Using rAAV-TIMP3 Vectors for the Improvement of Osteoarthritis in an Ovine Model

Presented By Crystal Collier
Osteoarthritis

(Articular Cartilage
Meniscus
Normal Joint Space
Bone Spurs
Cartilage Loss
Joint Space Narrowing)

(https://orthocenter-si.com
http://www.sciencemag.org
https://medical.azureedge.net

(Neogi, 2013)
Injury and Excessive Use
Obesity
Age (Menopause)
Genetics
Causes
Causes

Menopause

Injury and Excessive Use
Current Treatments

- Lifestyle Changes
- Corticosteroid Injections
- NSAIDS
- Physical Therapy
- Topical Pain Relievers
- Surgery

(Mandl et al, 2018)
Inducing Arthritis

- **CCLD** (Cranial Cruciate Ligament Desmotomy)
- **OVX** (Ovariectomy)
- **Oblique-Angle Forced Exercise**
Treating Arthritis

Aggrecanases – the enzymes responsible for degradation of aggrecan

Aggrecan = one of the main proteoglycan components of articular cartilage

Inhibits Matrix Metalloproteinases – example: aggrecanases

TIMP3

(Mason et al, 2013)
(Lim et al, 2010)
**Treating Arthritis**

<table>
<thead>
<tr>
<th>A vector is necessary to transport the gene</th>
<th>Viral DNA is modified to prevent replication</th>
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<tbody>
<tr>
<td><strong>rAAV-TIMP3</strong></td>
<td></td>
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<tr>
<td><strong>Cells in joint transduced to rebalance cartilage homeostasis</strong></td>
<td><strong>Predicted to slow the progression of disease</strong></td>
</tr>
</tbody>
</table>

(Mason *et al.*, 2013)
(Lim *et al.*, 2010)
Study Design

OVX

Virus

n=7

Control

n=3

Virus

n=3

Control

n=4

Exercise

n=15

CCLD

Virus

n=8

Control

n=3

Virus

n=3

Control

n=5
Osteophytosis on the femoral head of the hip joint.

Osteophytosis in the interphalangeal joints of the hand.

(Mandl et al, 2018)
Preliminary Results

OVX Control

Pre-Exercise

Week 15

Grade 0

Grade 4
Preliminary Results

Left
Grade 0

OVX Virus
Week 15

Right
Grade 1
Preliminary Results: Gait Analysis

Average of Left and Right By Group

<table>
<thead>
<tr>
<th>Experimental Group</th>
<th>Stance Time (Seconds)</th>
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<tbody>
<tr>
<td>OVX Virus</td>
<td>1.081</td>
</tr>
<tr>
<td>OVX Control</td>
<td>1.157</td>
</tr>
<tr>
<td>CCLD Virus</td>
<td>1.074</td>
</tr>
<tr>
<td>CCLD Control</td>
<td>1.104</td>
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</table>
Big Picture

The most common joint disease on earth.

23 Million Americans

630 Million People Worldwide

(Mandl et al, 2018)
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