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The Institute of Translational Health Sciences (ITHS) Technology Development Center

Tong Sun

Executive Director, Institute of Translational Health Sciences & Assistant Dean, Translational Health Sciences, University of Washington, School of Medicine

Abstract:

The Institute of Translational Health Sciences (ITHS), a CTSA hub at the University of Washington (UW) in partnership with the Fred Hutchinson Cancer Research Center (Fred Hutch), and Seattle Children's, is dedicated to speeding science to the clinic for the benefit of patients and communities throughout the Washington, Wyoming, Alaska, Montana, and Idaho (WWAMI) region. Through the Technology Development Center (TDC), ITHS consolidated and coordinated training, funding support, and services for academic innovators. The intent of this consolidation was to make it easier for translational researchers to find and connect with others who can help advance their scientific and technological developments beyond their laboratory "comfort zone" and through regulatory path definition, early clinical study, and preparation for commercialization.

Notes:

AI-Powered Neuromorphic Sensors for Medical Diagnostics

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Abstract:

Olfaction, an ancient sensory system, provides intricate information about the environment. In emulation of this biological process, neuromorphic devices in conjunction with machine learning algorithms, endeavor to replicate and digitize the olfactory capabilities. This presentation focuses on the gas discrimination and identification capabilities of neuromorphic nanosensors. These nanosensors, constructed with functionalized nano materials, were integrated into multi-channel gas sensor devices, and their sensing signals were recorded upon exposure to diverse gases. To unravel the temporal characteristics embedded in the sensing signals, we employ machine learning algorithms to extract meaningful patterns and discern specific gases. The integration of machine learning significantly enhances the electronic olfaction system's gas identification performance across a wide spectrum of gases. This innovative platform not only downsizes electronic noses but also digitizes olfactory information, enabling the precise detection and identification of various gases and volatile organic compounds (VOCs). By employing machine learning algorithms, we extract distinctive signal patterns that allow accurate classification of gaseous biomarkers. The resulting AI-enhanced electronic olfaction system offers significant potential for medical technology applications, including non-invasive disease diagnostics, infection monitoring, and controlled environments in clinical settings. The use of tailored biomaterials in sensor design ensures biocompatibility and scalability, paving the way for integration into smart medical devices and wearable platforms. This convergence of intelligent biomaterials, neuromorphic engineering, and data-driven analysis represents a powerful advance in the field of medical technology, highlighting the role of biomaterials science in enabling precision healthcare solutions.

Notes:

Ultrasound-Responsive Piezoelectric Biodegradable Nanoparticles for Drug-Free Anticancer Therapy

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Abstract:

Introduction: The ability to precisely and non-invasively modulate tumor cell activity through localized electric stimulation opens new frontiers in anticancer therapy. Our group was the first to demonstrate the possibility of electric cue delivery at the cellular level using ultrasound-responsive piezoelectric nanoparticles in neurons and tumor cells. Following these findings, several studies have corroborated and expanded upon our work, using inorganic and polymeric piezoelectric nanoparticles to achieve similar effects.

Materials and Methods: Here, we present the first piezoelectric nanoparticles synthesized from an FDA-approved material, chitosan, paving the way for safer, clinically translatable applications. The fabrication involves an emulsification technique, where a treatment with KOH likely induces crystallization and piezoelectricity. Piezo-response force microscopy confirmed that chitosan nanoparticles (ChNPs) exhibit a piezoelectric coefficient (d33) of 37.29 ± 4.45 pm/V, surpassing values reported for well-known polymeric nanoparticles (e.g., PVDF-TrFE). No prior reports have demonstrated piezoelectricity in chitosan at the nanoparticle level, underscoring the novelty of this work.

Results, Discussion and Conclusions: We further explored the biomedical applications of ChNPs by assessing their interactions with patient-derived glioblastoma cells. Biocompatibility studies confirmed the safe integration of ChNPs with cells even at elevated concentrations (1 mg/mL). Notably, ChNPs activated calcium waves and increased basal calcium levels upon acute ultrasound exposure, demonstrating successful cell stimulation. Chronic ultrasound stimulation of glioblastoma cells in the presence of ChNPs led to significant antiproliferative and pro-apoptotic effects, as evidenced by Ki-67 and p53 expression. Remarkably, unlike other polymeric piezoelectric nanoparticles, ChNPs induced pro-apoptotic effects without chemotherapeutic drug loading, highlighting their intrinsic therapeutic potential. This may be attributed to the piezocatalytic activity of ChNPs, which we demonstrated to enhance singlet oxygen levels upon ultrasound activation (20% increase). In conclusion, chitosan-based piezoelectric nanoparticles represent a biocompatible, biodegradable platform for ultrasound-mediated cancer therapy, offering drug-free, clinically translatable piezocatalytic anticancer stimulation.

