ISTITUTO ITALIANO DI TECNOLOGIA
NANOTECHNOLOGY FOR PRECISION MEDICINE

CONTROLLED RELEASE SOCIETY
CRS 2024 Annual Meeting AND Exposition
JULY 8-12, 2024 • BOLOGNA, ITALY

UNIVERSITY OF NORTH CAROLINA CHAPEL HILL

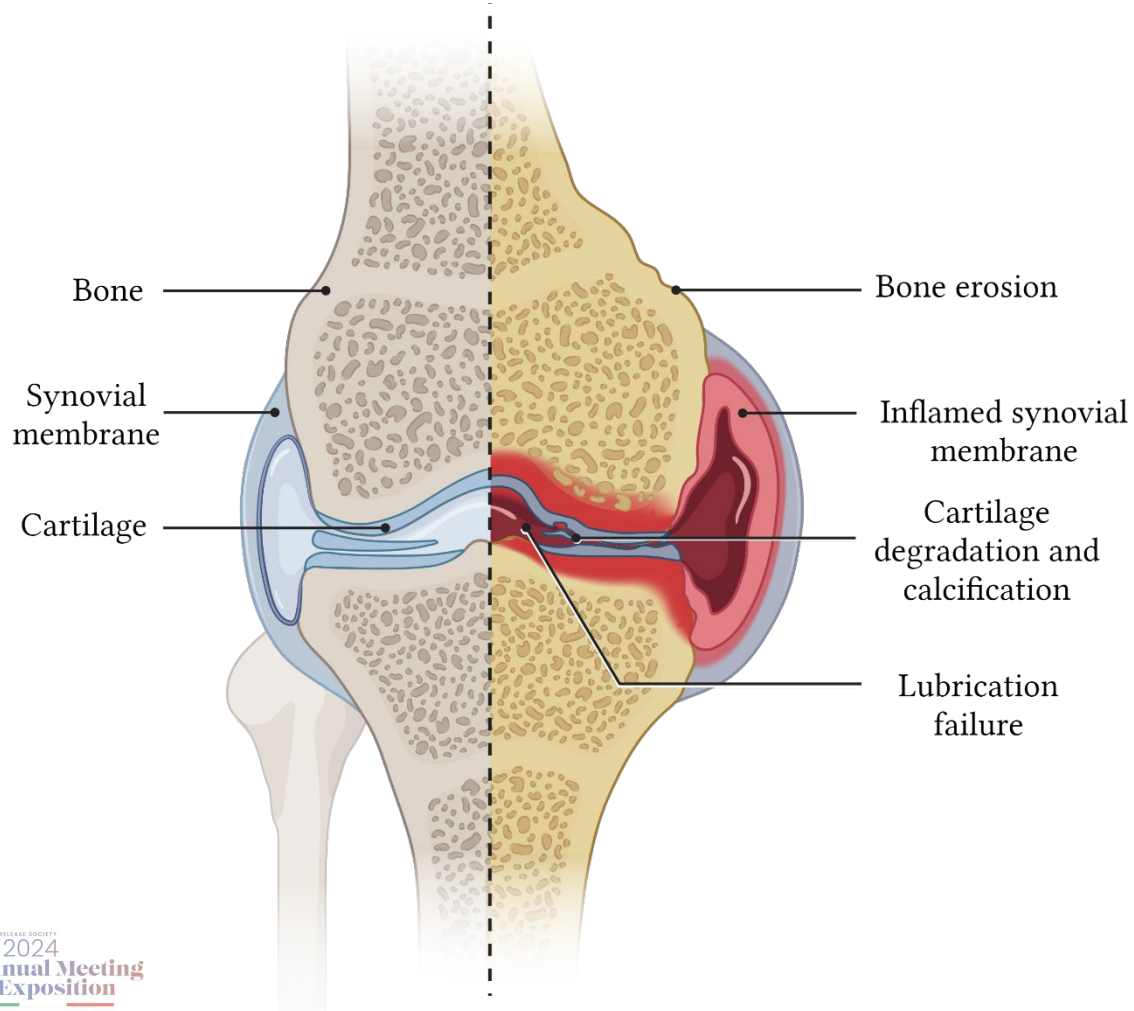
UNIVERSITA' DEGLI STUDI DI MILANO BICOCCA

RAVIOLI: A Hyaluronic Acid-Based Platform for the Treatment of post-traumatic Osteoarthritis

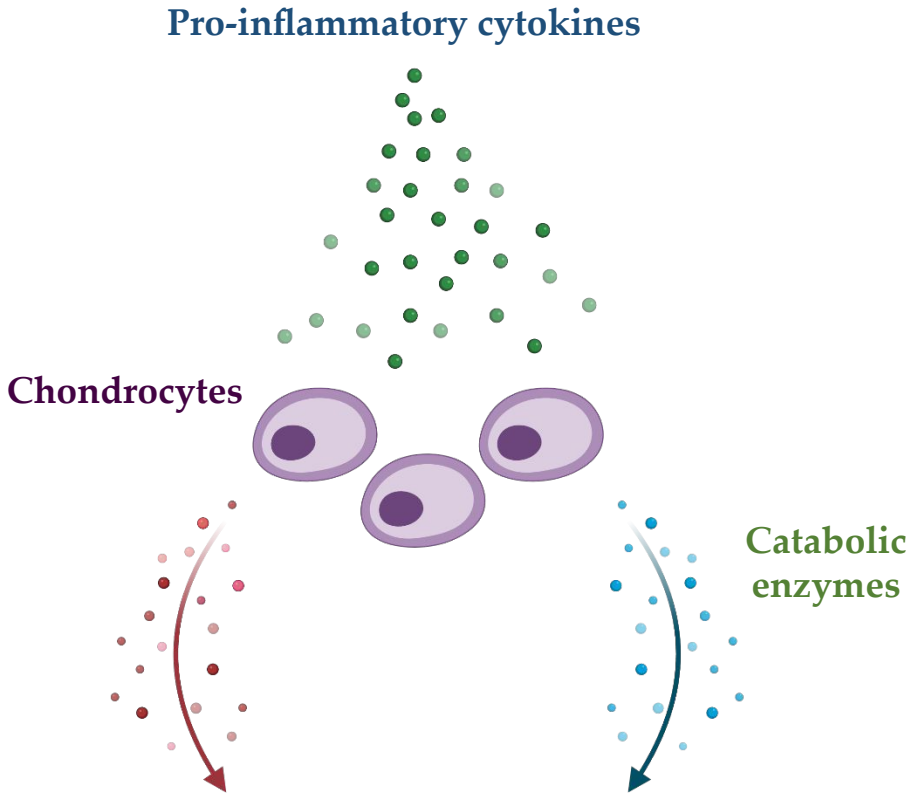
Dr. Antonietta Greco, PhD
antonietta.greco@unimib.it

