OPCAB in 5, CTx only in 1, and mitral valve repair in 1 patient simultaneously. Bone marrow was aspirated from iliac bone. Mean 1.5×10^9 mononuclear cells including mean 7.3×10^6 CD34+ cells and 2.4×10^6 AC133+ cells were obtained and concentrated with 10cc. These cells were transplanted into non-graftable ischemic myocardium. Heart function was evaluated in all patients using MIBI scan, echocardiogram and heart magnetic resonance imaging (MRI) preoperatively. The effect of CTx was evaluated using MIBI scan, echocardiogram, and MRI postoperatively. An average of 2 grafts were bypassed. Other territories were transplanted with isolated mononuclear cell. All patients had an uncomplicated postoperative course. After 2 to 7 months follow-up, there was improvement in symptom, ejection fraction (from 43% to 47%) on echocardiogram and myocardial perfusion on MIBI scan and MRI in all patients. These preliminary data showed improvement of heart function and myocardial perfusion and also showed the feasibility and safety of combined therapy with OPCAB and CTx in ischemic myocardium. However, the effectiveness of CTx alone cannot be readily assessed. Further randomized, controlled studies are required to evaluate the effectiveness of CTx alone.

Key Words: Autologous bone marrow cell transplantation, off-pump coronary artery bypass grafting, ischemic myocardium

Mid-term Clinical Results of Tissue-Engineered Vascular Autografts Seeded with Autologous Bone Marrow Cells

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Objective: Prosthetic and bioprosthetic materials currently in use lack growth potential and therefore must be repeatedly replaced in pediatric patients as they develop. Tissue engineering (TE) is a new discipline that offers the potential for creating replacement structures from autologous cells and biodegradable polymer scaffolds. In May 2000 we initiated clinical application of tissue-engineered vascular grafts seeded with cultured cells. However, cell culturing is time-consuming and xeno-serum must be used. To overcome these disadvantages, we started the usage of bone marrow cells (BMCs), readily available on the day of surgery, as a cell source. The aim of the study was to assess the safety and feasibility of this technique for creating pulmonary artery conduits. **Methods:** Since August 2000, TE grafts seeded with autologous BMCs have been implanted in thirty-five patients. The patients and/or their parents were fully informed and had given consent to the procedure. Five ml/kg of bone-marrow was aspirated under

general anesthesia prior to the skin incision. The polymer tube serving as a scaffold for the cells was composed of a co-polymer of l-lactide and ε-caprolactone (PCL-PLA, 50:50). This co-polymer is degraded by hydrolysis. The matrix is > 80% porous and the diameter of each pore is 100-200 μm. Polyglycolic acid (PGA) woven fabric with a thickness of 0.5 mm was used for reinforcement. Twenty-one TE conduits (TCPC grafts) and fourteen TE patches were used for the repair of congenital heart defects. The patients' ages ranged from 1 to 24 years (median, 5.5 years). All patients underwent a catheterization study and/or computed tomography (CT) scans for evaluation after operation. The patients received anti-coagulation therapy for 3 to 6 months after surgery. **Results:** Mean follow-up after surgery was 424 days (maximum, 38 months). There were no complications such as thrombosis, nor stenosis or obstruction of the tissue-engineered autografts. One late death at 3 months after TCPC was noted in HLHS patients, which was unrelated to the TE graft. There was no evidence of aneurys formation on cineangiography or CT. On examination in late period, all tube grafts were patent, and the diameter of the tube graft increased over time. (110 +/- % of the implanted size)

Conclusions: Biodegradable conduits or pulmonary vessel patches seeded with autologous BMCs showed normal function (good patency up to maximum follow-up of 38 months). As living tissues these vessels may have the potential for growth, repair and remodeling. The TE approach may provide an important alternative to the use of prosthetic materials in the field of pediatric cardiovascular surgery. Longer follow-up is necessary to confirm the feasibility of this approach.

Key Words: Tissue-engineered vascular autografts, bone marrow cells

Clinical Results of Transplantation of Tissue-Engineered Cartilage and Future Direction of Cartilage Repair - Novel Approach with Minimally Invasive Procedure -

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Articular cartilage has very limited potential to spontaneously heal, because it lacks vessels and is isolated from systemic regulation. No treatment has repaired the defects with long-lasting hyaline cartilage. Recently, a regenerative medicine by a tissue-engineering technique for cartilage repair has been given much attention in the orthopaedic field. In 1994, Brittberg et al. introduced a new technology in which chondrocytes expanded in monolayer culture were transplanted into the cartilage defect of the knee. As a second generation of chondrocyte transplantation, we have been performing transplantation of tissue-engineered cartilage made *ex vivo* for the treatment of osteochondral defects of the joints since 1996. This signifies a concept shift from cell transplantation to tissue transplantation made *ex vivo* using tissue-engineering technique. We have reported good clinical results with this surgical treatment. However, extensive basic research is vital to achieve better clinical results with this tissue-engineering technique. I would like to describe our recent research using a minimally invasive tissue-engineering technique to promote cartilage regeneration.

Key Words: Cartilage, tissue-engineering, scaffold

Role of Exocrine Pancreatic Progenitor Cells in Pancreatic Carcinogenesis

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Elucidating the mechanisms that regulates proliferation and differentiation in the pancreas and understanding the mechanisms leading to neoplastic transformation are essential steps for the development of novel diagnostic and therapeutic strategies in the management of pancreatic disorders, such as diabetes mellitus and pancreatic cancer.

The cellular origin of pancreatic carcinoma is one of the most recently studied questions. As a reason for this interest, the pancreas is an organ in which there is little cellular proliferation under normal circumstances, but the little proliferation that does occur is seen in all three components epithelia; ducts, acini and islets. The pancreatic cells, although