Notes:

New Ocular Biomaterials Utilizing Biomimetic Complexation for Controlled and Sustained Drug Delivery

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Abstract:

Introduction: More efficacious and efficient delivery of drugs to the eye is a significant unmet need. Over 2.2 billion people worldwide have vision impairment with approximately half preventable or untreated, according to the World Health Organization. Standard of care drug delivery strategies for the front of the eye are topical drops and significantly limited by the eye's normal protective barriers. Back of the eye diseases are even more difficult to treat with many treatments requiring ocular injections over a short time with numerous side effects. By exploiting long chain non-covalent interactions using a biomimetic strategy, we have synthesized and characterized a novel platform of optically clear, injectable, self-assembling gels for sustained release of drug-containing, nucleic acid (NA) nanoconjugates for ocular drug delivery to the anterior and posterior segments of the eye. Also, using a biomimetic strategy, we have produced several covalently crosslinked gels leading to novel contact and bandage lenses with controlled transport of various therapeutics that can deliver constant amounts of one or multiple therapeutics to the eye for the duration of lens wear from days to weeks.

Materials and Methods: Self-assembling gels were produced with non-covalent polycation and polyanion modifiers of varying molecular weight with poly (D, L-lactic-co-glycolic acid)-b- poly (ethylene glycol)-b-poly (D, L-lactic-co-glycolic acid) (PLGA-PEG-PLGA) triblock copolymers. Additional gel properties such as the lactic acid (LA) to glycolic acid (GA) ratio, the PLGA/PEG ratio, polymer solution composition, and homopolymer MW and concentration were varied. For covalently crosslinked silicone hydrogels, macromolecular memory was achieved by templating techniques, involving the formation of non-covalent pre-polymerization complexes between template therapeutic and monomers/oligomers. Polymerization occurred by free-radical photopolymerization in molds within conventional lens manufacturing processes. Concentration and diversity of monomer chemistry, template drug concentration, solvent amount, crosslinking and lens architecture, and polymerization kinetics were varied. Bromfenac extended-release silicone hydrogel contact lenses (BERCLs) were prepared (center thickness 85 µm, base curve 8.4 mm, diameter 14.8 mm) and were placed in white New Zealand rabbits post comprehensive ocular examination and compared to BromdayTM topical eye drops (bromfenac ophthalmic solution, 0.09%, Bausch+Lomb).

Results, Discussion, and Conclusions: Formulations have been tested both in-vitro and in-vivo with groundbreaking results for topical delivery compared to drops and the prevention of fibrotic ocular diseases such as posterior capsular opacification (PCO) and proliferative vitreoretinopathy (PVR). Drug-containing nucleic acid nanoconjugate release has been shown to be finely controlled by number and type of non-covalent interactions leading to release durations over 5 months compared to only 28-day release provided by unmodified gels. Extended release of NA nanocarriers specifically targeted and depleted myofibroblasts and progenitors with greater success than a bolus dose of nanocarriers, preventing PCO and PVR formation with minimal off-target effects. BERCL treated eyes showed a

continuous, stable, therapeutic bromfenac tear concentration of 256.4 ± 23.1 µg/mL for 8 days. Topical drops showed a quick peak concentration 213 ± 88 µg/mL and short duration of less than 100 minutes. Bioavailability (AUC0-8days) and mean residence time (MRT) of BERCL was 26 times and 155 times higher than topical eye drops, respectively. BERCLs were safe and well tolerated with no adverse events, and post-study ophthalmic exams were unremarkable. No histological difference was observed in corneal tissue. A meta-analysis revealed significantly higher concentrations and more sustained bioavailability, achieving longer drug exposure (100% of time) in the aqueous humor compared to drops (50% of time below therapeutic window), where a decrease in inflammatory cells is a primary endpoint. By utilizing new biomaterials, more efficient and efficacious treatment of ocular disease is on the horizon with strong potential to lead to better patient outcomes for preventable and untreated disease.

