# miRNA targets for Osteoarthritis

- miRNAs targets identified in early disease model of osteoarthritis (OA)
- Targets have the potential to be a first in class therapeutic to treat OA

The opportunity

Osteoarthritis (OA) is a degenerative disease of the joints, where the shock absorbing layer in the knee, the articular cartilage, breaks down (see Figure 1). Post-traumatic osteoarthritis is a subtype of OA that develops after a joint injury and accounts for 25% of osteoarthritis cases. Other risk factors include being overweight, increasing age, and joint malformation.

Pain and disability accompany OA and it is one of the leading causes of disability in the world. In the US alone, OA affects 39 million people and this market is expected to grow significantly as the US ageing population is predicted to growing by 50% in size by 2040.

Figure 1: Normal versus an osteoarthritic knee
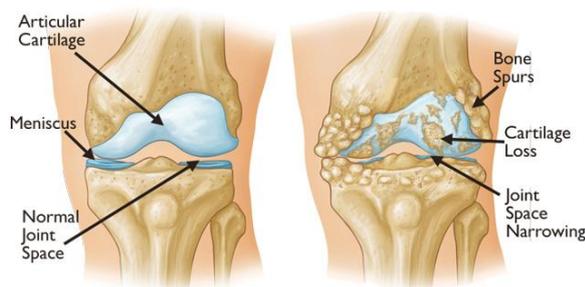
Current treatment options are limited and only treat the symptoms of OA. These include maintaining a healthy lifestyle, improving joint motion and controlling pain. There is currently no therapeutic intervention that can halt the onset or progression of OA. The global OA therapeutics market is estimated to be worth $4.9 billion in 2009 and is expected to grow to $9.6 billion by 2017.

A growing ageing population and the absence of disease-modifying treatments means that most patients must tolerate the burden of OA for decades.

MCRI researchers have used a post-injury mouse model of osteoarthritis and identified microRNA changes that are therapeutic targets for OA.

The technology

miRNAs are of particular relevance to OA as they are known to be important modulators to cartilage development and inflammatory processes. However, to date, clinical studies of osteoarthritis have relied on human tissue that can only be obtained at end-stage disease (at joint replacement). Information gathered from these studies provides little information on miRNAs involved in initiation, onset and early progression of osteoarthritis.

To identify miRNA targets which are involved in the pathogenic process of osteoarthritis MCRI researchers have:

1) **Used a well described process to induce OA in 10- 12 week mice by bilateral surgical destabilisation of the medial meniscus (DMM).**

2) **Conducted miRNA expression profiling (see figures 2-4) on RNA isolated from the medial tibial of the DMM and sham mice at 1 week and at 6 weeks post-surgery.**

Figure 2: 1 week DMM vs sham: 122 miRs $p < 0.05$ (green+blue+red); 42 miRs up-regulated > 1.5

fold with p < 0.05 (red); 2 miRs down-regulated > 1.5 fold with p < 0.05 (blue)
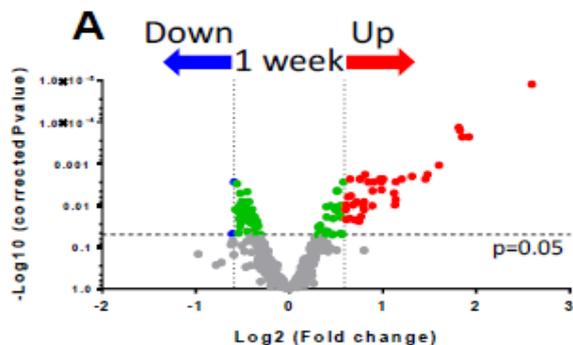
Figure 3: 6 week DMM vs sham: 74 miRs p < 0.05 (green+blue+red); 28 miRs up-regulated > 1.5 fold with p < 0.05 (red); 6 miRs down-regulated > 1.5 fold with p < 0.05 (blue)
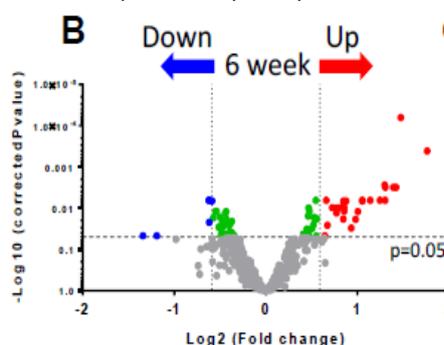
Figure 4: 57 dysregulated miRNAs were found to be common to both 1 and 6 week time points. In addition, differentially expressed miRNAs were also found to be exclusively associated with either 1 or 6 weeks post-surgery (65 miRNAs at 1 week and 17 miRNAs at 6 weeks).
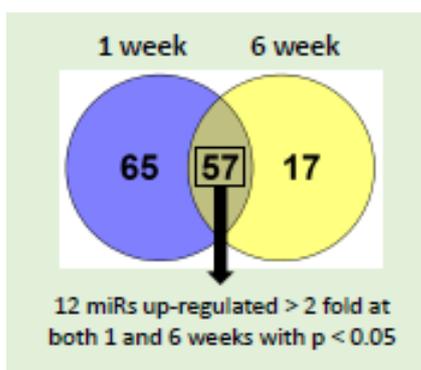
3) **Generated a network of predicted gene targets using paired miRNA:mRNA expression. Significantly, the miRNAs identified (Figure 4) are of known importance in late stage human OA and miRNAs that haven't previously been associated with OA i.e. novel candidates that are suitable for further investigation and development as prospective therapeutic targets for OA.**

Applications
The current data supports the development of a first-in-class therapeutic to prevent the onset and/or progression of osteoarthritis.

Other applications could include the development of a diagnostic test for OA.

Opportunity for partnership
The Murdoch Childrens Research Institute is seeking a partner to develop therapeutics for OA, through either a research development and option agreement or license agreement.

Intellectual Property
The technology is the subject of two provisional patent applications that relates to the use of such osteoarthritis miRNAs for diagnosing and treating osteoarthritis.

Key publications
MicroRNA expression profiling of articular cartilage from a mouse model of post-traumatic OA. Kung L.H, Rowley L, Ravi V. Bell K, Little C.B, Bateman J.F. Osteoarthritis and Cartilage. 24, (Supplement 1). S345-S346.

Contact: Dr Joanne Boag
Senior Manager, IP & Commercialisation
Murdoch Childrens Research Institute
P +613 8341 6445
joanne.boag@mcri.edu.au

Ms Lishia Singh
Business Development Officer
P +613 8341 6459
lishia.singh@mcri.edu.au