## Circadian rhythms, molecular clock and musculoskeletal health

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Disruption of circadian rhythms in humans and rodents has implicated a fundamental role for circadian rhythms in aging and the development of many chronic diseases including diabetes, cardiovascular disease, depression and cancer. The molecular clock mechanism underlies circadian rhythms and is defined by a transcription-translation feedback loop with *Bmal1* encoding a core molecular clock transcription factor. Germline *Bmal1* knockout (*Bmal1* KO) mice have a shortened lifespan, show features of advanced aging and exhibit significant weakness with decreased maximum specific tension at the whole muscle and single fibre levels.

We tested the role of the molecular clock in adult skeletal muscle by generating mice that allow for the inducible skeletal muscle-specific deletion of *Bmal1* (iMS*Bmal1*).

Here we show that disruption of the molecular clock, specifically in adult skeletal muscle is associated with a muscle phenotype including reductions in specific tension, increased oxidative fibre type, and increased muscle fibrosis similar to that seen in the *Bmal1* KO mouse. Remarkably, the phenotype observed in the iMS$Bmal1^{-/-}$ mice was not limited to changes in muscle. Similar to the germline *Bmal1* KO mice, we observed significant bone and cartilage changes throughout the body suggesting a role for the skeletal muscle molecular clock in both the skeletal muscle niche and the systemic milieu. This emerging area of circadian rhythms and the molecular clock in skeletal muscle holds potential to provide significant insight into intrinsic mechanisms of the maintenance of muscle quality and function as well as identifies a novel crosstalk between skeletal muscle, cartilage and bone.