Pathophysiological features of Osteoarthritis (OA)

Pathophysiological features of OA



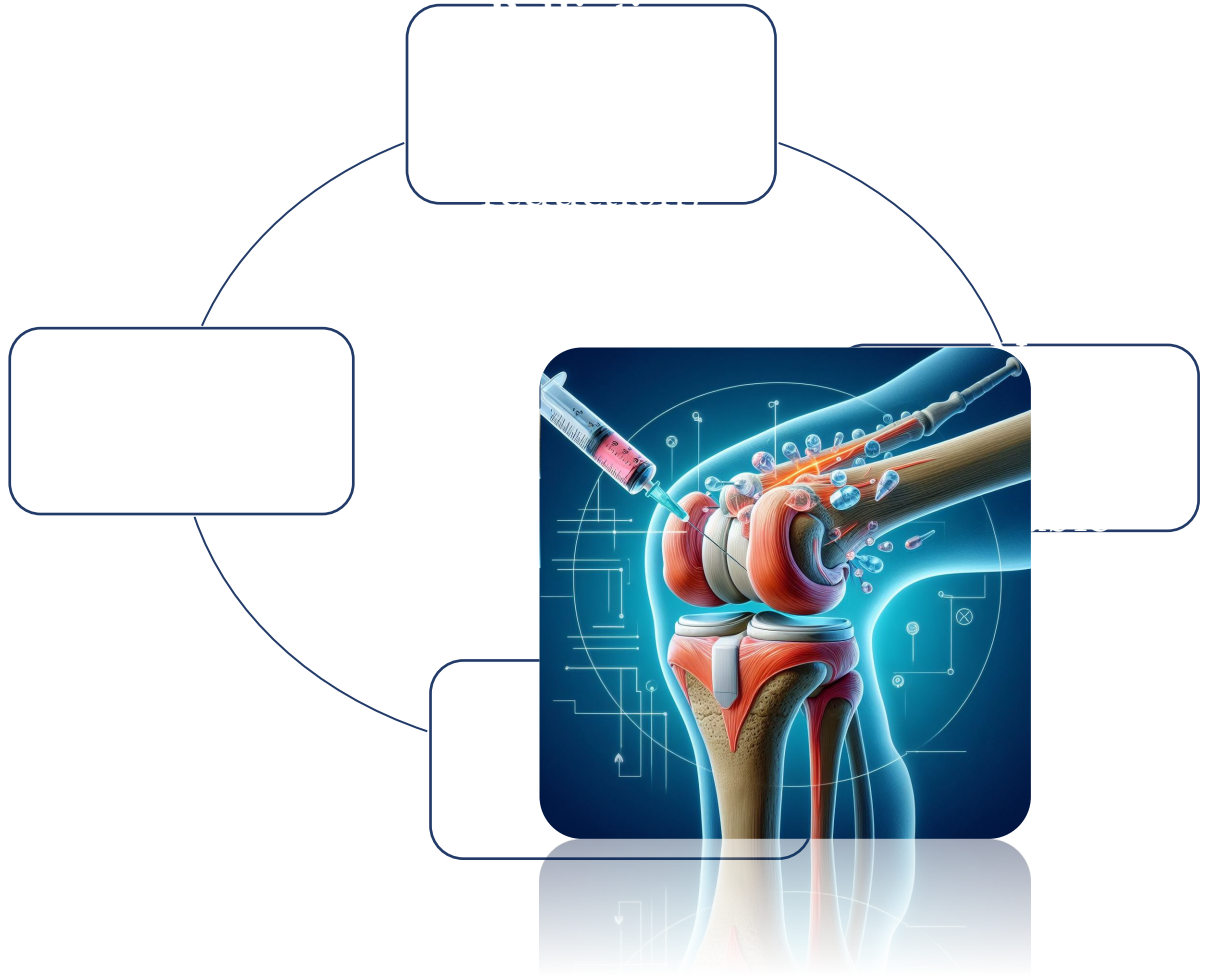
Soluble mediators driving cartilage degradation



Degradation of cartilage extracellular matrix

OA burden and conventional therapy

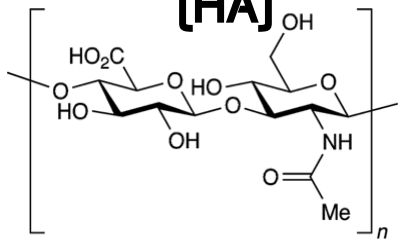
- Main cause of **pain** and **disability**
- Globally, **595 million** people suffer from osteoarthritis.
- 73% of osteoarthritis patients **are over 55** years old, with 60% being **female.**
- It imposes a **significant economic burden.**



***DMOADs:** disease modifying osteoarthritis drugs

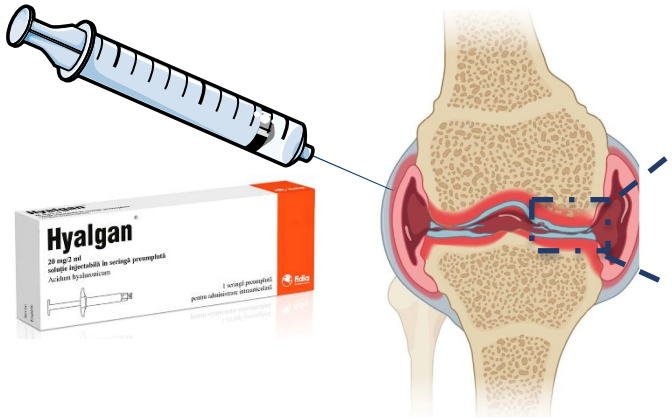
Targeting the lubrication failure

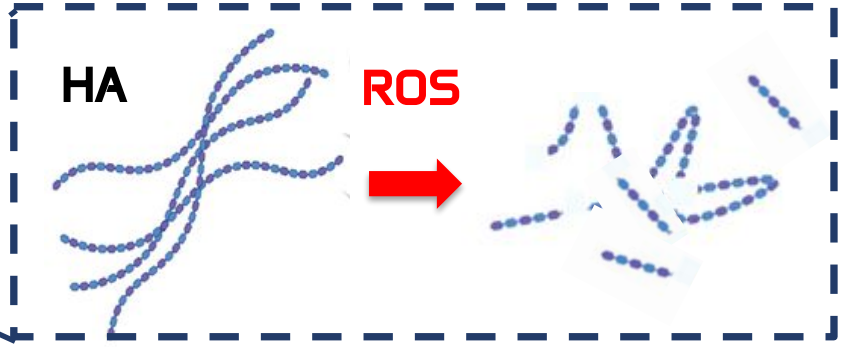
Hyaluronc Acid (HA)



