Syngeneic, minor mismatched, and major mismatched transplantation of synovial mesenchymal stem cells in a rat massive meniscal defect model

INTRODUCTION:
We previously reported that intraarticular injection of mesenchymal stem cells derived from synovium promoted meniscal regeneration in a rat massive meniscal defect model [1]. During this regeneration process, injected synovial MSCs adhered around the meniscal defect, then differentiated into meniscal cells directly. This was a syngeneic transplantation model, therefore, no immune reactions were observed.

Great number of reports described that bone marrow MSCs were immunoprivileged as well as immunosuppressive and that allogeneic transplantation of bone marrow MSCs enhanced regeneration in injury models. However, this is still controversial, and the opposite results were also reported [2]. As far as synovial MSCs, the influence of allogeneic transplantation have not been investigated at all.

In this study, we performed syngeneic transplantation and allogeneic transplantation of synovial MSCs in a rat massive meniscal defect model. For allogeneic transplantsations, major antigen mismatch and minor antigen mismatch were prepared. Meniscus 4 weeks after transplantation was evaluated in the 3 groups.

METHODS:

Cell isolation and culture.
This study was approved by institutional animal use committee. Synovium was harvested from the knee joint of 3 strains, F344, ACI, and LEW rats. After collagenase digestion, nucleated cells derived from synovium were expanded (Figure 1A) and colony forming cells were collected for transplantations. In vitro differentiation potentials for chondrogenesis, adiogenesis, and calcification were confirmed [3].

Meniscectomy.
As recipients, only F344 rats at 10-12 weeks of age were used. Under anesthesia, a straight incision was made on the anterior side of the right knee, the anteromedial side of the joint capsule was cut, and the anterior horn of the medial meniscus was dislocated anteriorly with a forceps. The meniscus was then cut vertically at the level of medial collateral ligament, and anterior half of medial meniscus was removed (Figure 1B).

Transplantation.
Immediately after the skin incision was closed, 5x10⁶ synovial MSCs in 50 µl PBS were injected into the right knee joint of F344 rats. Transplantation of synovial MSCs derived from F344 rat is a syngeneic model. Transplantation of synovial MSCs derived from LEW rat is a minor antigen mismatch model, in which histocompatibility antigens differ partly. Transplantation of synovial MSCs derived from ACI rat is a major antigen mismatch model, in which histocompatibility antigens differ greatly (Figure 2). Macroscopic features for tibial side of the knee joint at 4 weeks were evaluated (n=3).

RESULTS:
In the cases of synovial MSCs derived from F344 rat were transplanted, the meniscal defect was covered with synovium-like tissue in all 3 cases as reported previously [1]. In the cases of synovial MSCs derived from LEW rat were transplanted, the similar results were observed. In the cases of synovial MSCs derived from LEW rat were transplanted, the meniscal defect was covered with synovium-like tissue in 2 cases among 3 cases (Figure 3).

DISCUSSION:
Process of meniscal regeneration was observed similarly both in the syngeneic model and the minor mismatch model. In the major mismatch model, the repair process appeared to be slightly inferior to the other groups. This is a pilot study of allogeneic transplantation of synovial MSCs for cartilage defect, and further study is ongoing.

SIGNIFICANCE:
The effectiveness and safety of allogeneic transplantation of synovial MSCs for meniscal regeneration should be clarified in view of a possible future clinical use.

REFERENCES: