Nano- and Micro-carriers for Treatment of Osteoarthritis

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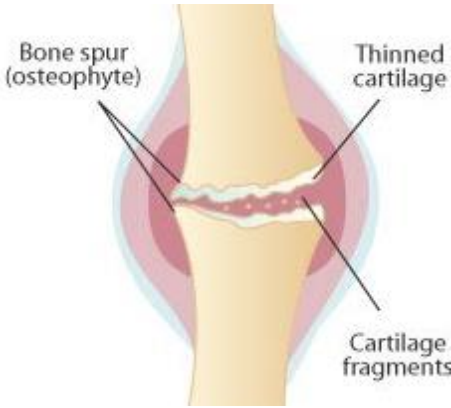
Osteoarthritis background



- Affects more than 300 million!
- Degradation of cartilage, typically in load-bearing joints
- Joint pain: No disease modifying OA drugs
- Increased levels of pro-inflammatory cytokines such as Interleukin-1β (IL-1β)
- High cell senescence and low autophagy
- Reduction of inflammatory processes: promising avenue for OA treatment

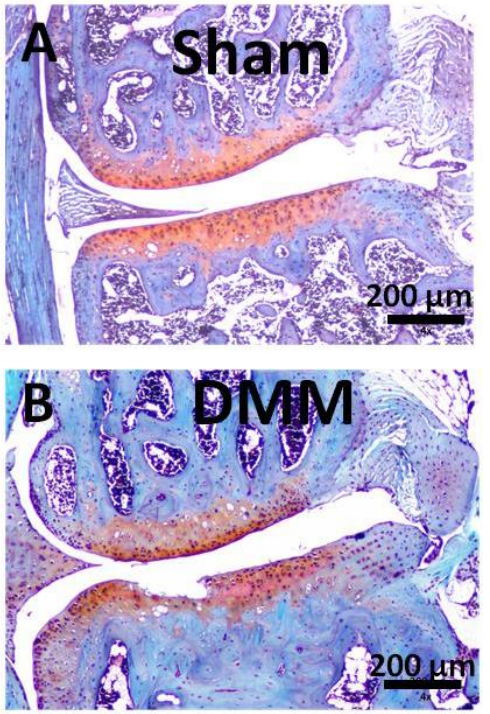
Current treatments

- Limited safety and efficacy of current anti-inflammatory treatments
  - Delivery of cytokine blockers not successful in human trials
    - Rapid clearance from the joint
    - Inability to completely reduce the inflammatory assault

Kapoor *et al.* Nat Rev Rheumatol, 7 (2011)

Blom *et al.* Osteoarthritis Cartilage, 12 (2004)

Objectives



- Our group has previously shown that delivery of rapamycin and resolvin D1 via biomaterial-based nano and micro-carriers can be used to treat in mice model of osteoarthritis
  - Dhanabalan K.M. *BioRxiv*. https://doi.org/10.1101/2021.07.20.453073
  - Dhanabalan K.M. *Biomaterials Science*. 8 (2020) 4308 – 4321
  - Dravid A.A. Bioengineering and Translational Medicine. Accepted

- The **major objectives** for this project will be to
  - ➢ Evaluate growth factor delivery via hydrogels and co-delivery of rapamycin and resolvin D1
  - ➢ Evaluate long term benefits (>6 months) of our treatment strategies in mice model of osteoarthritis
  - ➢ Translate the therapies to higher animal models such as sheep and dogs

Learnings and major techniques

Students working on this project will develop following expertise:

- Problem solving ability and time management!
- Engineering materials for biological applications
- Designing nanoparticles with various polymers and lipids (liposomes)
- Encapsulating drugs and strategies for sustained and controlled release of drugs
- Microscopic techniques such as fluorescence imaging, Scanning and transmission electron microscopy, histology
- Mammalian and bacterial cell culture, animal handling and surgeries
- Working with clinical samples

Further reading

- Dhanabalan K.M.; Dravid A.A.; Agarwal S.; Sharath R.K.; Padmanabhan A.K., **Agarwal R.,** Rapamycin microparticles induce autophagy, prevent senescence and are effective in treatment of Osteoarthritis. *BioRxiv*. https://doi.org/10.1101/2021.07.20.453073

- Dhanabalan K.M.; Gupta V.K.; **Agarwal R.,** Rapamycin-PLGA microspheres induce autophagy and prevent senescence in chondrocytes and exhibit prolonged retention in mice joints. *Biomaterials Science*. 8 (2020) 4308 – 4321.