

## **Takeshi Muneta**

### **1 .Topic in Research Achievements in the Year 2006**

Mesenchymal stem cells (MSCs) are fascinating sources for cell therapy and regenerative medicine. In vitro chondrogenesis of bone marrow-derived MSCs was first reported by Johnstone et al. We found that addition of BMPs to previous chondrogenesis medium enhanced cartilage formation (Biochem Biophys Res Commun 2001; Cell Tissue Res 2005). This simple model made it possible to define in detail the cellular and molecular events during chondrogenesis (Proc Natl Acad Sci USA, 2002).

There are increasing reports that MSCs are present in various tissues. We compared chondrogenic potential of MSCs derived from bone marrow, synovium, periosteum, skeletal muscle, adipose tissue and demonstrated synovial MSCs had greater chondrogenesis potential in vitro (Arth Rheuma 2005; J Cell Biochem 2006). Also, chondrogenic potential of synovial MSCs was similar in both young and elderly donors (Arth Rheuma 2006). Furthermore, synovial MSCs implanted into cartilage defect of rabbits differentiated into cartilage according to the local environment (Stem Cells 2006). These indicate superiority of synovium as a cell source for cartilage regeneration.

MSCs also exist in synovial fluid. We found that MSC number in synovial fluid was 100-folds more in anterior cruciate ligament injury patients than that in healthy volunteers. Gene profile analysis demonstrated synovial fluid-derived MSCs were more similar to synovial MSCs rather than bone marrow MSCs. After great amount of synovial MSCs were injected into the knee joint, the cells adhered to the injured sites and promoted ligament and meniscus injuries in animal models. This method has a potential of enhancing repair of joint injuries with little invasion.

For expansion of MSCs, supplementation of serum is necessary and fetal bovine serum should be away for clinical use to avoid bovine transmission disease. Fold increases of synovium-derived MSCs with human autologous serum were significantly higher than those with FBS. Contrary, fold increases of bone marrow-derived MSCs with autologous human serum were significantly lower than those with FBS. Synovial MSCs are practical for clinical applications with autologous human serum.

### **2 .Publications in the year 2006**

Koga H, Muneta T, Ju YJ, Nagase T, Nimura A, Mochizuki T, Ichinose S, von der Mark K, Sekiya I.

Synovial stem cells are regionally specified according to local micro environments after implantation for cartilage regeneration.

Stem Cells. 2006 Nov 30

Yoshimura H, Muneta T, Nimura A, Yokoyama A, Koga H, Sekiya I.

Comparison of rat mesenchymal stem cells derived from bone marrow, synovium, periosteum, adipose tissue, and muscle.

Cell Tissue Res. 2006 Oct 13

Okuda N, Takeda S, Shinomiya K, Muneta T, Itoh S, Noda M, Asou Y.

ED-71, a novel vitamin D analog, promotes bone formation and angiogenesis and inhibits bone resorption after bone marrow ablation.

Bone. 2006 Oct 13

Yoshimura H, Nakahama K, Safronova O, Tanaka N, Muneta T, Morita I.

Transforming growth factor-beta stimulates IL-1beta-induced monocyte chemoattractant protein-1 expression in human synovial cells via the ERK/AP-1 pathway.  
Inflamm Res. 2006 Oct 13

Nagatomo K, Komaki M, Sekiya I, Sakaguchi Y, Noguchi K, Oda S, Muneta T, Ishikawa I.  
Stem cell properties of human periodontal ligament cells.  
J Periodontal Res. Aug;41(4):303-10, 2006

Mochizuki T, Muneta T, Nagase T, Shirasawa S, Akita KI, Sekiya I.  
Cadaveric knee observation study for describing anatomic femoral tunnel placement for two-bundle anterior cruciate ligament reconstruction.  
Arthroscopy. 2006 Apr;22(4):356-61.

Muneta T, Koga H, Morito T, Yagishita K, Sekiya I.  
A retrospective study of the midterm outcome of two-bundle anterior cruciate ligament reconstruction using quadrupled semitendinosus tendon in comparison with one-bundle reconstruction.  
Arthroscopy. 2006 Mar;22(3):252-8.

Mochizuki T, Muneta T, Sakaguchi Y, Nimura A, Yokoyama A, Koga H, Sekiya I.  
Higher chondrogenic potential of fibrous synovium- and adipose synovium-derived cells compared with subcutaneous fat-derived cells: distinguishing properties of mesenchymal stem cells in humans.  
Arthritis Rheum. 2006 Mar;54(3):843-53.

