【Grant-in-Aid for Scientific Research (S)】

Biological Sciences (Medicine, Dentistry, and Pharmacy)

Title of Project : Development of innovative medical technology based on integrated understanding of both protection and destruction of articular cartilage homeostasis

Riko Nishimura
(Osaka University, Graduate School of Dentistry, Professor)

Research Project Number : 16H06393 Researcher Number : 60294112
Research Area : Oral Basic Science, Biochemistry, Molecular Biology
Keyword : Articular chondrocyte, Transcription factor, Osteoarthritis, Regeneration

【Purpose and Background of the Research】

When articular chondrocytes and their matrices are impaired by aging, inflammation, and excessive mechanical stress, cartilage diseases such as osteoarthritis occur. Because of super-aged society in Japan, patients of osteoarthritis are increasing to approximately twenty millions.

In articular cartilage lesions destroyed by osteoarthritis, histological phenomena and gene expression patterns resembled to hypertrophy of growth plate chondrocytes and the subsequent events including destruction of cartilage matrices are observed. Therefore, investigation of mechanisms of osteoarthritis have been performed based on molecular mechanisms of hypertrophy of chondrocytes and destruction of cartilage matrices.

Recently, it is getting clearer that articular chondrocytes have different properties from growth plate chondrocytes. However, it is still elusive what cellular and molecular properties articular cartilage chondrocytes have.

In this project, we have planned to characterize articular cartilage chondrocytes at cellular and molecular levels, understand molecular mechanisms how articular cartilage chondrocytes retain their homeostasis, investigate the signal resulted in osteoarthritis and reveal molecular pathogenesis of osteoarthritis. Moreover, we attempt to contribute to development of novel effective therapy and early diagnostic method for osteoarthritis.

【Research Methods】

1. It is very important for understanding of property of articular chondrocytes to identify specific transcription factors involved in regulation of articular chondrocytes homeostasis. We are planning to isolate them by performing enChIP cloning method and microarray analyses of articular chondrocytes.
2. We are attempting to identify transcription factors involved in osteoarthritis, based on human osteoarthritis data base. Subsequently, we will investigate functional roles of the transcription factors in vitro as well as in vivo.
3. We will analyze gene expression profiles of articular chondrocytes by performing microarray analyses, and then attempt to isolate molecules involved in articular cartilage homeostasis. After identification, we will examine their functional roles in articular cartilage by performing knockdown and/or Cas9 knockout systems against the genes.

【Expected Research Achievements and Scientific Significance】

We are expecting to open up articular cartilage biology, and develop new technologies that led to a paradigm shift in treatment of osteoarthritis.

【Publications Relevant to the Project】

・Hata K, Takashima R, Amano K, Ono K, Nakanishi M, Yoshida M, Wakabayashi M, Matsuda A, Maeda Y, Suzuki Y, Sugano S, Whitson R, Nishimura R, Yoneda Y (2013) Arid5b facilitates chondrogenesis by recruiting the histone demethylase Phf2 to Sox9-regulated genes. ***Nature Communications.*** 4: 2850 DOI: 10.1038/ncomms3850

・Yoshida M, Hata K, Takashima R, Ono K, Nakamura E, Takahata Y, Murakami T, Iseki S, Takano-Yamamoto T, Nishimura R, Yoneda T. (2015) The transcription factor Foxc1 is necessary for Ihh-Gli2-regulated endochondral ossification. ***Nature Communications*** 6: DOI: 10.1038/ncomms7653.

【Term of Project】

FY2016-2020

【Budget Allocation】

139,900 Thousand Yen

【Homepage Address and Other Contact Information】

http://www.dent.osaka-u.ac.jp/admission/admission_000294.html