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Report of "Research Award of Oral Sciences"

Major: Oral Sciences
Grade: 4
Department: Orthodontics and Dentofacial Orthopaedics
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Title: Conditioned medium from stem cells of human exfoliated deciduous teeth partially alters the expression of inflammation-associated molecules of mouse condylar chondrocytes via secreted frizzled-related protein 1

1. Aim of research and results obtained (Approximately 400 words):

Aim: Temporomandibular joint osteoarthritis (TMJOA) is the major pathological disease impairing the TMJs and affects about 9%-36% of the elder worldwide. Up to date, effective treatment to reverse the tissue degeneration in TMJOA remains unavailable. In our previous study, we found that intravenous administration of conditioned medium from stem cells of human exfoliated deciduous teeth (SHED-CM) effectively restores mechanically injured osteochondral tissues in mouse TMJOA. However, the underlying therapeutic mechanisms remain elusive. In this study, we aimed to investigate the direct therapeutic effects of SHED-CM on inflamed mouse primary condylar chondrocytes in vitro.

Results: Mouse primary condylar chondrocytes were isolated from 5-6-day-old ICR mice. Recombinant mouse IL-1ß was used to induce chondrocyte inflammation in vitro. Immunofluorescence staining revealed that interleukin-1ß-stimulated chondrocytes showed increased expression of the catabolic marker inducible nitric oxide synthase (iNOS) and reduced expression of the anabolic marker aggrecan (ACAN). We found that SHED-CM treatment, and not conditioned medium from bone marrow mesenchymal stem cells (BMSC-CM), effectively suppressed iNOS expression and elevated ACAN levels, indicating that SHED-CM converted the catabolic phenotype of inflamed chondrocytes to an anabolic phenotype. Liquid chromatography with tandem mass spectrometry analysis of SHED-CM and BMSC-CM identified eight proteins enriched in SHED-CM that are related to anti-inflammatory and/or chondrogenic processes: SFRP1,

PDGFD, TGFB2, FRZB, MXRA5, A2M, SEMA3A, and MDK. Of these proteins, the Wnt signal inhibitor secreted frizzled-related protein 1 (SFRP1) was the most abundantly enriched in SHED-CM. We found that treatment with the selective SFRP1 inhibitor WAY-316606 abolished the anti-catabolic and pro-anabolic effects of SHED-CM.

2. Self-evaluation of research achievement:

Our results showed that SHED-CM directly converted the catabolic phenotype of inflamed chondrocytes to an anabolic phenotype, which supports that SHED-CM directly repair the injured TMJ. Moreover, we found that blocking the function of the most abundant protein in SHED-CM relative to BMSC-CM, the Wnt signalling inhibitor SFPR1, using WAY-316606 remarkably reduced the therapeutic effects of SHED-CM. These results demonstrated that SHED-CM restored the metabolic homeostasis of inflamed chondrocytes partially via SFRP1-mediated Wnt signalling inhibition. The direct action of SHED-CM may be useful to treat inflammatory cartilage diseases.

3. Meeting presentation:

Conditioned Medium from M2 Macrophages Alleviates Murine Temporomandibular Joint Osteoarthritis. The 22nd Annual Meeting of Japanese Society for Regenerative Medicine, Kyoto, 2023/03, Linze Xia, Fumiya Kano, Noboru Hashimoto, Eiji Tanaka, Akihito Yamamoto. Oral presentation.

4. Journal publication:

Conditioned Medium from Stem Cells of Human Exfoliated Deciduous Teeth Partially Alters the Expression of Inflammation-associated Molecules of Mouse Condylar Chondrocytes via Secreted Frizzled-related Protein 1. Journal of Oral Health and Biosciences. 2023;35(2):52–60. Xia L, Kano F, Hashimoto N, Ding C, Xu Y, Hibi H, et al.