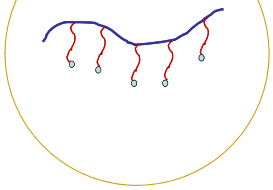
Putnam Research Group
Biolubrication Project



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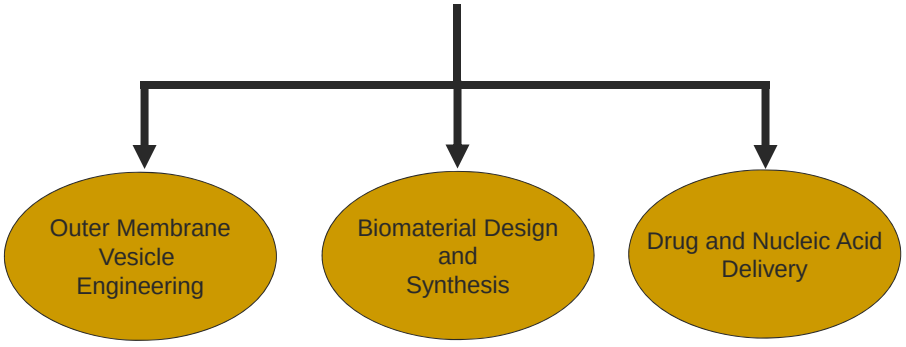
The Putnam Lab

Project Distributions



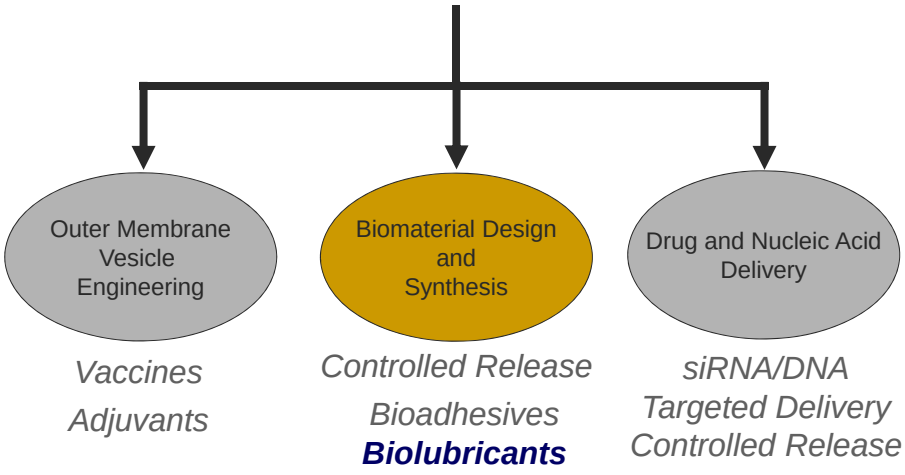
Vaccines
Adjuvants

Controlled Release
Bioadhesives
Biolubricants

siRNA/DNA
Targeted Delivery
Controlled Release

The Putnam Lab

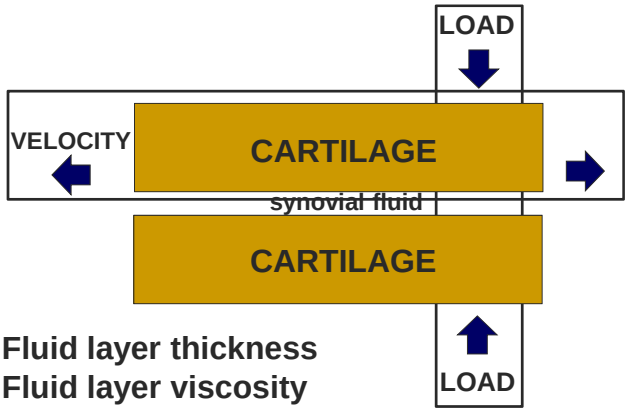
Project Distributions



Osteoarthritis

- Leading cause of morbidity in adults
- Afflicts over 50 million individuals in the developed world, and growing.
- Economic impact exceeds $30B annually in United States alone
- Current treatments are palliative
  - Not disease altering

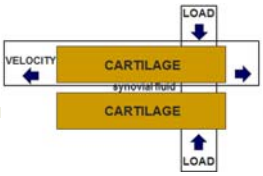
Biolubrication 101
Stribeck curve

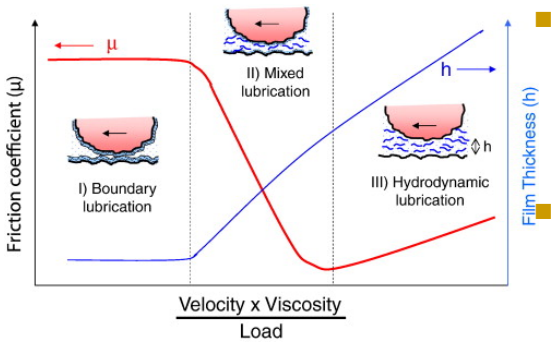


- **Fluid layer thickness**
- **Fluid layer viscosity**

Coefficient of friction (μ)