Notes:

Stimuli-Responsive Polymers for Biomedical Technologies

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Abstract:

Introduction: Stimuli-responsive materials (SRMs) can be used to produce devices for the controlled delivery of drugs, neuromodulation, tissue engineering and regenerative medicine. Our specific interest is the development of SRMs capable of responding to one or more stimuli (particularly electricity, light and magnetism) and demonstrating their efficacy in vitro/vivo. We employ a multidisciplinary approach (including chemistry, materials science and engineering, and biology) to produce and characterize SRMs via techniques including biological assays, mechanical tests, microscopy, spectroscopy, etc. Our particular interest is carbon-based conductive/electroactive SRMs (i.e., based on derivatives of oligomers, polymers, and 2D materials, etc.), and our multidisciplinary approach has enabled us to explore how to design materials/devices with task-specific properties designed for drug delivery, neuromodulation, and tissue scaffolds to control cell behavior, potentially mimicking endogenous tissue electrical properties for tissue scaffolds enabling fundamental biological studies, drug screening in the short term, as well as providing bioactive cues to aid in tissue regeneration in the long term.

Materials and Methods: We employ an interdisciplinary approach combining chemistry (synthesis), materials science and engineering to prepare and characterize SRMs (e.g., mechanics, microscopy and spectroscopy). The SRMs are subsequently exposed to stimuli, and the release profiles of their payloads (e.g., drugs) is quantified (typically spectroscopically, optionally via cell assays).

Results, Discussion and Conclusions: The SRMs can respond to one or more stimuli, and we have controlled the behavior of cells via the delivery of stimuli (e.g., electrical/light signals, chemical signals), including therapeutically relevant quantities of ions, drugs or biologics of various molecular weights, including anti-microbials, anti-cancer agents, anti-inflammatories and growth factors. The stimulation paradigms are either designed to be adaptable to integration in existing medical devices or technologies (e.g., catheter balloons inserted via minimally invasive surgery, medical electronics such as bionic eyes, cochlear implants, electrodes for deep brain stimulation, etc.), and believe such carbon-based SRMs will be translated to real world applications for technical and medical applications in the foreseeable future.

Notes:

Precise Functionalization of DNA Scaffold Particles for Enhanced NK Cell Antitumor Efficacy

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Abstract:

Introduction: Natural killer (NK) cells play a central role in innate anticancer immunity through their ability to recognize and kill cancer cells without prior antigen priming. Despite their therapeutic promise, clinical translation of NK cell–based immunotherapies have been hindered by limited persistence, functional exhaustion, and insufficient activation within the immunosuppressive tumor microenvironment. Strategies that enable precise and sustained engagement of activating receptors on NK cells, while simultaneously promoting tumor-specific targeting, are of significant interest. Engineered NK cell engagers and biomaterial-based delivery platforms are promising approaches to address these challenges by improving spatial control and multivalency of immune activation. While Surface-functionalized polymeric particles offer opportunities to present immune ligands in defined densities and ratios, conventional conjugation strategies often lack the modularity and quantitative control needed to systematically optimize immune receptor engagement. Here, we introduce a biocompatible DNA-scaffolded poly (lactic-co-glycolic acid) (PLGA) particle platform that enables ratiometric and programmable antibody loading. This system is designed to precisely control the presentation of NK cell–activating antibodies alongside tumor-targeting ligands, providing a platform to enhance NK cell mediated cytotoxicity against solid tumors.

Materials and Methods: PLGA particles were fabricated using an emulsion-based technique and surface-functionalized with short synthetic DNA oligonucleotides via a PLGA–PEG–DNA conjugation strategy. Complementary DNA sequences were used as modular scaffolds to enable quantitative and ratiometric attachment of monoclonal antibodies (mAbs) through sequence-specific DNA hybridization. Selected mAbs targeting NK cell activating receptors, together with an anti-EGFR antibody, were conjugated to the particle surface at defined densities and ratios. Particle size and antibody loading efficiency were characterized using electron microscopy, and fluorescence-based quantification. A series of formulations with varying antibody compositions were evaluated in vitro for their ability to promote NK cell activation and cytotoxicity against colorectal and glioblastoma cancer cell lines. In vivo efficacy was evaluated in colorectal tumor–bearing mice following local administration of selected immune-engaging particle formulations, with tumor growth kinetics and survival monitored as study endpoints.