Lubricant and biological properties

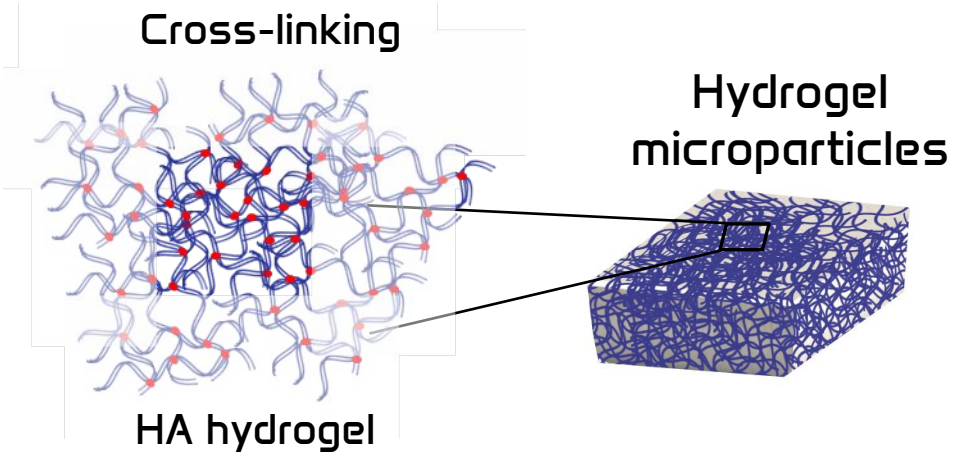
Viscosupplementation for OA treatment





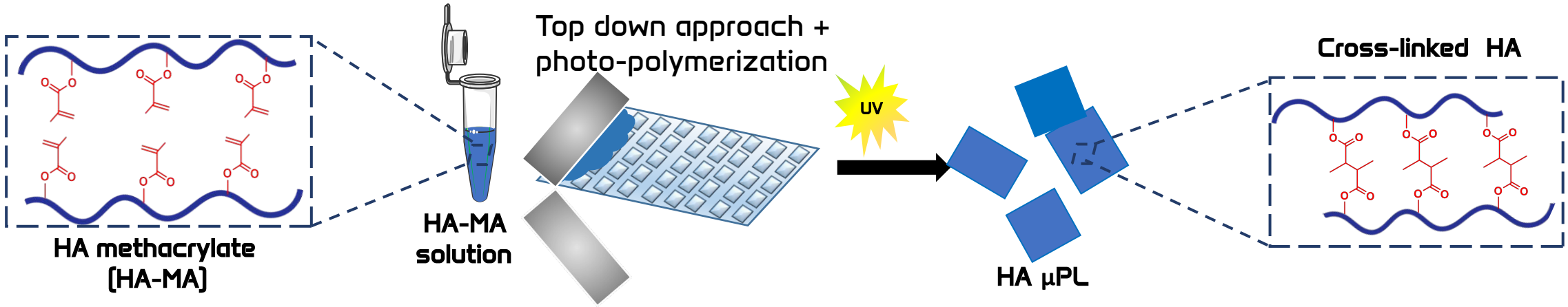
The injected HA rapidly degraded by ROS, **limiting its time of intra-articular residence**

Strategy for increasing the joint retention time of HA

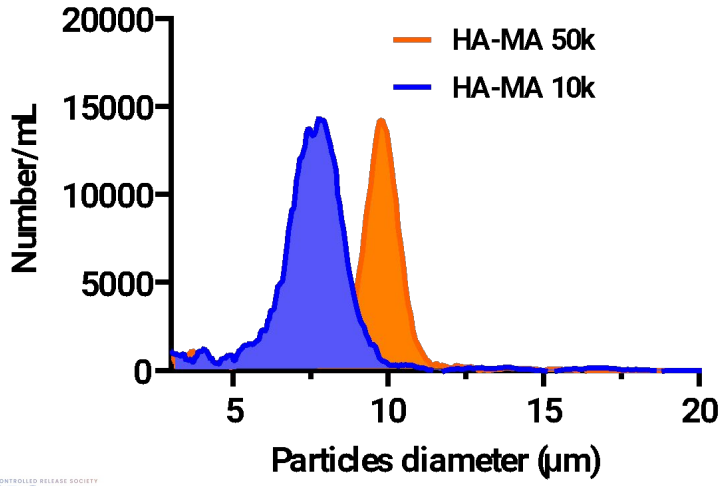


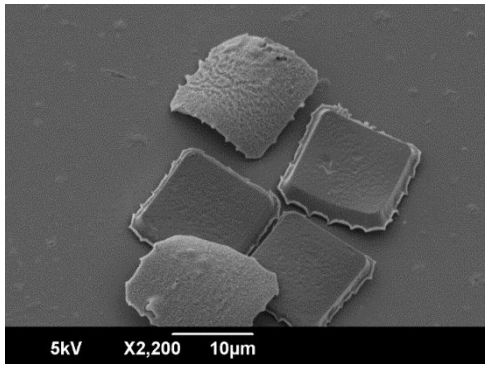
Formulation of HA into hydrogel microparticles to tackle lubrication dysfunction and simultaneously address clearance issues

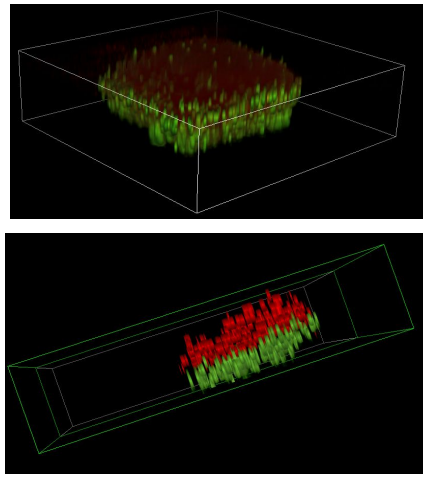
Fabrication and characterization of HA micro-particles

