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Letter to the Editor

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

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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. When examined in detail, the location of the 508 bp product on chromosome 5 (chr5:60541290-60541797; accession number: NC_000005.10) matched with the sequence known as prostate androgen-regulated transcript 1 (*PART1*, also known as NCRNA00206; GeneID: 25859). Furthermore, this 508 bp PCR product included a single BseYI cut site resulting in 148 and 360 bp DNA fragments after endonuclease digestion with this enzyme.

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*,

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it was *PART1*. Recent literature supports the involvement of lncRNA PART1 in OA pathogenesis.

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