CDB SEMINAR

Naoki Nakayama

Center for Stem Cell and Regenerative Medicine, Brown Foundation Institute of Molecular Medicine, The University of Texas Health Science Center at Houston

Monday, June 18, 2012

17:00~18:00 A7F Seminar Room

(This seminar will start as soon as the preceding seminar finishes)

Cell culture engineering toward large scale chondroprogenitor production from human pluripotent stem cells

Abstract

There has been considerable interest in the potential clinical application of stem cells in the repair of cartilage damage that does not heal spontaneously. However, current therapies, which have used mainly adult mesenchymal stromal cells (MSCs) from bone and fat and dedifferentiated chondrocytes from joint cartilage, are far from ideal. Large numbers of chondrogenic cells are required for cellular cartilage repair in humans. The low yield of the cells described necessitates expansion in culture, which leads to a loss of chondrogenesis activity and the formation of the wrong type of cartilage that fails to integrate stably into the joint. An alternative, scalable source of chondroprogenitor cells would resolve the problem. Because joint formation and the development of joint cartilage occur during embryogenesis (chondrocytes are derived from lateral plate mesoderm, paraxial mesoderm and cranial neural crest), the repair process may need to recapture such embryonic processes. For humans, pluripotent stem (PS) cells are the only practical source for obtaining embryonic cells. Human (h)PS cells can be maintained in culture for a long time without loss of their developmental potential. The culture is also scalable. Therefore, theoretically, it is possible to obtain a number of desired progeny representing a particular embryonic cell type, such as paraxial mesoderm, once the differentiation protocol has been optimized and the isolation/purification protocol established. However, clinical-scale production of differentiated progeny from hPS cells is a major undertaking; therefore it is critically important that large numbers are achievable by simple expansion of the progeny. Chondrogenesis from human pluripotent embryonic stem (hES) cells has been reported extensively. However, most reports thus far have failed to effectively generate and prospectively isolate the chondrogenic progeny of defined developmental origin, and demonstrate their robust cartilage-forming capacity. I will present first directed specification and prospective isolation of KDR-PDGFRα+ chondrogenic paraxial mesoderm cells from hPS cells and their strong chondrogenic properties compared with STRO1+ human bone marrow MSCs. Furthermore, the reported methods for expanding mesenchymal cells from hPS cells (and adult MSCs) cause the loss of chondrogenic activity over several passages, highlighting the need for improved culture conditions for stable expansion of chondrogenic mesenchymal cells. I will also describe specification, prospective isolation and mid-to-long term expansion of CD271+PDGFRα+CD73+ chondrogenic ectomesenchymal cells derived from hPS cell-derived neural crest-like progeny. The CD271+PDGFRα+CD73+ chondrogenic ectomesenchymal cells maintained in our chemically defined medium constitutively express SOX9 protein and are robustly chondrogenic at least till 10 passages. We believe that hPS cell-derived chondrogenic cells with their unmatched advantage of long-term chondrogenic activity are set to become a competitive alternative to adult marrow or fat MSCs for clinical application to cartilage regeneration in future.

Host:
Shinichi Nishikawa
Stem Cell Biology, CDB
nishikawa@cdb.riken.jp
Tel:078-306-1893
(ext : 5301)