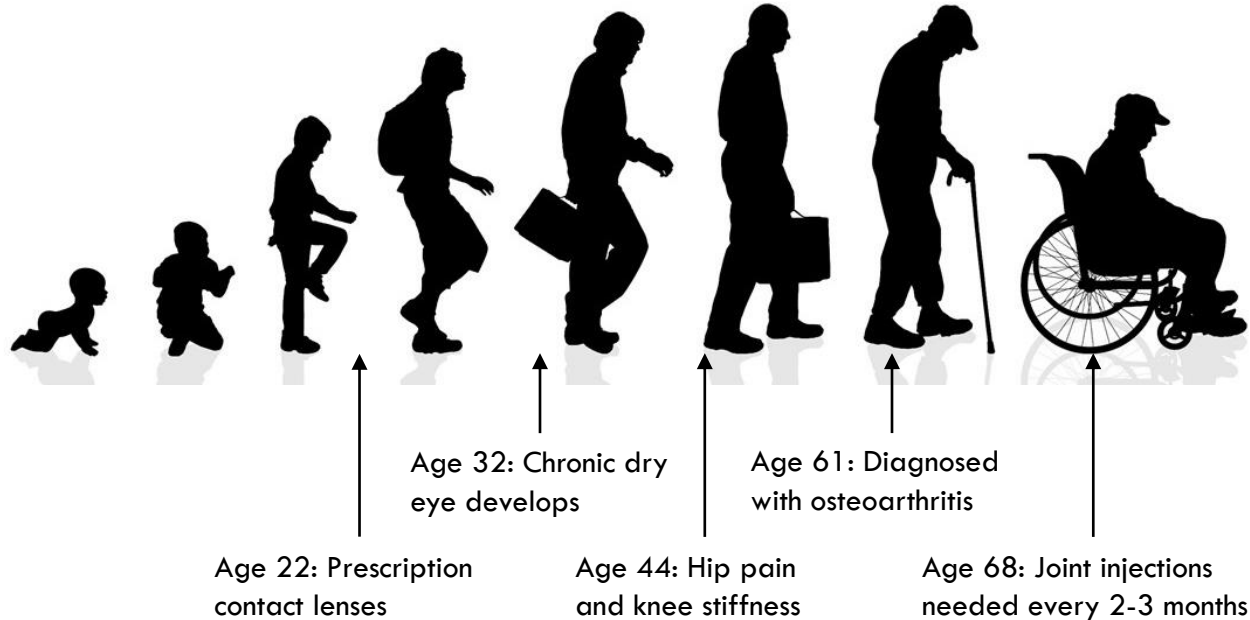


Matthew Paszek and Heidi Reesink
synLubricin™



Lubricating the Human Body

- Daily tasks require dynamic movements in joints and eyes
- Aging and other factors can reduce natural lubrication



Current Lubrication Solutions

- **Cortisone and Hyaluronic Acid**
 - Two joint injection treatments for various arthritis ailments
 - Reduces inflammation and temporarily lubricates joints, respectively
 - Quickly broken down, thus injections are needed every few months
 - No non-surgical, medium- to long-term solutions on the market
- **Glycols, Glycerin, and Mineral Oils**
 - Artificial tears often contain a cocktail of exogenous lubricants
 - Preservatives can irritate the eyes
 - Multiple daily reapplications required to relieve dry eye symptoms
 - No non-surgical, medium- to long-term solutions on the market

synLubricin™

- Recombinant glycoprotein for long-term *in-vivo* biolubrication

Codon-scrambling strategy enables recombinant production in FDA-approved human embryonic kidney 293-F cells

Extended half-life of >2 months, compared to conventional hyaluronic acid of ~12 hours

Engineered bottlebrush proteins that protect biological tissue by maintaining hydration and resisting abrasion

Treatment for osteoarthritis, rheumatic disease, chronic dry eye, and other use cases

