Mesenchymal stem cell sheet encapsulated cartilage debris provides great potential for cartilage defects repair in osteoarthritis

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ABSTRACT

The restoration of the degenerated articular cartilage in patients with osteoarthritis (OA) is still a challenge for researchers and clinicians. Drug interventions and surgical treatments have been widely attempted for cartilage regeneration in OA. However, the results were largely unsatisfactory. Autologous chondrocyte implantation (ACI) or matrix-induced autologous chondrocyte implantation (MACI) offers potential for the regeneration of cartilage over the long-term. However, due to the limitations and disadvantages of ACI, alternative therapies for cartilage regeneration are in need. The availability of large quantities of mesenchymal stem cells (MSCs) and the multilineage differentiation, especially their chondrogenic differentiation property, have made MSCs the most promising cell source for cartilage regeneration. In addition, MSCs have been shown the ability to undergo site-specific differentiation. MSCs can be obtained as MSC sheets using the temperature-responsive culture dish method. The MSC sheet can provide amounts of cells and extracellular matrix, which might provide the continuity between the implant and host cartilage, thus improving integrative cartilage repair. Moreover, OA is associated with progressive and often severe inflammation. MSCs not only have the ability to contribute structurally to tissue repair, but also possess potent immunomodulatory and anti-inflammatory effects. Taken together, these properties make MSC sheet promising candidate for cartilage repair in OA. We hypothesize that MSC sheet encapsulated cartilage debris can efficiently promote cartilage repair in OA patients. Chondrocytes can be obtained and cultured from small cartilage debris in vitro. Therefore, the chondrocytes may grow from the debris in cartilage defect and improve cartilage regeneration. MSC sheet provide amounts of cells, ECM and protein for cartilage regeneration and integration, and may play some roles of periosteum. The operation of MSC sheet encapsulated cartilage debris for cartilage repair is simple and practical. Moreover, the cell sheet/cartilage debris constructs can be easily shaped based on the size and shape of cartilage defects. The new method might have great potential in treating cartilage defects clinically, especially for OA patients.

Osteoarthritis (OA) is a degenerative disease of the articular cartilage. Drug interventions for OA primarily aim to alleviate symptoms, reduce pain, and control inflammation and have little impact on the progressive degeneration of cartilage [1]. Surgical treatments for cartilage repair in OA, such as microfracture, abrasion, drilling, and osteochondral grafting can relieve pain temporarily but are unsatisfactory over the long term [2].

Autologous chondrocyte implantation (ACI) or matrix-induced autologous chondrocyte implantation (MACI) offers potential for the regeneration of cartilage over the long term [3]. However, a major disadvantages of ACI or MACI is the inability to treat large cartilage defects [4], thus excluding patients with OA. In addition, donor site morbidity, the de-differentiation and limited lifespan of chondrocytes [5], low cell numbers upon harvest, potential cell leakage upon implantation of chondrocyte suspension [6], and uneven distribution of cells in three dimensional cartilage defects [7] need to be concerned. Owing to the fact that no current treatment can fully and consistently restore normal joint function of OA patients [3], alternative therapies for cartilage regeneration in OA are in need.

The availability of amounts of mesenchymal stem cells (MSCs) and their multilineage differentiation, especially the chondrogenic differentiation property, made MSCs the most promising cell source for cartilage regeneration. MSCs can be obtained from many tissues, such as bone marrow, adipose tissue, muscle and so on. MSCs can overcome the disadvantages of chondrocytes, such as low cell number upon harvest, loss of chondrocyte markers and dedifferentiation in vitro culture and chondrocytes' limited lifespan. In addition, MSCs have been shown the ability to undergo site-specific differentiation [8].

In previous studies, MSCs seeded onto different materials were shown to improve cartilage repair [9,10]. However, a major challenge is to achieve successful integration of the regenerated cartilage tissue with surrounding native cartilage. Integrative cartilage repair might be hindered by the lack of matrix-producing cells in the interface area [11]. If integration does not occur, the regenerated cartilage might deteriorate and fail over the long term [2].

Mesenchymal stem cells can be obtained as MSC sheet using the temperature-responsive culture dish method [12]. The MSC sheet can provide amounts of cells and extracellular matrix (ECM), which might improve integrative cartilage repair. Moreover, OA is associated with progressive and often severe inflammation. Current interventions could not have effects on the alleviation of inflammation. MSCs not only have the ability to contribute structurally to tissue repair, but also possess potent immunomodulatory and anti-inflammatory effects [8,13]. Taken together, these properties make MSC sheet promising candidate for cartilage repair in OA.

We hypothesize that MSC sheet encapsulated cartilage debris can efficiently promote cartilage repair in OA patients. Previous study showed that chondrocytes could creep out from nearby normal cartilage and participate in cartilage repair [14]. Chondrocytes

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can be obtained and cultured from small cartilage debris in vitro. Therefore, the chondrocytes may grow from the cartilage debris in cartilage defects and improve cartilage regeneration. MSC sheet provide amounts of cells, ECM and proteins, especially the collagen, for cartilage regeneration and integration, and may play some roles of periosteum. The MSC sheet might activate the function of chondrocytes through paracrine secretion.

The operation of MSC sheet encapsulated cartilage debris for cartilage repair is simple and practical. In addition, the cell sheet/cartilage debris constructs can be easily shaped based on the size and shape of cartilage defects in OA patients. The new method might have great potential in treating large and complex cartilage defects clinically, especially for OA patients.

Conflict of interest statement

None declared.

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MicroRNA changes in advanced radiotherapy techniques and its effect to secondary cancers

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ABSTRACT

MicroRNAs (miRNAs) are a kind of RNA, produced copies of endogenous hairpin-shaped, are 21–25 nucleotide length, small, and single chain. Recent studies have revealed that hundreds of miRNAs are found in the human genome and are responsible for diverse cellular processes including the control of developmental timing, cell proliferation, apoptosis and tumorigenesis. miRNAs can activate the initiation of apoptosis, cessation of the cell cycle and aging in case of DNA damage by stimulating the tumor suppressor target gene p53 directly and indirectly. DNA damage is composed by multiple stress factors including ionizing radiation, reactive oxygen species, UV exposure and drugs like doxorubicin and camptothecin. Radiation is used widely in health, academic area, and industry for producing electricity. As a result of using radiation widely in different fields, environmental radiation exposure is increasing as well. Whereas high dose radiation exposure causes DNA damage and gives rise to ionization to molecules of living cells by accelerating malignant tumor formation. Fields receiving high dose radiation are evaluated in terms of adverse effects, therapeutic efficacy and secondary malignancies in radiotherapy applications. Dose distributions are re-created when it is required. On the other hand, fields received low dose and the doses that the patient is exposure in simulation and/or portal imaging are often overlooked. The changes in miRNA levels arising in low dose radiation field and its effect to neoplastic process in cell will be pathfinder in terms of secondary cancers or second primary cancers. It is shown that there are differences between the level changes of miRNA in low dose fields which are overlooked in daily practical applications because of not resulting with acute or chronic side effect and the level changes of miRNA in high dose fields.

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