Results, Discussion and Conclusions: DNA scaffolding enabled precise, reproducible, and ratiometric loading of multiple antibodies onto PLGA particles, overcoming key limitations of conventional surface conjugation approaches. Systematic modulation of surface antibody density and composition demonstrated that NK cell activity was strongly dependent on both the total antibody surface density and the relative stoichiometric ratios of the conjugated antibodies. An optimized ratio achieved maximal enhancement of NK-mediated cytotoxicity against cancer cells in vitro, compared to single-ligand or non-optimized controls across both colorectal and glioblastoma models. In vivo study showed that intratumoral administration of immune-engaging particles resulted in enhanced NK cell antitumor activity and significantly prolonged survival compared to control treatments. Together, these results indicate that quantitative control of immune ligand surface presentation is an important design consideration for engineering immune-engaging biomaterials to support NK cell–mediated immunotherapy. Additionally, this study demonstrates that DNA-scaffolded PLGA particles provide a tunable platform for controlled immune cell engagement and offer practical design guidance for the development of NK cell–based therapeutic strategies in solid tumor models.

Revealing Novel Structures and Benefits of *Pseudomonas aeruginosa* Biofilms through Bioprinted Models

Goodness Ogechi Osondu Chuka [1], G. Subbiahdoss [1], Stephan Schandl [2], Alexandr Ovsianikov [2], **Erik Reimhult [1*]**

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Abstract:

Introduction: Chronic lung infections in cystic fibrosis (CF) patients are associated with *Pseudomonas aeruginosa* (PA) biofilms exhibiting high antibiotic tolerance, with no clear explanation for this phenomenon. We investigate the role of the biofilm matrix in antibiotic tolerance using 3D biofilm models based on acetylated alginate and DNA, which mimic mucoid biofilms. By incorporating additional components, such as DNA, into alginate bioinks, we investigated the protective effects of these components within the mucoid extracellular matrix (ECM) to enable PA to achieve antibiotic tolerance, and we compared these protective effects with those for native in vitro biofilms. Additionally, much is unknown about how mucoid PA organizes in biofilms compared to the well-studied PAO1 biofilms that form dense, mesh-like glycoconjugate biofilms. A quantitative understanding of the internal structure of mucoid biofilms could aid in understanding their growth, spread, and their remarkable ability to promote antibiotic tolerance in PA biofilms, which hampers the development of treatments for cystic fibrosis. Quantitative imaging methods from biophysics have only recently been applied to elucidate biofilm organization and have not yet been applied to mucoid PA biofilms.

Materials and Methods: We synthetically acetylate alginate to mimic bacterial alginate. Alginate-based bioinks seeded with PA are printed, and the resulting biofilm models are characterized for their rheological and transport properties compared with native biofilms. The diffusion of antibiotics through printed and native biofilm disks is compared, as is PA antibiotic tolerance in the various biofilm formats. Additionally, we use cryo-SEM and confocal microscopy to image the organization of PAO1 and mucoid PA cells, as well as their ECM ultrastructures, in biofilms. Advanced mage analysis is used to segment 2D and 3D imaging data with purpose-written scripts to extract the spatial and orientational distribution of PA in several-day-old PAO1 and mucoid PA biofilms. This data is analyzed for spatial and orientational order using statistical measures with additional scripts.

Results, Discussion and Conclusions: Using model biofilms with controlled components, we demonstrated that being surrounded by an alginate biofilm induces extreme antibiotic tolerance in PA. However, the tolerance is not due to restricted diffusion or antibiotic sequestration. Antibiotic diffusion also shows a nontrivial dependence on charge and molecular weight: acetylation of alginate increases tolerance to several critical antibiotics, whereas DNA, contrary to standard expectations, reduces tolerance. We will focus our presentation on our unpublished results regarding using quantitative cryo-SEM and confocal microscopy to reveal the ultrastructure and organization of bacteria in model and native PA biofilms. We revealed that mucoid PA forms much thicker biofilms and exhibits a more dispersed bacterial distribution than the well-studied PAO1, which is commonly used as a reference for biofilm studies. Although they are assumed to form microcolonies within the biofilm, such microcolonies were generally absent in early-stage biofilms and were visible only as artefacts when improper sample-preparation methods that dehydrated the biofilms were used. Despite the pronounced bacterial separation, mucoid PA exhibited high levels of organization in biofilms. Additionally, cryo-SEM revealed aligned fibrous features in the ECM ultrastructure of mucoid biofilms, which were absent from the mesh-like ECMs of PAO1. We conclude that mucoid PA phenotypes form

biofilms that are not only alginate-rich but also structurally distinct from PAO1 reference biofilms in ECM and cell distribution, with implications for biofilm growth, internal transport, mechanics, and bacterial communication.