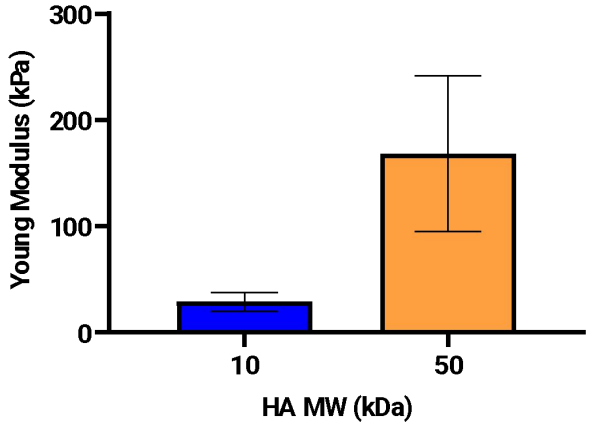


Defined shape, tunable density and mechanical properties









Targeting cartilage calcification

Pathological calcification of cartilage is a hallmark of OA

Anti-inflammatory effect

Antagonist of TGF- β and BMP receptor

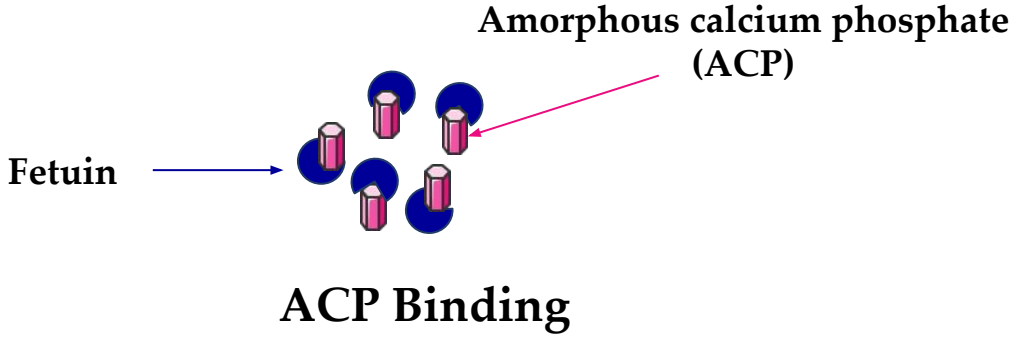
Fetuin

In patients with OA, serum **Fetuin-A levels are lower** than in healthy individuals

OA severity

Fetuin-A level

Inhibitor of calcification in OA



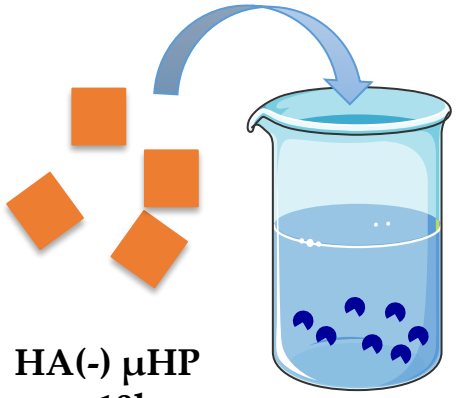
ACP Binding

AIM

Employing HA microparticles as drug delivery system of Fetuin to form a long-term drug depot in the joint

Fabrication and characterization of RAVIOLI

Charge-based loading

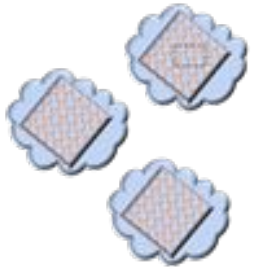


HA(-) µHP
10k

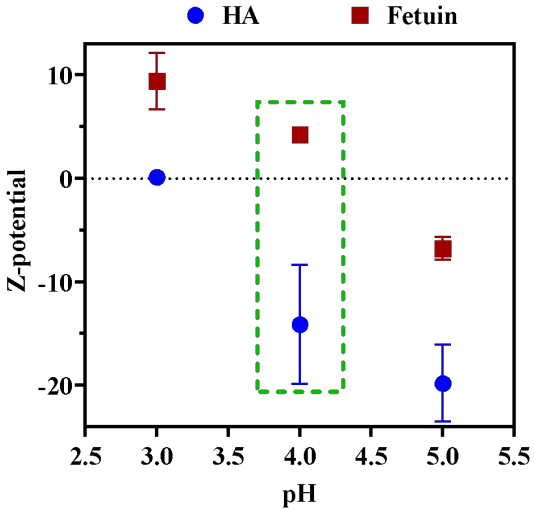
Fetuin (+) in acetate buffer
(pH=4)

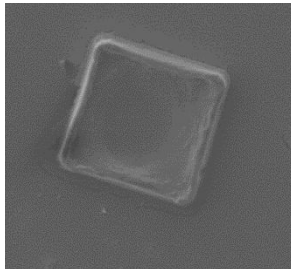
2 hours of incubation

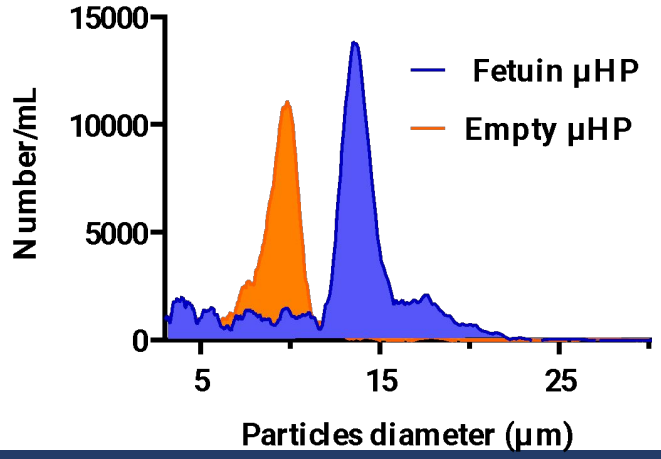
Purification

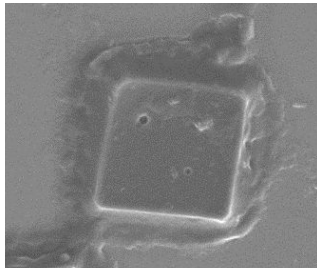


RAVIOLI
(EE% = 50)