Zhang B, Muneta T, Yagishita K, Sekiya I.  
Substance P immunoreactive fibers of synovial tissue in patients with anterior cruciate ligament injury.  
Knee Surg Sports Traumatol Arthrosc. 2006 May;14(5):404-10.

Ju YJ, Tohyama H, Kondo E, Yoshikawa T, Muneta T, Shinomiya K, Yasuda K.  
Effects of local administration of vascular endothelial growth factor on properties of the in situ frozen-thawed anterior cruciate ligament in rabbits.  
Am J Sports Med. 2006 Jan;34(1):84-91.

Shirasawa S, Sekiya I, Sakaguchi Y, Yagishita K, Ichinose S, Muneta T.  
In vitro chondrogenesis of human synovium-derived mesenchymal stem cells: optimal condition and comparison with bone marrow-derived cells.  
J Cell Biochem. 2006 Jan 1;97(1):84-97.

Ylostalo J, Smith JR, Pochampally RR, Matz R, Sekiya I, Larson BL, Vuoristo JT, Prockop DJ.  
Use of differentiating adult stem cells (marrow stromal cells) to identify new downstream target genes for transcription factors.  
Stem Cells. 2006 Mar;24(3):642-52.

### 3 . Abstracts in the year 2006

53<sup>rd</sup> Annual Meeting of the Orthopaedic Research Society (ORS) San Diego, California, USA. 2007.2.11-14

Intraarticular Osteoprotegerin Administration Prevents Cartilage Destruction in a Murine Model of Osteoarthritis

Shimizu S

53<sup>nd</sup> Annual Meeting of the Orthopaedic Research Society (ORS) San Diego, California, USA. 2007.2.11-14

Synovium-derived mesenchymal stem cells enhance tendon-bone healing by producing collagen fibers

53<sup>nd</sup> Annual Meeting of the Orthopaedic Research Society (ORS) San Diego, California, USA. 2007.2.11-14

Distribution of vascular niche and parameters during expansion of mesenchymal stem cells from synovium in medial osteoarthritis knee with the objective of cell source for cartilage regeneration.

Nagase T

52nd Annual Meeting Orthopaedic Research Society

2006.3.19-22 Chicago

OSTEOPONTIN DEFICIENCY IMPAIRS WEAR DEBRIS-INDUCED OSTEOLYSIS

Shimizu S

52nd Annual Meeting Orthopaedic Research Society

2006.3.19-22 Chicago

SYNOVIUM -DERIVED MESENCHYMAL STEM CELLS ARE MORE PRACTICAL FOR CLINICAL APPLICATIONS WITH AUTOLOGOUS HUMAN SERUM THAN BONE MARROW DERIVED CELLS: THE EFFECT OF DIFFERENT SERUMS ON PROLIFERATION AND DIFFERENTIATION DEPENDS ON CELL SOURCES

Nimura A

52nd Annual Meeting Orthopaedic Research Society

2006.3.19-22 Chicago

SEQUENTIAL QUANTITATIVE STUDY OF MESENCHYMAL STEM CELLS IN SYNOVIAL FLUID AFTER LIGAMENT SURGERY OF THE KNEE IN HUMANS: A POSSIBLE ROLE FOR ENHANCEMENT OF HEALING POTENTIAL

Morito T

52nd Annual Meeting Orthopaedic Research Society

2006.3.19-22 Chicago

IN VIVO CHONDROGENESIS OF SYNOVIUM-DERIVED MESENCHYMAL STEM CELLS

Koga H

52nd Annual Meeting Orthopaedic Research Society

2006.3.19-22 Chicago

THE ROLE OF MONOCYTE CHEMOATTRACTANT PROTEIN-1 (MCP-1) IN THE PATHOGENESIS OF ARTHROFIBROSIS.

Yoshimura H

International Cartilage Repair Society Symposium (San Diego)

2006.1.8-11

CELLULAR EVENTS OF SYNOVIUM-DERIVED MESENCHYMAL STEM CELLS  
AFTER THEIR IN  
VIVO TRANSPLANTATION INTO ARTICULAR CARTILAGE DEFECTS

Sekiya I

28<sup>th</sup> Annual Meeting of the American Society for Bone and Mineral Research (ASBMR)  
Philadelphia, Pennsylvania, USA. Poster Presentation.

2006.9.18

□Osteopontin Facilitates Titanium Particle-Induced Osteolysis via TNF-□ Signaling

Shimizu S