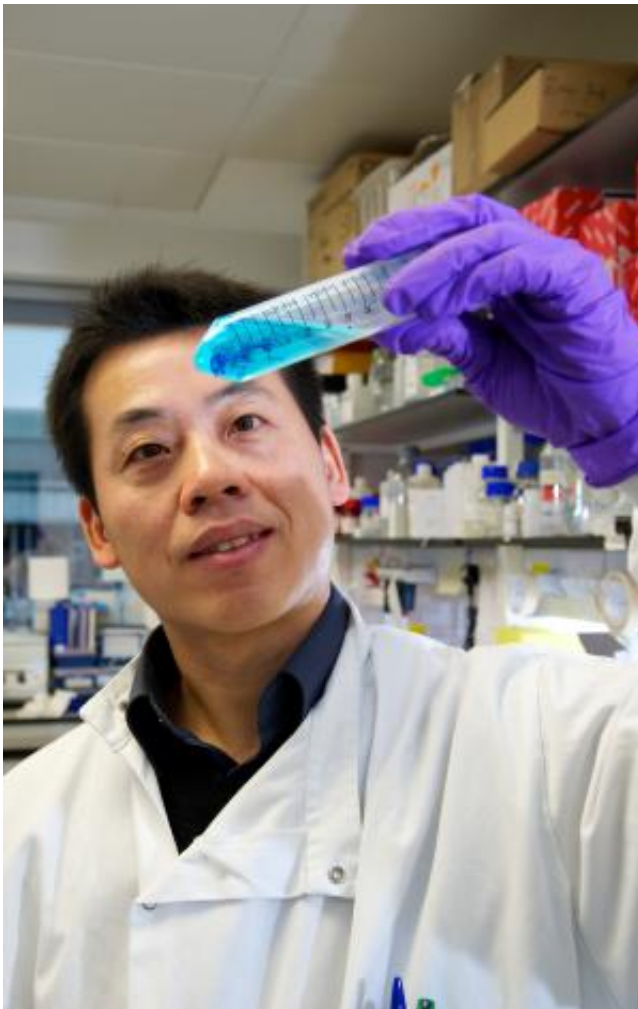


New research links body clocks to osteoarthritis

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This image shows Dr. Qing-Jun Meng from The University of Manchester carrying out research into the effect of body clocks in cartilage tissue and how they can be manipulated to better manage osteoarthritis. Credit: The University of Manchester

Scheduled exercise, regular meals and the periodic warming and cooling of joints could be used to relieve the symptoms of osteoarthritis according to scientists at The University of Manchester. Their research may also help explain why older people are more prone to developing this common joint disorder.

The team in the Faculty of Life Sciences has established for the first time that [cartilage cells](#) have a functioning [body clock](#) that switches on and off genes controlling tissue function. The rhythm of the [cartilage](#) clock perhaps goes some way to explain why [osteoarthritis](#) sufferers find the symptoms of the disease worse at certain times of the day.

When Dr Qing-Jun Meng and his team studied cartilage tissue in older [mice](#) they found that the tissue's body clock was 40% weaker than in younger mice. This suggested that clock deterioration could contribute to an increased risk of developing osteoarthritis in later life. The researchers then looked at cartilage cells affected by damage similar to osteoarthritis and found that components of the body clock are altered during the early stages of the disease.

Following these discoveries the researchers tested what would happen to cartilage tissue in mice and human cartilage cells if they imposed an artificial rhythm mimicking daily changes of body temperature. By raising the temperature by two degrees at 12 hour intervals they found that after three applications the body clock in the cells had been reset and was working in a more robust state. This change lasted for between five and seven days even after the temperature cycles were removed. Further study may show the change continues for longer.

Dr Meng says: "By imposing a rhythm to boost the internal rhythm in cartilage, our data suggests the aged cartilage clock might be re-tuned. This could be done using systemic approaches such as scheduled exercise, restricted meal times or by targeting the joint itself with

scheduled warming and cooling. We believe imposing a rhythm could have a significant impact on the future management of joint diseases and with further study it could relieve sufferers' symptoms."

This ground breaking research also suggests that taking drug treatments for joint diseases according to the cartilage clock time could increase their effectiveness, which would allow a lower dosage and consequently reduce side effects.

Dr Meng, a Medical Research Council (MRC) Fellow, has been studying body clocks for a number of years: "Mounting evidence suggests that disruption to body clocks by changes like shift work or jet lag contribute to a number of conditions such as obesity, cardiovascular diseases, cancer and mood disorders. Our next step is to test our theory that body clock disruption also contributes to osteoarthritis."

The research has been published in the journal *Arthritis and Rheumatism*. Osteoarthritis is the most common joint disorder, affecting around 6 million people in the UK. However, the mechanisms behind the disease are poorly understood and treatment options are limited.

Professor Ray Boot-Handford from the Wellcome Trust Centre for Cell Matrix Research, which is based at the university, has been studying cartilage and osteoarthritis for more than 20 years. He worked with Dr Meng on this research and says: "Osteoarthritis is a complex disease caused by multiple factors, although it's well known that one of the major risk factors is aging. Our findings that the cartilage cells show circadian rhythm and that this rhythm is weakened with age is exciting and may help explain how osteoarthritis develops as we get older. Future research will directly examine the link between cartilage clock changes and osteoarthritis and highlight potential new avenues for treating this disease."

One of the key aspects of this research was the identification of the rhythmic genes that are expressed in [cartilage tissue](#). The scientists found that 615 genes, or 4% of the genes in cartilage, were time-dependently expressed with peaks every 24 hours. They also found that many of the [genes](#) have previously been linked to osteoarthritis.

Nicole Gossan worked on the study as part of her PhD. She says: "This research has been incredible to work on. It is the first to show a functioning clock in mouse and human cartilage cells and identify its genome-wide targets. Disruption of these targets during aging could seriously impact joint health and we are the first to establish a link between clock disruption and osteoarthritis."

Dr Meng and his team have now been awarded an MRC grant of half a million pounds to establish the causal relationship between clock disruptions and the onset and severity of osteoarthritis as well as identifying novel therapeutic targets. This will include the targeting of clocks by imposing an artificial rhythm as well as the timed delivery of drugs. It's hoped the research will ultimately lead to better treatments for osteoarthritis.

More information: "The circadian clock in chondrocytes regulates genes controlling key aspects of cartilage homeostasis" *Arthritis and Rheumatism*, 2013.

Provided by University of Manchester

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