Notes:

Functional Nanobiomaterials in Tissue Engineering

Prabir Patra

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Abstract:

Introduction: Various tissues in the body, such as but not limited to, connective tissue, bones, skin, and blood vessels, are all formed by some structured and regulated arrangement of nanofibers, usually made up of proteins or polysaccharides Because the natural extracellular matrix (ECM) is composed of fibrillar collagens approximately 50 to 150 nm in diameter mimicking similar features has led to the development of ordered nanoscaffolds in the same dimensional scale. As a model system we showed that 3T3 fibroblast, which is a precursor to primary fibroblasts, could be used for wound-healing bandages. We constructed electrospun PCL scaffolds over a range of diameters (117–1,647 nm) while checking other major morphological properties like pore size. We then systematically investigated cell adhesion and proliferation activities on these scaffolds. We also report the modification of the electrospun system conducive to cardiomyocyte and neuronal growth.

Materials and Methods: PCL with an average molecular weight of 80,000 g/mole was obtained from Sigma-Aldrich (St. Louis, MO) and dissolved in acetone (Fisher Scientific, Pittsburgh, PA) under gentle stirring to obtain various weight fractions ranging from 8 to 20 wt%. Filtration was not performed before electrospinning. We prepared our PCL in acetone (w/w) solution by warming the solution to 508C. After we observed a visually clear solution, we filtered it out and did not observe any unreacted monomer left; the solution had optimum viscosity for easy electrospinning. We also prepared graphene PCL system (G-PCL) nanoscaffold. Graphene was from cheap tubes Inc.

Results, Discussion and Conclusions: The effect of electrospun fiber morphology on skin cell adhesion and proliferation was explored to optimize tissue-engineering scaffolds. We fabricated electrospun PCL scaffolds with average fiber diameters ranging from 117 to 1,647 nm; 117-nm scaffolds were beaded and significantly decreased cell attachment and proliferation. For scaffolds that ranged from 428 to 1,051 nm, cell attachment and proliferation rate were higher for smaller-diameter scaffolds. G-PCL scaffold was found to be effective in neurite growth as well as cardiomyocyte adhesion and functions. Adaptive tissue structures were also reported in connection with brain tissue engineering

Notes:

Integrating Organoid Models and Milk Fat Globule Proteomics to Study Transporter Biology in Human Lactation

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Abstract:

Introduction: Human lactation is a highly coordinated physiological process requiring precise regulation of nutrient, ion, and lipid transport to support milk synthesis and secretion. Transporter proteins, including solute carriers (SLCs), ATP-binding cassette (ABC) transporters, and ATPases, are central to these processes, yet their regulation during human lactation remains poorly defined. This gap largely stems from the lack of physiologically relevant human models that capture lactation-specific features. The present study was guided by the hypothesis that lactogenic and non-lactogenic states are associated with distinct transporter proteomic profiles, reflecting functional metabolic reprogramming of mammary epithelial cells. To test this hypothesis, we established lactating human mammary organoids derived from reduction mammoplasty tissue and induced pluripotent stem cells (iPSCs), alongside proteomic analysis of human milk fat globules. This combined approach allows parallel interrogation of transporter expression in both secretory cells and milk-derived membrane fractions. Given the exploratory nature of this work, our aim was not to draw definitive mechanistic conclusions but to identify initial transporter signatures associated with lactogenic differentiation, assess sex-based trends in iPSC-derived organoids, and generate leads for future functional and disease-oriented studies.

Methodology: Human mammary organoids were generated from reduction mammoplasty tissue and iPSCs derived from male and female donors. iPSCs were differentiated toward the mammary lineage and cultured under lactogenic conditions using defined hormonal supplementation. Functional lactation was assessed using BODIPY and Oil Red O staining to evaluate intracellular lipid accumulation and milk fat globule formation. Human milk samples were obtained from healthy donors, and milk fat globules were isolated and processed for proteomic analysis using LC–MS/MS. Transporter proteins from the SLC, ABC, and ATPase families were identified and quantified. A total of four biological replicates (n=4) were analyzed. Statistical significance was assessed using t-tests and ANOVA, as appropriate. Comparative analyses included lactogenic versus non-lactogenic conditions and sex-based differences in iPSC-derived organoids. This methodology represents an initial framework, with expanded validation and mechanistic assays currently ongoing.

