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OSTEOARTHRITIS

mRNA decay in OA

"A number of mRNAs differ in their decay rates in normal compared to osteoarthritic chondrocytes," says Simon Tew, the corresponding author of a new study published in the journal *Arthritis & Rheumatology*. With a transcriptome-wide analysis, the researchers from the University of Liverpool, UK, discovered that mRNAs in cartilage from patients with osteoarthritis (OA) had a shorter mRNA half-life than their counterparts from a non-OA control group. "Surprisingly," exclaims Tew, "many of these transcripts actually exhibited higher steady state expression levels indicating that they are produced and then destroyed at a much greater rate in the osteoarthritic cells."

A now defunct understanding of gene expression is that the rate of transcription is the main determinant of protein production. Tew's work, which is the first publication of a transcriptome-wide analysis of mRNA decay in chondrocytes, contributes to a growing pool of evidence showing that the rate of mRNA decay is an equally important regulatory mechanism, thereby complicating our understanding of post-transcriptional regulation of the pathogenesis of OA.

Tew says he and his colleagues had previously studied "how altered mRNA turnover affected specific genes in cartilage cells. We reasoned that they wouldn't be the only genes regulated in this way and so we decided to examine how mRNA half-life varied across the transcriptome in normal and osteoarthritic chondrocytes."

To achieve this objective the researchers tested mRNA decay with microarray analysis and RT-PCR validation, a methodology previously applied to embryonic stem cells. Tew explains that his team "decided to examine isolated cultured chondrocytes, as they offered a simple experimental system with the caveat that their isolation will have induced some phenotypic changes".

Knee osteochondral tissue was taken from patients being treated either for osteosarcoma ($n = 5$) or for OA ($n = 8$). Chondrocytes were isolated from the tissue and cultured with the transcriptional blocker actinomycin D.

Although most chondrocyte mRNAs were stable, the number of short-lived transcripts was higher in OA chondrocytes than in non-OA chondrocytes.

The researchers found 395 mRNAs with different decay rates in OA and non-OA chondrocytes. Most of these mRNAs were less stable in the OA chondrocytes, only 8 mRNAs (2%) were more stable.

Many of the differentially regulated genes are nuclear and are involved in programmed cell death and embryonic development, but genes encoding ADAMTS proteins and hyaluronan synthase 2 also had rapid rates of decay in OA chondrocytes.

Tew says of ongoing experiments, "We are now interested in determining the molecular mechanisms responsible for controlling mRNA decay in OA and understanding how altered mRNA decay influences gene function."

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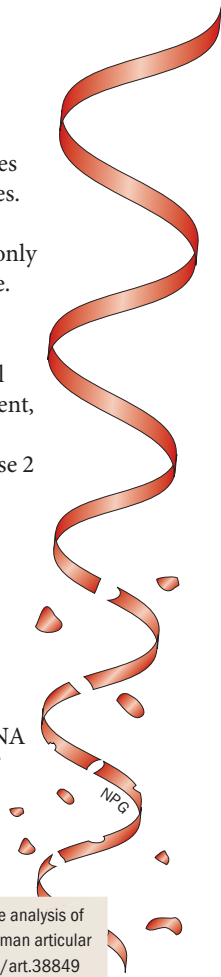

Original article Tew, S. R. Transcriptome-wide analysis of mRNA decay in normal and osteoarthritic human articular chondrocytes. *Arthritis Rheum*. doi:10.1002/art.38849