Transition of microRNA expression in peripheral mononuclear cell according to the prognosis of osteoarthritis

+1Atsushi Okuhara; +1Tomoyuki Nakasa; +1Hayatoshi Shibuya; +1Takuya Niimoto
+1Nobuo Adachi; +1Masataka Deie; +1Mitsuo Ochi
+1Hiroshima University, Hiroshima, Japan
atshushioku@yahoo.co.jp

INTRODUCTION: Osteoarthritis (OA) is the most widespread acquired connective tissue disorder that affects the synovial joints. Several studies demonstrated that mononuclear cells such as T cells aggregated in OA synovial tissues, which participated in the cartilage degradation. Many evidence clarified that OA might be the systemic diseases rather than a joint disease.

Recently, a new class of small non-coding RNAs, named microRNA(miRNA) s, regulates gene expression. Many miRNAs are evolutionarily conserved across phyla, and several miRNAs exhibit a tissue-specific or developmental stage-specific expression pattern and have been reported to be associated with human diseases such as cancer, leukemia, and viral infection. miRNAs might play a role in joint disorder, such as rheumatoid arthritis (RA) and OA.

The objective of this study was to investigate the expression pattern of miRNAs in PBMCs from patients with OA compared to RA patients and healthy subjects, as a new biomarker for OA diagnosis.

METHODS: This study was approved by the institutional Review Board of Hiroshima University and was conducted in accordance with the Helsinki Declaration. Thirty six patients (seven males, twenty eight females) with OA, 6 patients (three males, three females) with RA and 36 healthy subjects (nineteen males, seventeen females) were included in this study. OA was diagnosed according to the American College of Rheumatology criteria. We chose 4 miRNAs, miR-146a, miR-155, miR-181a and miR-223, which express in immune cells and regulate immune function and inflammation. Human peripheral blood was collected from healthy subjects, RA patients and OA patients. The expression of miR-146a, miR-155, miR-181a and miR-223 was analyzed using real-time PCR. To examine the expression level of miR-146a, miR-155, miR-181a and miR-223 in OA PBMCs, these samples were divided into four grades (grade I, II, III and IV) according to Kellgren-Lawrence classification.

The expression of miR-146a, miR-155, miR-181a and miR-223 in PBMCs were analyzed using quantitative reverse transcription polymerase chain reaction(qPCR), we investigated the expression pattern of the miRNA expression in OA progressions, and its relationships with parameters that include age, body mass index(BMI), femoro-tibial angle(FTA) and serum keratan sulfate(KS).

Statistical analysis was performed using Stat View version 5.0 statistical package. Significance was set at P<0.05.

RESULTS: The average relative expression levels of miR-146, miR-155, miR-181a and miR-223 were 3.8-, 1.9-, 1.4- and 2.9-fold, respectively, higher for OA patients than for healthy subjects (P<0.01 for miR-146a, miR-155 and miR-223 and P<0.05 for miR-181a, as determined by Mann-Whitney U test). (Figure 1).

As for the relative expression levels of miR-146a, miR-155 and miR-223 according to Kellgren-Lawrence classification, that of miR-146, and -223 were intensely expressed in OA PBMCs with a low grade of the Kellgren-Lawrence classification. That of miR-155 was significantly higher in the late stage of OA (Figure 2).

In OA patients, miR-146a is positively correlated with age. BMI did not affect the expression of miRNAs. In healthy subjects, age and BMI did not affect the expression of miRNAs (Table 1). And there was no significant correlation between miRNAs expression and FTA (Figure 3).

miR-223 is positively correlated with the concentration of KS (Figure 4).

DISCUSSION: miRNAs which express in immune cells and regulate immune function and inflammation are expressed intensely in OA patients, compared with healthy subjects. This results suggests that these miRNAs which express specifically in OA peripheral blood play a role in OA pathogenesis, and especially the expression of miRNAs is concerned with progressive OA. This evidence could lead to the elucidation the mechanism underlying OA pathogenesis and new therapeutic target for treatment of OA.

And by combining miRNA expression level and clinicopathological marker, the pathogenesis of OA may be elucidated.