Biolubrication 101
Stribeck curve





- Boundary mode
  - heavy load
  - slow speeds
- Hydrodynamic mode
  - light load
  - fast speeds

Both are important, depending on need

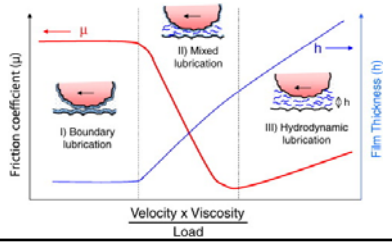
The knee
Both lubrication modes are required

- Boundary mode
  - heavy load
  - slow speeds
- Hydrodynamic mode
  - heavy load
  - slow speeds

Absence of both modes of lubrication leads to osteoarthritis progression

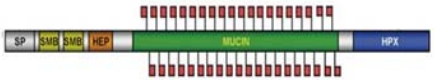
Osteoarthritis
Hydrodynamic lubrication

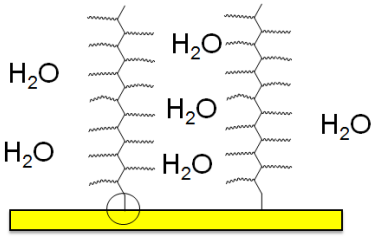
- Hyaluronic acid
  - Natural hydrodynamic lubricant in synovial fluid
  - Replacement injections decrease pain
- Not disease altering
- Boundary mode lubrication also required



Osteoarthritis
Boundary mode lubrication

- Lubricin
  - Natural boundary lubricant in joint
  - Brush architecture
  - Binds orthogonally to cartilage surface
  - Maintains ordered water layer at surface
- Lubricin replacement prevents OA progression
- **Problem**
  - Manufacturing costs
  - ~$10,000/mg

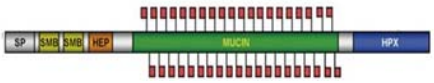


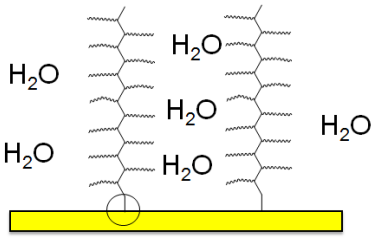


Elsaid, K. et al *Arth. and Rheumatism* **2005** 52:1746-1755
Jay, GD et al. *Arth. and Rheumatism* **2010** 62(8): 2382-91

Synthetic lubricin mimetics

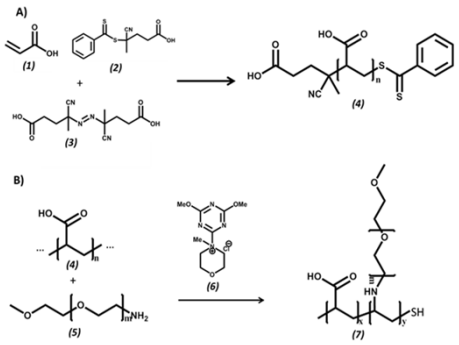
- Design criteria
  - Polyanionic backbone
  - Hydrophilic brushes
  - Biocompatible
  - Orthogonal cartilage binding
  - Inexpensive and reproducible manufacture
- **Boundary mode lubricant!**

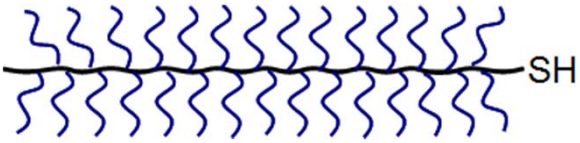




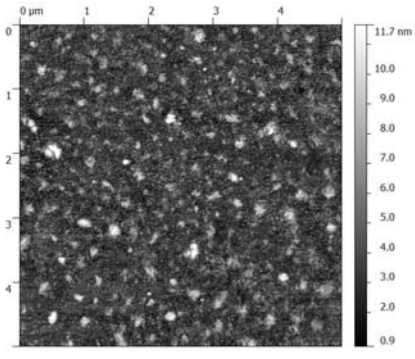
Synthetic lubricin mimetics
Synthesis

- Synthesis and structure
  - Poly acrylic acid via RAFT polymerization
  - PEG side chains via DMTMM conjugation



