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Next generation viscosupplements: Design specifications of lubricity, cushioning, and residence time

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Osteoarthritis (OA) is characterized by the breakdown of hyaline cartilage and synovial fluid (SF) in articular joints. This debilitating disease affects 27 million people in the US. An important pathophysiologic change associated with OA is a decrease in the lubricity of SF due to a decrease in both the concentration and molecular weight of hyaluronic acid (HA) which adversely affects the rheological properties of SF. No pharmacologic treatments have been proven to ameliorate the progressive destruction of articular cartilage associated with OA. Currently, HA or crosslinked HA is injected intra-articularly to treat patients (i.e., viscosupplementation), and yet this procedure has major drawbacks: 1) HA is rapidly enzymatically degraded; 2) injected HA has not been shown to reside in the joint for longer than 28 days (half-life of only 8.8 days, even when crosslinked); 3) HA synthesis and purification is costly; and 4) HA has not been demonstrated clinically to prevent cartilage wear, and several meta-analyses of randomized controlled studies have challenged this procedure's efficacy. To address this unmet need of a treatment for early and mid stage OA, we are synthesizing and evaluating novel synthetic polymers which are designed to specifically lubricate healthy and worn cartilage, provide cushioning, and reside in the joint after intra-articular injection for more than 30 days. In this lecture, I will discuss the synthesis and characterization of two novel biolubricants, the performance of these biolubricants in ex vivo and in vivo models, and the design rationale for this approach.

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A diagnostic tool for detection of brain fever by epitope-imprinted piezoelectric device

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Neisseria meningitides, a human-specific bacterial pathogen causes bacterial meningitis by invading the meninges of central nervous system. High mortality rate associated with the disease therefore requires proper medical diagnosis and early treatment. Diagnosing bacterial meningitis is currently cumbersome and involves isolating the bacteria from sterile cerebrospinal fluid (CSF) through lumbar puncture followed by observing presence of meningococci under microscope by a neurologist. A computational approach identified candidate T-cell epitopes from outer membrane proteins Por B- (^{273}KGLVDDADI^{282} in loop VII and ^{170}GRHNSESYH179 in loop IV) present on the exposed surface of immunogenic loops of class 3 OMP allele of *N. Meningitides* as well as another epitope sequence identified from N. meningitides iron acquisition protein viz. an iron regulated outer membrane protein frpB. These epitopes are used for designing a diagnostic tool via molecularly imprinted piezoelectric sensor (MIP-QCM) for N. meningitides strain MC58. Methacrylic acid (MAA) and acrylic acid (AA) with ethylene glycol dimethacrylate (EGDMA) and azo-isobutyronitrile (AIBN) were used as functional monomers, crosslinker and initiator, respectively. The epitope can be simultaneously bound to functional monomer and fitted into the shape-selective cavities. On extraction of epitope sequence from thus grafted polymeric film, shape-selective and sensitive sites were generated on EQCM crystal i.e known as epitope imprinted polymers (EIPs). Imprinting was characterized by atomic force microscopy images. The epitope-imprinted sensor was able to selectively bind Neisseria meningitides proteins present in blood serum of patients suffering from brain fever. Thus, fabricated sensor can be used as a diagnostic tool for meningitis disease.

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