Hydrogel Delivery System for Osteoarthritis Treatment

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HEALTHY KNEE JOINT

KNEE JOINT WITH OSTEOARTHRITIS


Osteoarthritis and its Limited Treatment

Osteoarthritis:

○ Most chronic joint disease

○ Affects 27 million Americans today [Murphy+2012]

○ No cure- existing treatments mainly involve pain management

Risk Factors [Felson+1997]:

○ Age

○ Joint injury (causing inflammation)

○ Mechanical stress (obesity)
A Closer Look...

Non-pharmacological treatments

- Exercise
- Physical therapy
- Weight loss

- Surgery
  - Joint replacement and/or osteophyte removal

Problem: Current forms of intra-articular treatment are only temporary due to short retention rate of medicine within joints

Proposal: Using Injectable Hydrogel

- Highly hydrated cross-linked polymer networks, acts as delivery vehicle, that can encapsulate biomolecules

- Consists of: 4-arm PEG-MAL (polyethylene glycol maleimide), crosslinkers (DDT and/or VPM), buffer solution

- Benefits
  - Biodegradable
  - Biocompatible
  - Minimally invasive
  - Stimuli responsive

Therefore, encapsulating OA therapeutics into hydrogel creates a longlasting delivery system that can degrade in response to a product of the inflammatory response.
Matrix metalloproteinases
Objectives

#1: To determine release behavior over time without any stimuli

An effective delivery system should degrade minimally

#2: To understand the effect of collagenase on hydrogels degradation and therapeutic release

○ There must be a direct relationship between collagenase concentration and the rate of release

#3: To track the response of hydrogels to multiple spikes of collagenase

An effective delivery system must continue degradation in response to multiple exposures to collagenase
Method

Summary

Gels made with certain number of FITC beads (fluorescent nanoparticles) and surrounded in buffer solution and/or collagenase solution

After gels plates were put in incubator, supernatant would collected and analyzed using flow cytometry

| Study #1 | 2.5, 5, 10, & 20% PEG MAL gels in PBS buffer solution for 15 days, run through flow daily |
| Study #2 | 5 & 10% PEG MAL gels made with 0, 50, 100% VPM in collagenase solution, run through flow after 3 hrs |
| Study #3 | 5 & 10% PEG MAL gels made with 0, 50, 100% VPM in PBS for five days with daily spikes in collagenase concentration, run through flow after 3 hrs (surrounding fluid then replaced with PBS) |
Flow Cytometry


Limited Release of FITC Beads from Unperturbed Hydrogels

* All gels 50:50 DTT and VPM
Hydrogels Began Degrading under Collagenase Concentration of 10U/ul
After Initial Surge in FITC Release, Gels Release the Same Amount to Same Collagenase

- 0 U/ul C-Day 1
- 0.1 U/ul C-Day 1
- 10U/ul-Day 1
The Next Step?

● Testing therapeutic with intra-articular hydrogel injections *in vivo* using a mouse model
● Mouse knees will be loaded via cyclic tibial compression that results in load-induced OA
● Knees will be injected with hydrogel containing therapeutic with Green Fluorescent Protein binded to it
● Both the knee joint health and GFP density in the knee synovial joint will be recorded

Predicting cortical bone adaptation to axial loading in the mouse tibia[accessed 2017 Aug. 8] http://rsif.royalsocietypublishing.org/content/12/110/20150590
Conclusions

➢ Using hydrogel provides a single injection therapy in which therapeutic agent is released in response to persisting activation by a catabolic process allowing for a more advantageous approach in treating osteoarthritis than current methods.

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