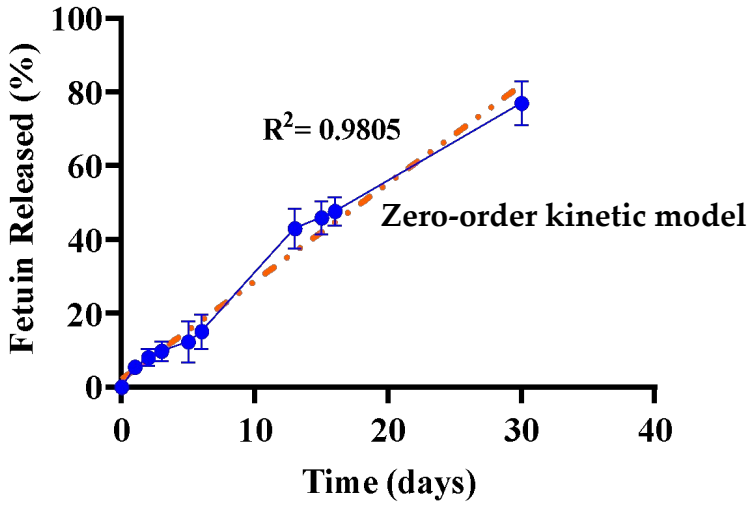






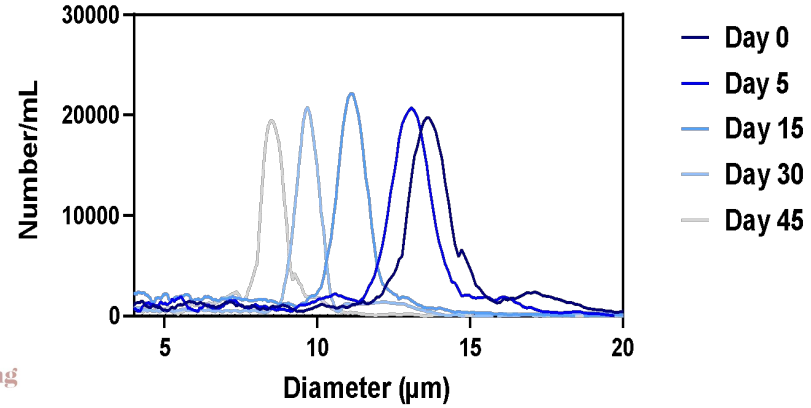
Fabrication and characterization of RAVIOLI

Release study
(500 µL PBS 1x, pH: 7.4, 37°C)