Results, Discussion, and Conclusion: All organoid models successfully exhibited lactogenic features, including organized acinar structures and robust lipid accumulation, as confirmed by BODIPY and Oil Red O staining. These functional assays provided validation beyond proteomic identification, supporting active milk lipid synthesis rather than passive protein expression. Female iPSC-derived organoids consistently showed higher lipid accumulation compared to male counterparts, suggesting sex-linked regulatory differences, although this observation remains preliminary. Proteomic analysis revealed distinct transporter expression patterns between lactogenic and non-lactogenic conditions, supporting our central hypothesis. Identified transporters spanned key SLC families involved in nutrient uptake, ABC transporters linked to lipid handling, and ATPases critical for ion homeostasis. At this stage, direct links between the observed transporter profiles and lactation associated disorders or therapeutic targets cannot yet be defined. However, the datasets generated provide an important starting point for investigating how transporter dysregulation may contribute to impaired milk production or composition. In conclusion, this study establishes a human-relevant, dual-platform

approach combining lactating organoids and milk fat globule proteomics to profile transporter dynamics during lactation. As an initial exploratory effort, it generates foundational insights and testable hypotheses that will guide ongoing functional, mechanistic, and disease-focused investigations.

Notes:

Engineering an Artificial Lymph Node for Antigen-Specific Immunomodulation in Type I Diabetes

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Abstract:

Introduction: Type 1 diabetes (T1D) is driven by autoreactive T cells that destroy pancreatic β cells, requiring lifelong insulin therapy. Current immunotherapies rely on systemic immunosuppression, which carries significant toxicity. We aim to develop an implantable device acting as a subcutaneous artificial lymph node that locally induces antigen-specific immune tolerance. We hypothesize that device-mediated recruitment and tolerization of dendritic cells (DCs), in the presence of islet antigen, will generate antigen-specific regulatory T cells (Tregs) capable of protecting β cells.

Materials and Methods: Our device is a 3D-printed implant containing two refillable drug reservoirs flanking a central collagen-based cell reservoir. The drug reservoirs are separated from the cell compartment by nanoporous membranes for controlled release of drugs, while a microporous mesh isolates the niche from surrounding tissue but permits vascular and lymphatic integration. We used the BDC2.5 TCR-transgenic system and its cognate p79 mimotope to enable antigen-specific readouts. DC chemotaxis toward CCL2, CCL7, CCL20, and CCL21 was quantified in vitro. Bone marrow-derived DC (BMDC) tolerization with dexamethasone sodium phosphate (DexNaP) or IL-10 was assessed by CD80, CD86, and PD-L1 expression. p79-pulsed tolerogenic DCs (TolDCs) were co-cultured with BDC2.5 ($CD45.2^+$) and polyclonal NOD ($CD45.1^+$) naïve T cells to measure proliferation (CellTrace Violet) and FOXP3/CD25 induction. In vivo, devices were implanted for 4 weeks to permit vascularization, then loaded with CCL21 ± DexNaP before explantation and flow cytometric analysis.

Results, Discussion, and Conclusions: CCL21 was the most potent chemokine for recruiting immature DCs. DexNaP and IL-10 generated CD80lowCD86lowPD-L1+ TolDCs, with DexNaP producing the strongest effect. p79-pulsed tolDCs induced BDC2.5 T-cell proliferation and significantly increased antigen-specific $FOXP3^+CD25^+$ Tregs. Implanted devices developed functional blood and lymphatic vessels by 4 weeks. CCL21-loaded devices had significantly more DCs and naive T cells than controls. DexNaP and IL-10 support TolDC programming. These TolDCs promote the conversion of naïve T cells into antigen-specific Tregs in vitro. Our device establishes a vascularized, immune-accessible niche that recruits immune cells in vivo. Ongoing studies will determine whether our device and drug cocktail can induce these processes in situ and whether this response can halt or delay autoimmune β-cell destruction in T1D.

Notes:

Leveraging Sensors and AI for Wound Healing: Opportunities and Challenges

Shekhar Bhansali

Cornelius Vanderbilt Professor of Engineering and Chair, Electrical & Computer Engineering, Vanderbilt University, Nashville, TN

Abstract:

Introduction: Wounds that do not heal over long periods of time (3 months) are classified as Chronic wounds. Chronic wounds in the United States, such as diabetic foot ulcers, pressure ulcers, and venous leg ulcers, represent an estimated 2-4% of total healthcare spending, and the wound care market is pegged at 50 billion U.S. dollars by 2025. Chronic wounds need to be managed to prevent complications, preserve tissue function, and facilitate healing. Sensors and AI offer new opportunities in managing wound care but have multiple challenges to overcome for widespread adoption. The talk presents the opportunities in leveraging sensors and AI for wound healing.

