Form8

ABSTRACT OF DISSERTATION

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 (乳歯歯髄幹細胞培養上清は分泌型 Frizzled 関連タンパク 1 を介してマウス下顎頭軟骨細胞における炎症関連分子の発現を部分的に変化させる)
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Intravenous administration of conditioned medium from stem cells of human exfoliated deciduous teeth (SHED-CM) effectively restores mechanically injured osteochondral tissues in mouse temporomandibular joint osteoarthritis. However, the underlying therapeutic mechanisms remain elusive. Here, we investigated the direct therapeutic effects of SHED-CM on inflamed primary condylar chondrocytes 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. 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. Collectively, our study suggests that SHED-CM directly suppresses catabolism and promotes anabolic responses of inflamed primary condylar chondrocytes, which partially rely on SFRP1 function in SHED-CM. The direct action of SHED-CM may be useful to treat inflammatory cartilage diseases.