A single-nucleotide polymorphism (rs8176070) of lncRNA PART1 may reflect the risk for knee osteoarthritis

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Letter to the Editor

Dear Editor,

An original article titled “Clinical significance of Matrilin-3 gene polymorphism in Egyptian patients with primary knee osteoarthritis” was published in your journal by Diab et al. (1) in 2017 as a potential follow-up study published elsewhere previously by Gu et al. (2). Both studies indicated that a specific single-nucleotide polymorphism (SNP) (rs8176070) presenting as Matrilin-3 (MATN3) SNP6 was associated with osteoarthritis (OA) and may reflect the risk and severity of knee OA. However, SNP6 of MATN3 was first identified by Stefánsson et al. (3) through a genome wide scan for hand OA. Two other studies described a similar relationship between the SNP6 of MATN3 and hand OA, but they were unable to relate it to knee OA (4, 5).

A study was planned to investigate the significance of suggested MATN3 polymorphism in patients with primary knee OA in the Turkish population. The PCR-RFLP-based approach was used as described by Diab et al. (1) and Gu et al. (2). Briefly, the 501 bp product of MATN3-specific PCR was supposed to be digested with BseYI restriction enzyme. The wild type genotype was supposed to produce a double band at 149 and 352 bp; heterozygotes were supposed to produce three bands at 501, 149, and 352 bp; and homozygotes were supposed to produce only one band at 501 bp.

Before further investigation, the primer pair (forward primer: 5’-GGACAGGATCCCACAAAAAG-3’, and reverse primer: 5’-GAAAGAGGGGCTACAACAGG-3’) utilized in both studies described above was reexamined through a Standard Nucleotide BLAST search (https://blast.ncbi.nlm.nih.gov/Blast.cgi). Unlike claimed in these studies, these primers did not match with MATN3, which is known to be located on the short arm of the chromosome 2 region 2p24-p23 (1). Instead, they matched with sequences on chromosome 5 (accession numbers AC022428.7 and AC016591.6). In addition, when searched in detail, the known MATN3 sequence (accession number: NM_002381.5, GeneID: 4148) does not include a BseYI restriction enzyme cut site.

These primers were further validated through UCSC Genome Browser’s UCSC In-Silico PCR tool (https://genome.ucsc.edu/cgi-bin/hgPcr) against the Human Genome [Assembly: Dec. 2013 (GRCh38/hg38)] (6). Results revealed a 508 bp product on chromosome 5, and the Standard Nucleotide BLAST search of this product revealed the same sequences with the accession numbers AC022428.7 and AC016591.6. In addition, when searched in detail, the known MATN3 sequence (accession number: NM_002381.5, GeneID: 4148) does not include a BseYI restriction enzyme cut site.

Finally, the search for SNP (rs8176070) in NCBI-SNP Database (www.ncbi.nlm.nih.gov/snp) revealed that it was defined on chromosome 5 at location 60541649, which matched PART1 but not MATN3.

These results were confirmed by sequencing analysis of the 508 bp PCR product, amplified from the genomic DNA isolated from peripheral blood of a 49-year-old male volunteer.

It has recently been reported that long non-coding RNA (lncRNA) PART1 expression was detected in cartilage tissues and chondrocytes (7). It has been suggested that PART1 promoted OA progression by regulating miR-373-3p/SOX4 axis (7).

In conclusion, the reports by Diab et al. (1) and Gu et al. (2) are misleading for two reasons: 1) SNP (rs8176070) of PART1 was mistakenly defined as SNP6 of MATN3, and 2) the analyzed sequence in both studies was not MATN3.
Recent literature supports the involvement of IncRNA PART1 in OA pathogenesis.

Peer review: Externally peer-reviewed.


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