Methods: The Wearable wound monitoring platform was designed by incorporating flexible electrochemical sensors, ultra-low-power electronics, and wireless communication modules to enable continuous acquisition of data. Uric acid (UA), as one of the most significant metabolic biomarkers associated with cellular necrosis and inflammation, was selected as an indicator of wound status. This system was equipped with 4 independent UA sensors and sampled sequentially, with the information being transmitted to a custom software application. It senses and actively measures UA for 7 days, allowing long-term monitoring. Pilot in vivo experiments on patients with venous leg ulcers also tested the functionality of the system, continuity of data, and wearability. The output data was introduced to AI-based analytics to combine biochemical sensor data with physiological data. Current models are trained to recover the long-term patterns, creating an individualized baseline, and anomalies that reflect the wound healing.

Results and Conclusions: Constant wearable sensing made it possible to detect dynamic temporal wound behavior using uric acid as a biomarker for 7 days via Bluetooth integration, collecting data on the system and remotely. AI-based personalization improved sensitivity to deviations from baseline compared to population-level thresholds. However, salient challenges that were also found in the findings are sensor degradation due to biofouling and signal drift, heterogeneous and asynchronous data streams, and connectivity limitations due to wearable encapsulation materials. Finally, real intelligence is a result of a sensor-model co-design and not individual algorithms. This presentation highlights the promise and the practical limitations of the implementation of sensor- and AI-based wound care systems on a large scale.

Notes:

Nanostructured Biosensor for the Dual Detection of Glucose and Ascorbic Acid

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Abstract:

Introduction: Biosensors are very useful in our daily lives and play an important role in several areas. Biosensing in medicine is the most promising application in the field, and so there is always need for new devices with high sensitivity, specificity. Complete blood tests are considered the gold standard in clinical diagnosis as it provides a comprehensive overview of a patient's health status. One of the most important biomarkers is glucose, an essential metabolic intermediary. Blood glucose levels are key indicators of various diseases, so frequent or continuous glucose monitoring is essential for medical diagnosis. There have been significant advances in glucose measurement technology. However, despite these important advances, the field of glucose biosensors still has room for improvement. First-generation glucose biosensors are known to have had the major disadvantage that ascorbic acid significantly influenced the signal generated, reducing their selectivity and accuracy. This work presents a dual nanostructure biosensor that can detect glucose and ascorbic acid with the same device by simply modifying its operating voltage.

Methods: Iridium oxide (IrO2) nanostructures were electrodeposited onto stainless steel electrodes, according to reference. Prussian Blue (PB) nanoparticles were prepared following the protocol of Shokouhimehr and drop casted onto the electrodeposited electrode. Finally, GOx enzyme solution in PBS (2.5mg/mL) was also drop casted on the modified surface. The surfaces were characterized by scanning electron microscopy (SEM) and X-ray energy dispersion (EDS) using a Carl Zeiss Supra 55VP scanning electron microscope. They were also characterized electrochemically using the Solartron 12508W potentiostat and impedance analyzer composed of a Solartron 1287 Electrochemical Analyzer and a Solartron 1250 Frequency Response Analyzer, commanded by the software provided by the manufacturer (ZPlot®, Scribner Associates Incorporated).

Results: SEM and EDS studies demonstrated the presence of the electrodeposited IrO2, and also the PB nanoparticles, with their characteristic cubic shape, adhering to the surface. The correct functionalization of the steel electrode was monitored using cyclic voltammetry and EIS. As a result of electrodeposition, the impedance drops abruptly, as was previously observed. When PB is added, a slight change in impedance was observed at low frequencies, showing a decrease in charge transfer resistance (Rct). Finally, an increase in Rct is observed as a result of the presence of GOx. The electrochemical response of the biosensor to different glucose concentrations (1-15 mM) was studied by cyclic voltammetry. Within the cathodic zone, a slight change in the reduction current peak (0V) was observed, along with another much more prominent and differentiated peak at -0.59V. Calibration yielded a straight line with a correlation coefficient of 0.982, with a sensitivity of 55.3$\mu A \cdot mM^{-1} \cdot cm^{-2}$. When the biosensor was evaluated against ascorbic acid concentrations (1-5 mM), a complete change in behavior was observed, showing increases in anodic current and response to voltages greater than 0.4V. In this case, calibration showed logarithmic behavior with am R2 of 0.99 and a sensitivity of 94.7$\mu A \cdot mM^{-1} \cdot cm^{-2}$.