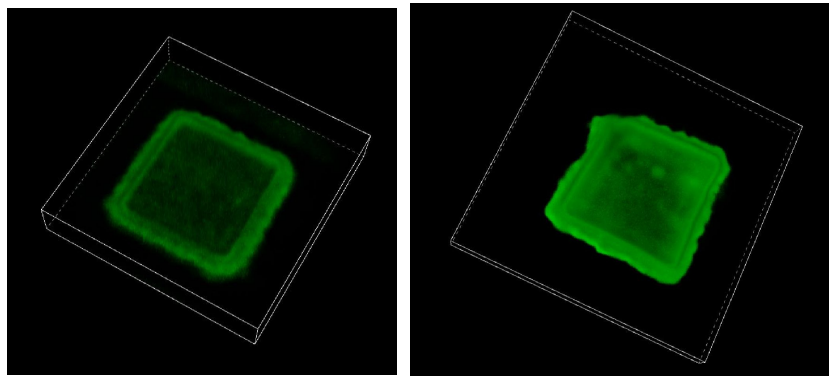


Coomassie brilliant blue G-250 staining

Multisizer characterization



Fetuin Distribution inside Ravioli – confocal microscopy



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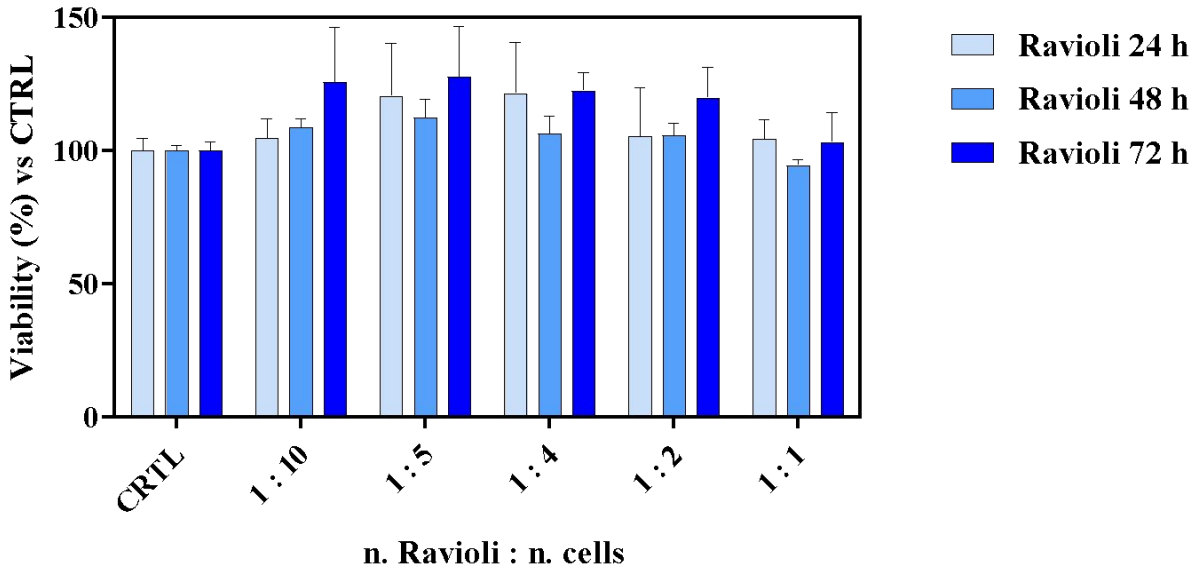
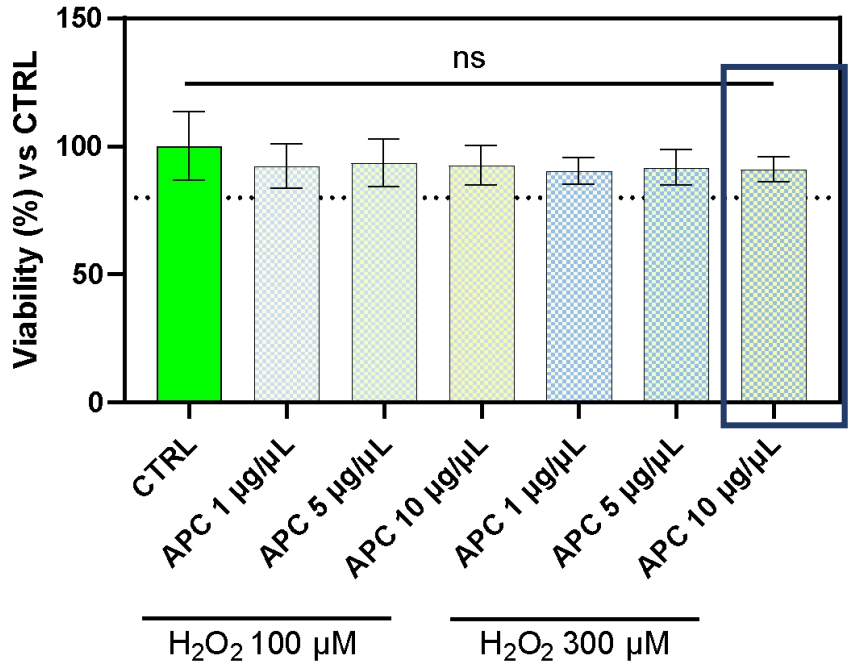
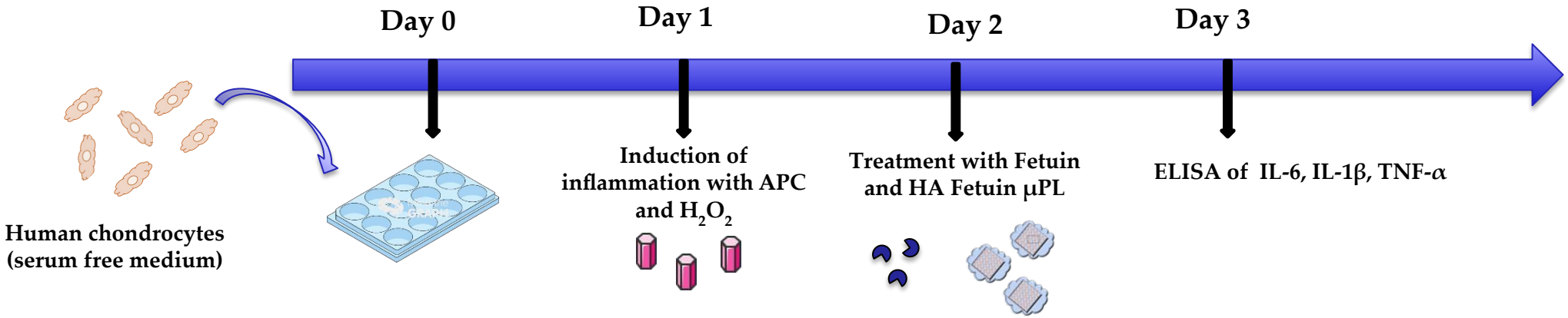
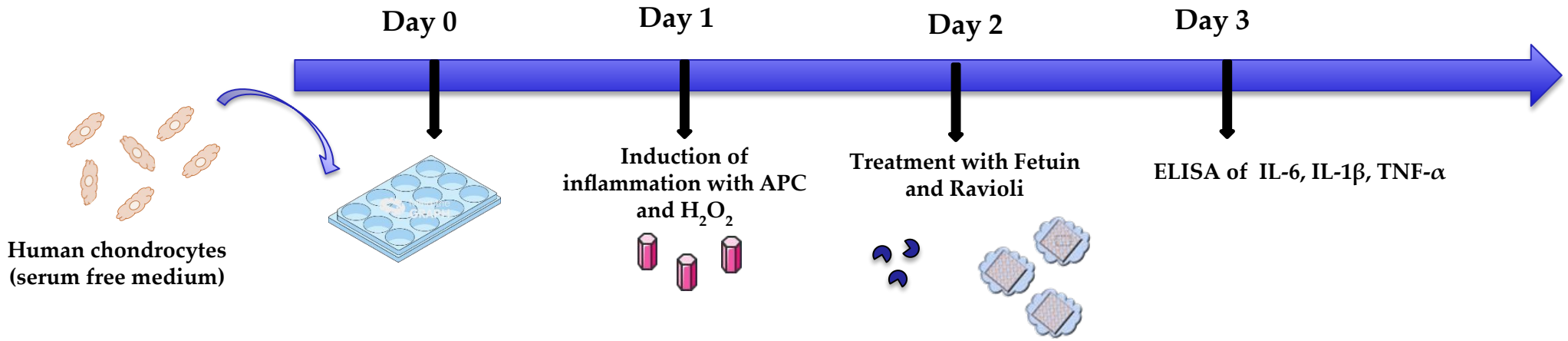
In vitro therapeutic efficacy of RAVIOLI