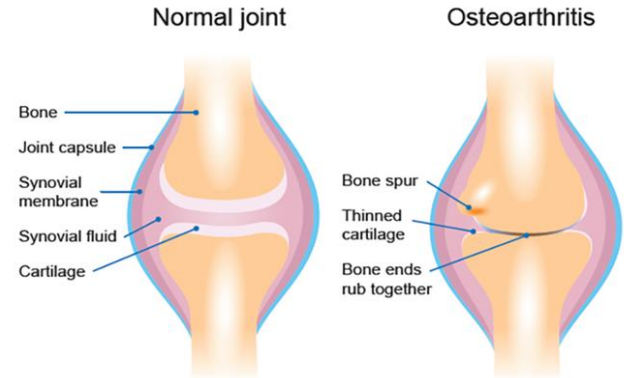
Markets for synLubricin™

| Affliction | U.S. Patients | U.S. Treatment Revenue | Source |
|----------------------|--------------------|--|-----------------------------|
| Arthritis (all) | 86 million (2010) | \$15.1 billion (2010) CAGR 9.9% (2003-10) | Frost & Sullivan A772 |
| Rheumatoid arthritis | 2.6 million (2017) | \$8.3 billion (2017) | Frost & Sullivan N96E-52 |
| Psoriatic arthritis | 796,400 (2017) | \$1.3 billion (2017) | Frost & Sullivan NB3A |
| Chronic Dry Eye | 7.0 million (2014) | \$573 million (2014) CAGR 11.1% (2007-2014) | Frost & Sullivan N500 |

| Treatment | Global Market | Source |
|---|---|--|
| Joint Pain Injections (all treatments) | \$3 billion (2018) CAGR 8.8% (2018-2026) | Transparency Market Research |
| Hyaluronic Acid (all uses) | \$9.1 billion (2019) CAGR 8.1% (2020-2027) | Grand View Research |

Treatments for osteoarthritis

- Natural wearing-down of joints causes pain and stiffness
- Age and weight are contributing factors
- Similar symptoms as rheumatic arthritis (autoimmune disease)



