Project Summary and Outcome Report

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PROJECT TITLE

Synthetic joint bio-lubricants for mitigating osteoarthritis and associated chronic pain

PROJECT INVESTIGATORS

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PROJECT SUMMARY

A significant factor contributing to the pathogenesis and progression of osteoarthritis (OA) is the impaired lubrication of joints. The disruption in lubricating system reduces the generation of natural lubricant, resulting in increased friction, cartilage wear, and subsequent joint damage. To address this, this project aimed to develop an innovative class of synthetic biolubricants for mitigating osteoarthritis and associated chronic pain. By injecting these synthetic biolubricants into the joint cavity, we aimed to restore the lubricant function, improve joint mobility, and prevent the degenerative process of OA. The specific tasks of this project included the synthesis of novel biocompatible biomolecule-based molecular brushes using advanced molecular engineering and the investigation of their lubrication properties for potential OA treatment.

PROJECT ACHIEVEMENT

1. Development of molecular brushes as synthetic biolubricants for OA treatment

1.1 Successful synthesis of molecular brushes

We have successfully synthesised a series of novel molecular brushes that have glycol chitosan, a natural polysaccharide, as the backbone, and PMSEA, a cutting-edge hydrophilic polymer imparting hydration lubrication properties, as the side brushes (Figure 1). To further facilitate the molecular brushes to adhere to the cartilage surface, we also incorporated mussel-inspired

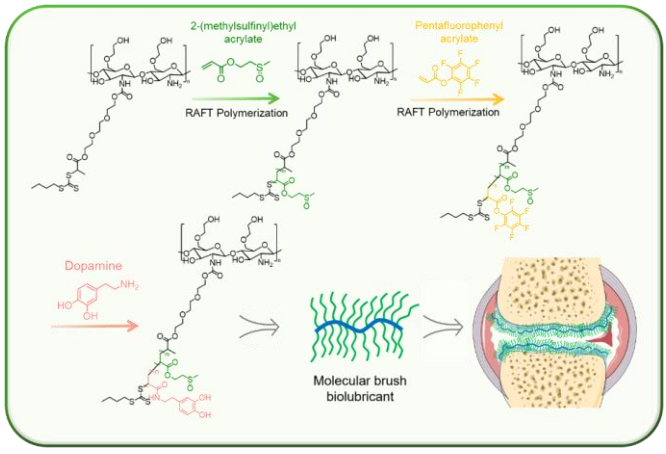

Figure 1. Schematic Illustration of the Synthesis of Biolubricants Based on Molecular Polymer Brushes.

polydopamine, a known molecular “adhesive”, to the chain end of the side PMSEA brushes.

1.2 Confirmation of lubrication properties of the molecular brushes

Using a ball-on-disc model, we conducted tribological studies of the synthesised molecular brushes. We demonstrated that these molecular brushes exhibited a lower coefficient of frication (COF) compared to hyaluronic acid, a commercial injectable lubricant for osteoarthritis treatment. Furthermore, by optimising the molecular characteristics of the brushes, we achieved a COF of approximately 0.005, which is significantly lower than the COF (0.01-0.02) of natural synovial liquid in joint. This demonstrates the potential of the synthesised molecular brushes as synthetic biolubricants for improving surface lubrication.

1.3 Investigation of lubricating function on small animals with OA

We are currently collaborating with the clinicians at Peking Union Medical College Hospital to investigate the function of the synthesised molecular brush biolubricants in small animals (guinea pigs) with established osteoarthritis (OA).

2. Publications

We have submitted two publications and drafted two manuscripts that acknowledge the support of Arthritis Australia.

Pub 1. Xin Xu, Yuhao Zhang, Yuan Xu, Yingjie Wang, JiaoJiao Li, Felicity Han, Kevin Tetsworth, Jason Stoke, Andrew Whittaker, and Changkui Fu. *Synthetic Biolubricants Based on Molecular Polymer Brushes for the Treatment of Osteoarthritis*. To be submitted.

Pub 2. Xin Xu, Youliang Zhu, Yixin Chang, Yuhao Zhang, Wenting Zhang, Hui Peng, Zhong-Yuan Lu, Andrew Whittaker, and Changkui Fu. *Polymerisation-Induced Self-Assembly on Planar Surfaces: A New Approach for Controlling Surface Topography and Modulating Material-Bio Interactions*. To be submitted.

Pub 3. Yixin Chang, Gayathri Ediriweera, Weizhi Xu, Qiaoyun Wang, Xin Xu, Yuhao Zhang, Hui Peng, Kun Liu, Amnon Bar-Shir, Andrew K. Whittaker, and Changkui Fu. *Efficient Synthesis of Polymeric Fluorinated Nanoparticles with High Fluorine Content via Aqueous Photo-PISA for 19F MRI Application*. Submitted to ACS Nano.

Pub 4. Wenting Yang, Shangqian Li, Siqi Yu, Alex G. C. de Sá, Tanmayee Sai Sivani Ita, Tian Liang, Helen Forgham, Ruirui Qiao, Jiulong Li, Patrick S. Stayton, David B. Ascher, Huan Meng, Andrew K. Whittaker, and Changkui Fu. *Combinatorial Discovery of RAFT Cationic Polymers for mRNA Delivery: Structure-Function Insights from High-Throughput Screening and Machine Learning*. Submitted to Advanced Healthcare Materials.

3. Conferences/Seminars

I have presented research related to this project and acknowledged the support of Arthritis Australia at many conferences and seminars. These include:

1. Eight seminars at different universities, including the School of Chemical Engineering of University of New South Wales, School of Chemical Engineering of University of Melbourne,

School of Chemistry and School of Material Engineering of Monash University, School of Chemistry of Queensland University of Technology, School of Chemistry of Flinders University, School of Biomedical Engineering of Sun Yat-sen University, School of Materials and Energy of Guangdong University of Technology.

Seminar title: *Sulfoxide Polymers: A New Paradigm for Polymer Design and Applications*.

2. Three conference presentations, including 1) *Antifouling and Antibacterial Polymers and Surfaces*. The 20th International Congress on Marine Corrosion and Fouling (ICMCF), June 16-21, 2024, Guangzhou, China; 2) *Polymeric Metal-Fee MRI Contrast Agents*. The 14th International NanoMedicine Conference, June 24-26, 2024, Sydney, Australia; and 3) *Delivery of Proteins and mRNA using Advanced Synthetic Polymers*. International Conference on Advanced Materials for Energy, Environment, and Health (ICAMEEH), September 24-27, 2024, Adelaide, Australia

4. Research impact

Our research on developing synthetic biolubricants has been featured in our institution's website (https://aibn.uq.edu.au/article/2024/02/targeting-lasting-osteoarthritis-relief-injectable-biolubricant). This research has sparked conversions and discussions with OA patient on the potential for translating this invention into a real medical treatment for OA.

5. Acknowledgement

We are sincerely grateful to Arthritis Australia for supporting this cutting-edge research. This is just a beginning of this research, and we will continue to build upon it as we strive to develop an effective medical solution for the better treatment of OA.