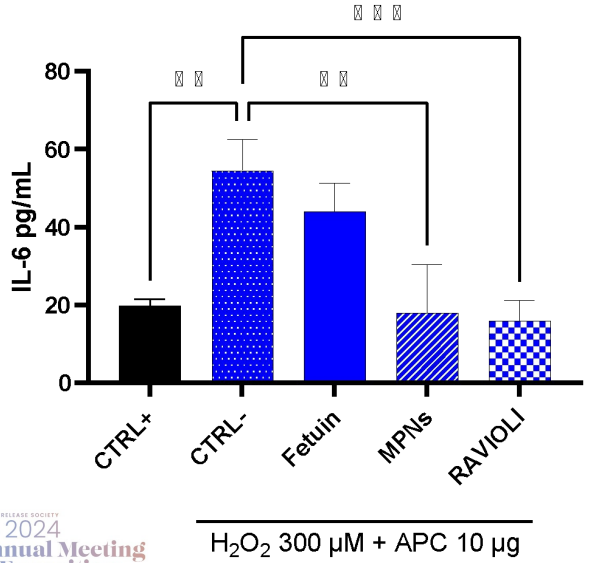


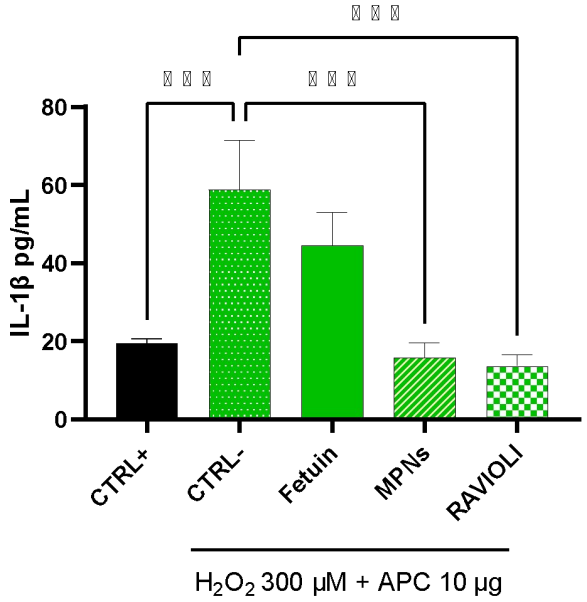


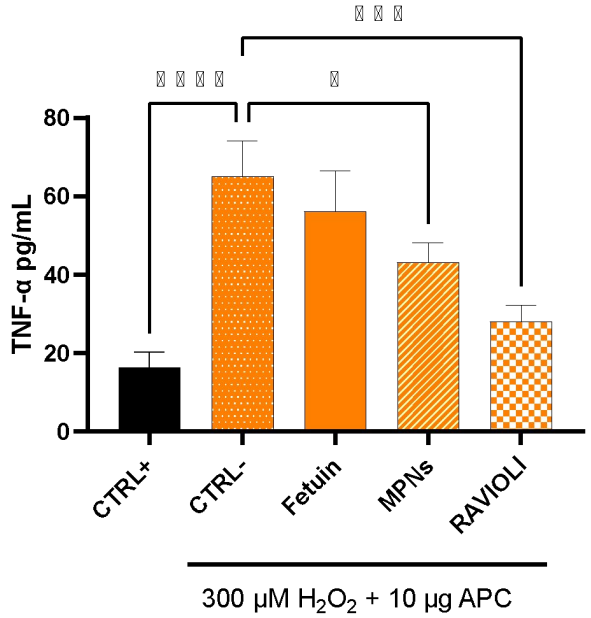


In vitro therapeutic efficacy of RAVIOLI





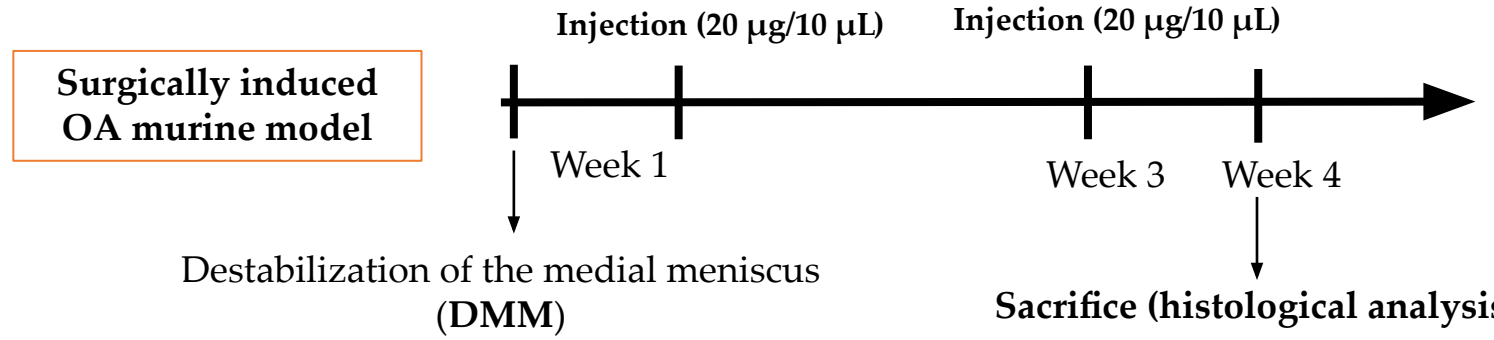




Greco, Fragassi, Palomba et al., in preparation

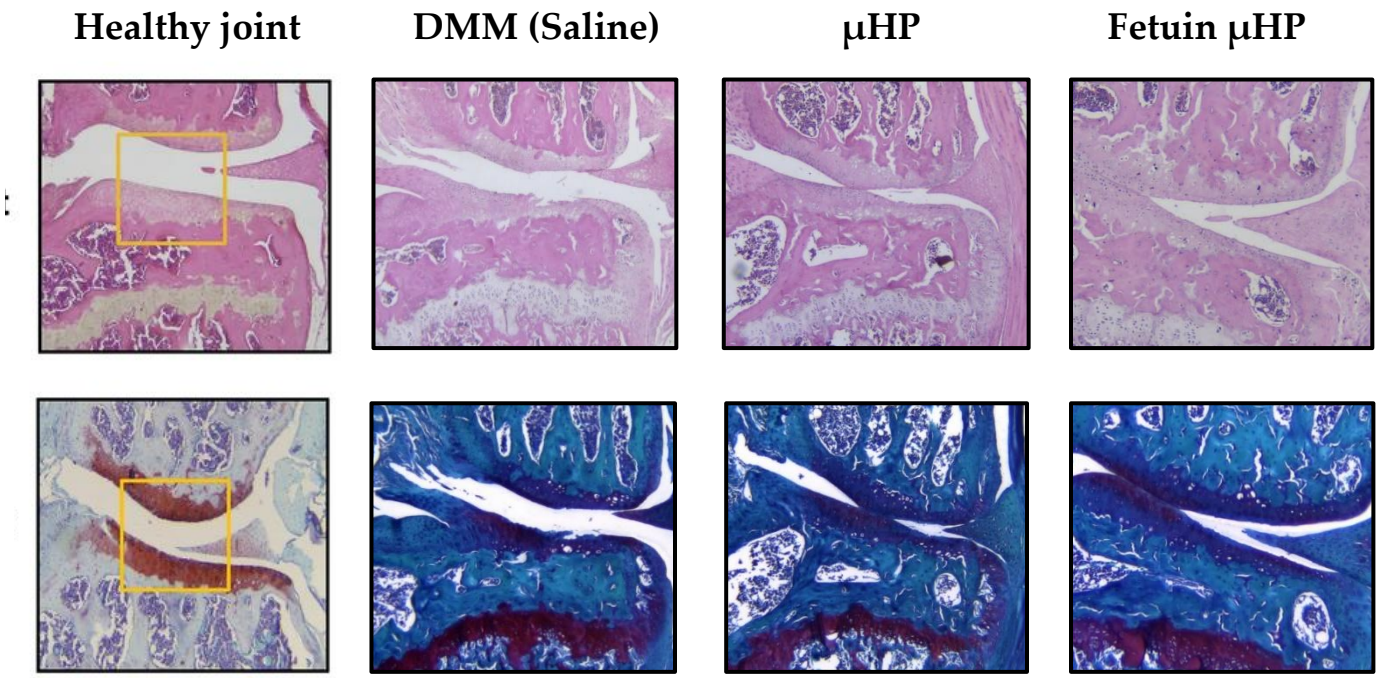
In vivo therapeutic efficacy of RAVIOLI

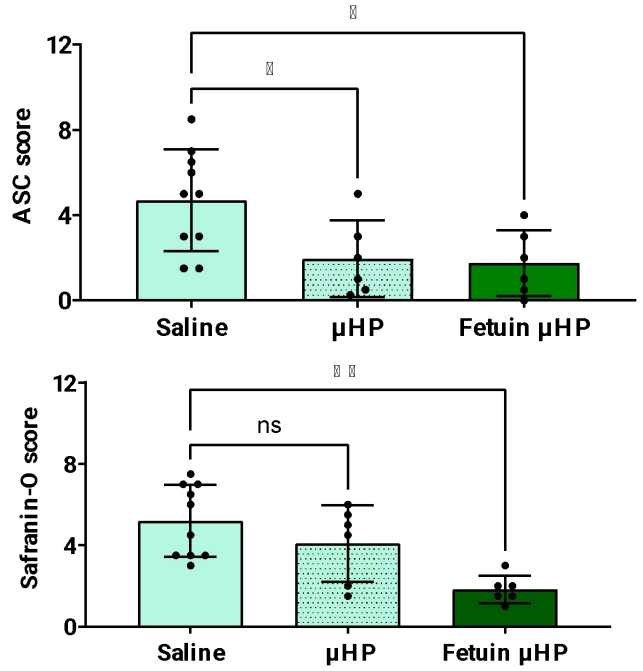
Surgically induced OA murine model