Conservative Treatments

Invasive Treatments

Therapy

- Physical
- Occupational
- Weight-loss/exercise

Medication

- Acetaminophen
- NSAIDs
- Duloxetine

Joint Injections

- Cortisone
- Hyaluronic acid
- **synLubricin™**

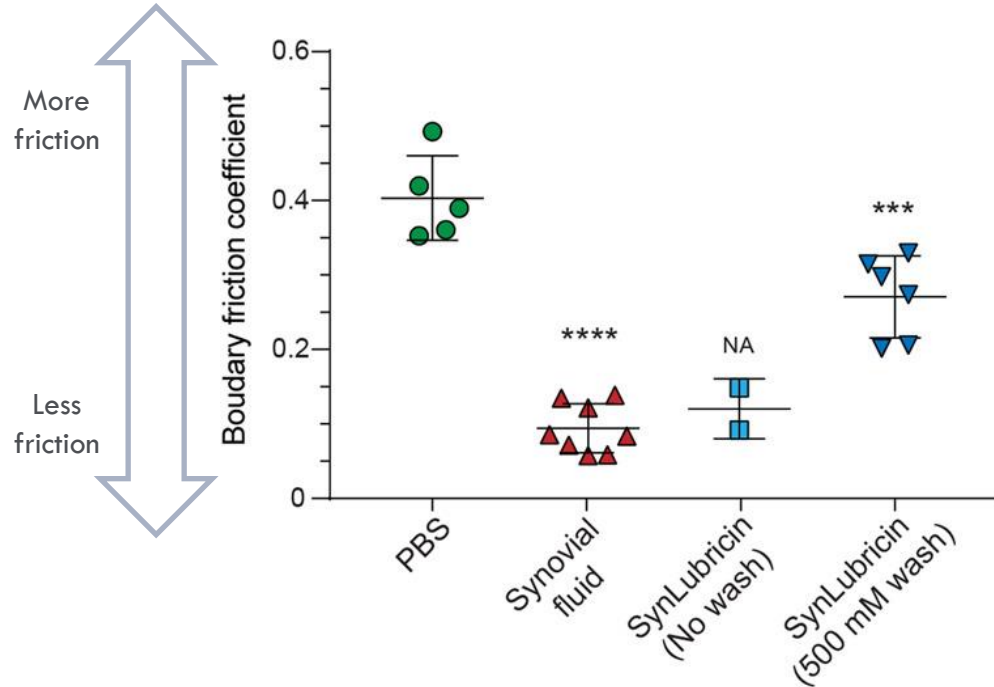
Surgery

- Bone realignment
- Joint replacement

Joint Injections

| Treatment | Action | Cons |
|-----------------|---|---|
| Cortisone | Treats inflammation Multiple use cases | Not recommended for diabetics Wears off after a few months Limited to 4 injections per year |
| Hyaluronic Acid | Supplements natural joint lubrication | Debatable efficacy Does not provide immediate relief Multiple injections often required |
| synLubricin™ | Long-term lubrication of joints | New medication |

Efficacy of synLubricin™



Cartilage Lubrication

- synLubricin™ applied to cartilage explants demonstrates similar lubrication to bovine synovial fluid
- Even after washing with 500 mM NaCl, synLubricin™ exhibits significantly better lubrication than PBS saline solution (control)

Treatments for chronic dry eye

- Dry eyes are unable to produce enough tears for lubrication
- Estimated more than 4.88 million Americans have this condition



Conservative Treatments

Invasive Treatments

OTC Medication

- Eye drops
- Ointments
- **synLubricin™**

Prescription Drugs

- Anti-inflammatory
- Antibiotics

Procedures

- Eye inserts
- Scleral or bandage contacts
- Closing tear ducts
- Clearing oil glands

OTC Medication

| Treatment | Action | Cons |
|--------------|--|---|
| Eye drops | Moistens eyes Decreases evaporation | Requires constant application Irritating preservatives |
| Ointments | Lubricates eyes | Daily overnight application Temporary blurred vision |
| synLubricin™ | Lubricates eyes for long periods of time | New medication |

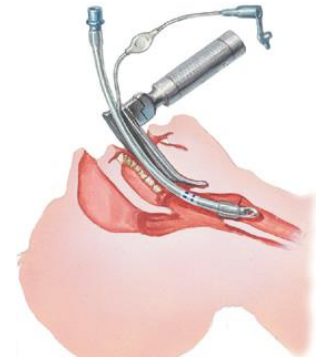
Alternative uses for synLubricin™

Medical

- Medical device lubrication
- Obstetrical and vaginal lubrication

Biotechnology

- Machine lubrication

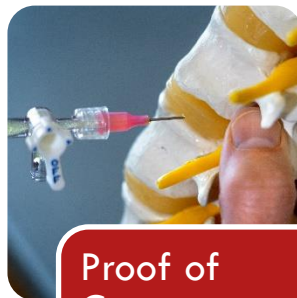


Technology Readiness



Invention

- synLubricin™ created, isolated, and characterized on lab-scale



Proof of Concept

- Demonstration of safety and efficacy in rat models



Prototype

- Successful production in human embryonic kidney 293-T cells



Next:
Scale-up and
Regulatory

PCT application filed – publication #WO2020150396A

Matthew Paszek Lab



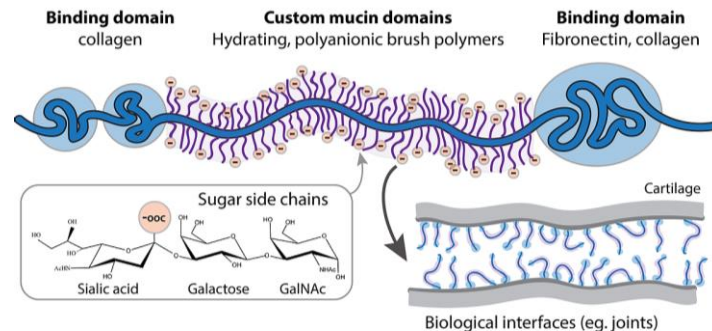
Cornell Engineering

- Matthew Paszek, Ph.D.
- Associate Professor of Chemical and Biomolecular Engineering, Cornell University

