# 第1112回生物科学セミナー

日時： **9月23日（金） 10:00−11:30**

演者： Dr. Qing-Jun Meng（University of Manchester, UK）

## 演題: Understanding circadian rhythms in the musculoskeletal system towards therapies for osteoarthritis and low back pain

Osteoarthritis (OA) is the most prevalent joint disease, causing severe pain, deformity and a loss of mobility. Low back pain (LBP), frequently associated with degeneration of the intervertebral disc (IVD), is the No.1 cause of Years Lived with Disability, with over 80% of the population predicted to experience back pain within their lifetime.　Age is a major risk factor for both skeletal conditions. However, the reasons why susceptibility to these conditions increases with age are poorly understood. Consequently, current treatments are limited focusing solely on symptomatic pain relief rather than correcting the underlying pathogenesis and aberrant cell biology.　The circadian (24 hourly) clocks in the brain and periphery direct key aspects of physiology through rhythmic control of tissue-specific sets of downstream genes. Symptoms of both conditions are known to show time-of-day effect, suggesting a possible involvement of the clock mechanisms. Work from our group focuses on the roles of circadian clocks in the articular cartilage and IVD. We show that the daily rhythm in these tissues becomes dampened and out-of-phase during ageing. Further, our data identify circadian clock disruption in cartilage and IVD as a new target of inflammation. Moreover, we show that mice with targeted knockout of an essential clock gene (BMAL1) in chondrocytes and disc cells have profound, yet tissue-specific degeneration in the articular cartilage and IVD. These findings implicate the local skeletal clock as a key regulatory mechanism for tissue homeostasis. This new avenue of research holds potential to better understand, and eventually treat these debilitating conditions.　In this seminar, I will summarize our key findings on skeletal clocks and their potential implications in health and disease of the joint/spine.

References:


1. Dudek et al. (2016) The chondrocyte clock gene Bmal1 controls cartilage homeostasis and integrity. J Clin. Invest. 126 (1), 365-376.
2. Berenbaum and Meng. (2016) The brain-joint axis in osteoarthritis: nerves, circadian clocks and beyond. Nature Reviews Rheumatology.
3. Dudek et al. (2016) The intervertebral disc contains intrinsic circadian clocks that are regulated by age and cytokines and linked to degeneration. Annals of the Rheumatic Diseases,
4. Guo et al (2015) Catabolic cytokines disrupt the circadian clock and the expression of clock-controlled genes in cartilage via an NFkB-dependent pathway. Osteoarthritis and Cartilage, Special Issue: Inflammation in Osteoarthritis. 23, 1981-1988.
5. Gossan et al (2013) The circadian clock in chondrocytes regulates genes controlling key aspects of cartilage homeostasis.　Arthritis and Rheumatism; 65(9):2334-2345.


場所： **理学部　3号館327号室**

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