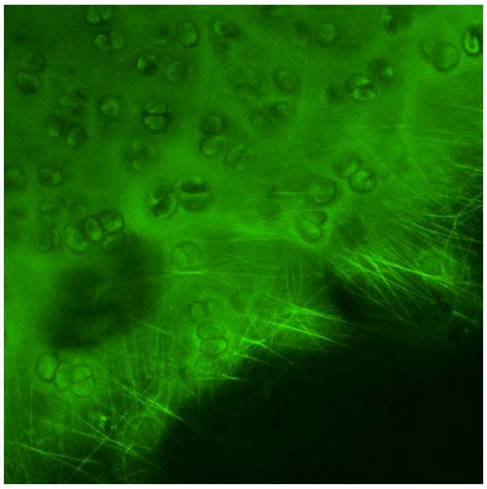


Synthetic lubricin mimetics
Surface coverage (gold)



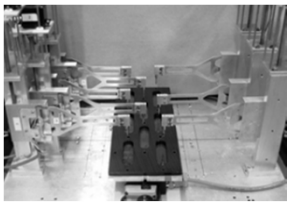
- **Structure**
  - pAA backbone: 60K
  - PEG side chains: 2K
  - PEG substitution: ~78%

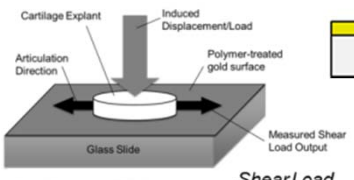
Synthetic lubricin mimetics
Surface coverage (cartilage)

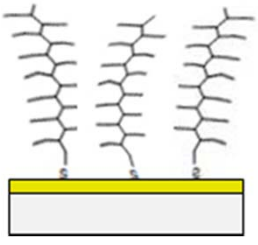


Synthetic lubricin mimetics
Lubrication analysis in vitro

- Custom tribometer (Bonassar group)

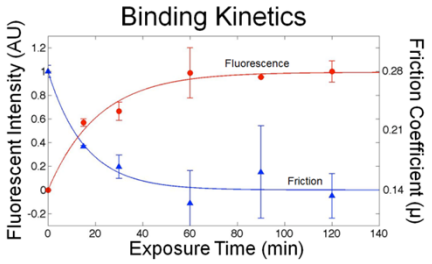


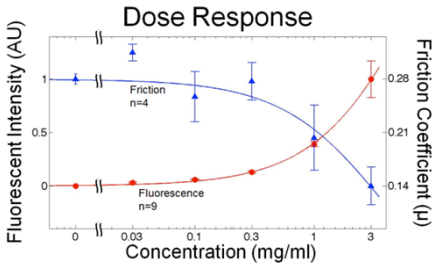


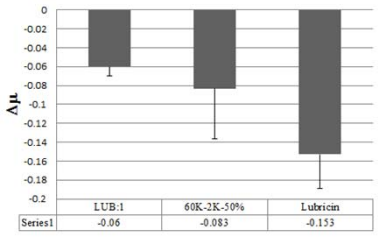


$$Coefficient of Friction(\mu) = \frac{Shear Load}{Normal Load}$$

Synthetic lubricin mimetics
Lubrication analysis in vitro

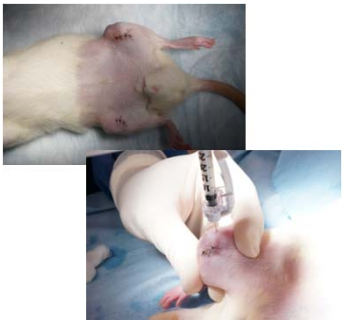


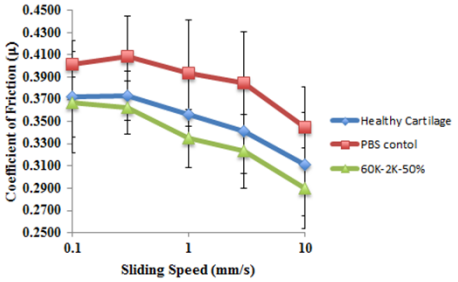




Synthetic lubricin mimetics
Lubrication analysis in vivo

- Rat ACL transection model
- Lubrication equal to native cartilage





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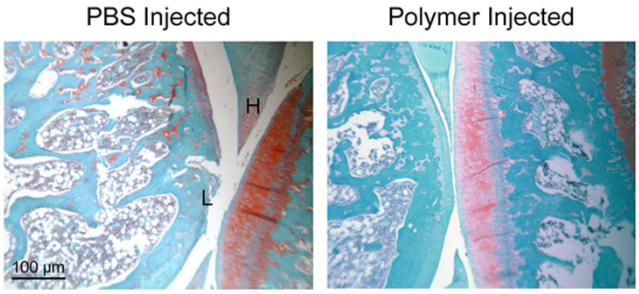
Synthetic lubricin mimetics
Lubrication analysis in vivo

- Excellent biocompatibility



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