H&E (surface of the lamina)

Safranin-O (extracellular matrix)





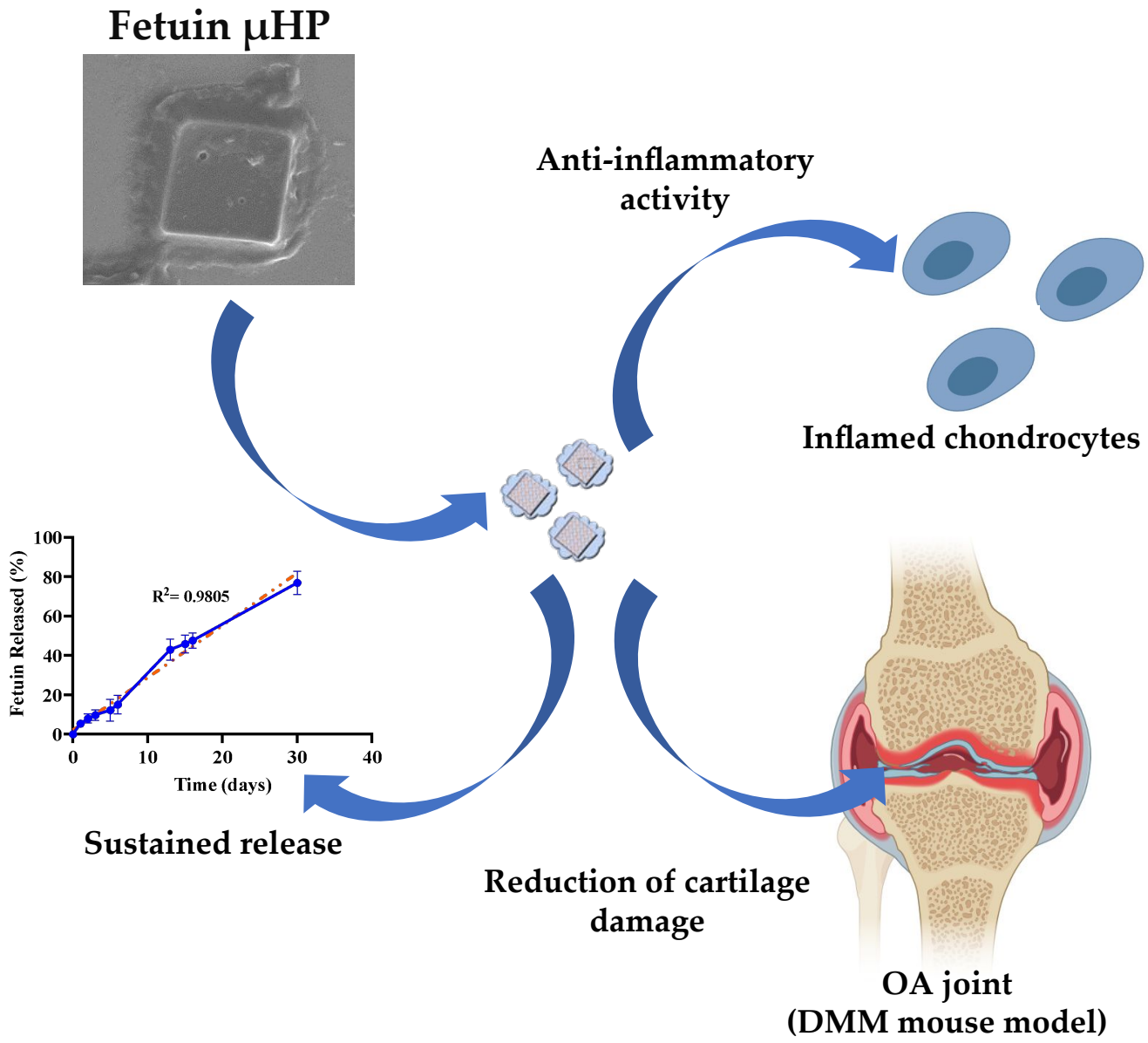
Conclusions

Fetuin was incorporated into HA μHP via **electrostatic interaction.**

RAVIOLI enables a **sustained FETUIN delivery** over 30 days.

RAVIOLI **reduce ACP-mediated inflammation** in human chondrocytes.

In DMM mice, RAVIOLI **decreased cartilage damage**.



Greco, Fragassi, Palomba et al., in preparation