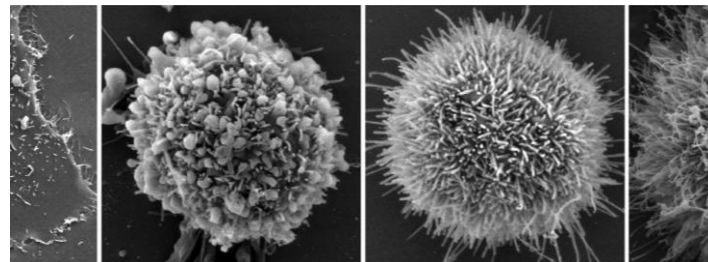
Paszek Lab at Cornell is applying materials science and synthetic biology to develop therapeutic biotechnologies

- Mucin-based biolubricants for long-term treatment of joint diseases and other biomedical challenges
- Engineering cellular system platforms for scalable biomanufacturing
- Clinical translation of novel therapeutics

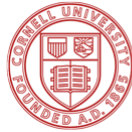
Engineered Biolubricants



Novel Cell Platforms



Heidi Reesink Lab



Cornell University
College of Veterinary Medicine

- Heidi L. Reesink, VMD, PhD, DACVS-LA
- Harry M. Zweig Assistant Professor in Equine Health

The Reesink Lab at Cornell studies the pathophysiology, epidemiology and treatment of osteoarthritis and racehorse fractures

- Investigating how synovial fluid glycans and glycoproteins, including lubricin and hyaluronic acid, are altered in osteoarthritis and traumatic joint injury
- Elucidating how lubricin and hyaluronic acid synergistically enhance joint lubrication, mitigate inflammation and promote cartilage health
- Developing novel therapeutic strategies for osteoarthritis

Regenerative Medicine and Lubricin Therapy



Equine Sports Medicine and Lameness



D-7839: Novel Recombinant Lubricin (“synLubricin™”) with Long-Term *in-vivo* Bio-Lubrication

Technology Overview

Commercial interest in recombinant mucin technology has emerged due to the unique ability of mucin glycoproteins to hydrate, protect, and lubricate biological surfaces. However, recombinant production of the large, highly repetitive domains that are characteristic of mucins remains a challenge in bio-manufacturing.

The secreted mucin-like glycoprotein called proteoglycan 4, or lubricin, has garnered particular interest as lubricin binds to cells and tissue interfaces, including cartilage and ocular surfaces to enable low friction lubrication and protection. In fact, low concentrations of synovial fluid lubricin are associated with anterior cruciate ligament injury, osteoarthritis, and rheumatoid arthritis.

Although there has been significant interest in the development of recombinant lubricin as an injectable for the treatment of osteoarthritis and rheumatic disease, and as a topical for chronic dry eye, recombinantly producing lubricin has proven to be challenging.

Using a novel codon-scrambling strategy, stable, long-term recombinant production in human suspension cell culture (human embryonic kidney 293-F cells) has been achieved for synLubricin™. Moreover, as shown in the figure below, cartilage explant studies demonstrated that synLubricin performed as well as synovial fluid, while *in vivo* studies in rats showed a prolonged half-life of over 2 months.

Potential Applications

- Treatment for arthritic joints and chronic dry eye
- Medical device lubrication

Advantages

- Extended half-life of over 2 months as compared to hyaluronic acid (12 hours) improves patient quality of life by reducing subsequent booster injections
- Stable and scalable recombinant production system developed

[Read more on Flintbox](#)

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PCT/US20/13752

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Publication:

Stable recombinant production of codon-scrambled lubricin and mucin in human cells. Shurer, C.R., et al. [Biotechnology and Bioengineering](#) (2019). <https://doi.org/10.1002/bit.26940>

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