Conclusions: The preliminary design and evaluation of a dual biosensor for the detection of glucose and ascorbic acid using different working potentials was carried out. It is possible to detect glucose with this simple biosensor, even in the presence of ascorbic acid (interfering substance). This device is

capable of detecting glucose in negative potentials, thus eliminating the possibility of oxidizing or reducing other compounds that could interfere with the measurement.

Notes:

Antifouling Polymer Brush-Based Biosensors for Rapid and Reusable On-Site Diagnostics

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Abstract:

Introduction: Numerous biosensor concepts demonstrate excellent analytical performance under laboratory conditions, yet only a few succeed in real-world on-site analysis of complex, non-model samples or in point-of-care diagnostics. Advancing biosensing platforms and antifouling bio-functional coatings toward practical applications requires interdisciplinary efforts spanning nanomaterials, synthetic chemistry, biophysics, and life sciences. We combined multi-methodological experimental studies with theoretical predictions to provide new molecular-level insights into biofouling mechanisms. Based on these findings, we developed a tunable antifouling terpolymer brush nano-coating that exhibits high resistance to protein fouling and bacterial adhesion, while supporting macrophage activity and osteoblast proliferation. To overcome limitations of standard surface-initiated oxygen-free polymerization methods, we designed scalable fabrication approaches employing microfluidic stacks and capillary-based reactors. These advances enabled a new generation of antifouling polymer brush-assisted label-free biosensors for rapid, reagent-free detection of clinically relevant analytes in complex matrices.

Methods: Biomolecular fouling mechanisms were studied by combining surface plasmon resonance (SPR), mass spectrometry (MS), and molecular dynamics simulations (MDS) to analyze interactions of zwitterionic and non-ionic polymer brushes and their copolymers with proteins from crude human plasma. Monomers included carboxybetaine methacrylamide (CBMAA), sulfobetaine methacrylamide (SBMAA), and N-(2-hydroxypropyl) methacrylamide (HPMAA). A terpolymer nano-brush with tailored monomer ratios were synthesized via ATRP using custom-designed flow-based approaches to yield stable, homogeneous antifouling coatings on diverse substrates. These ranged from upconversion nanoparticles for enhanced sensing to TiO_2-coated lossy mode resonance (LMR) optical fibers and gold coated SPR/QCM chips. DNA origami nanostructures were integrated within antifouling scaffolds to provide high-precision control of aptamer distribution. The coatings were characterized by XPS, FT-IRRAS, ellipsometry, QCM-D, SPR, AFM, and contact angle measurements and implemented in QCM and LMR biosensors.

Results: By tuning CBMAA, HPMAA, and SBMAA ratios, we established interfaces balancing antifouling performance with bioactivity. The optimized poly (CBMAA 20 mol% – co – HPMAA 77 mol% – co – SBMAA 3 mol%) composition reduced protein adsorption by 98% and bacterial adhesion by >99% compared to uncoated surfaces. The terpolymer brush promoted macrophage motility and phagocytic activity, enabling efficient bacterial clearance. RGD peptide functionalization enhanced osteoblast-like cell adhesion and spreading, yielding a 118-fold increase in cell attachment while maintaining antifouling performance. The LMR fiber sensor achieved femtomolar detection of Tau protein in plasma, demonstrating promise for early Alzheimer's diagnostics. QCM biosensors provided rapid (<30 min), label-free detection of pathogens such as Legionella and E. coli O157:H7 in food, river, and wastewater, with detection limits in the range of hundreds of CFU/mL, without sample preprocessing and with retained reusability.

Conclusion: Antifouling polymer brush-based biosensors and biointerfaces provide a versatile platform that bridges molecular-level understanding with robust, field-deployable technologies. They enable

new avenues in point-of-care diagnostics, food safety monitoring, and advanced cell studies, offering fertile ground for interdisciplinary collaboration in biomedical engineering.

Notes:

Shaping Surfaces: How Polymer Patterns Affect Early Bacterial Adhesion

Frank, Alexis, Dávalos, Renatta; Calvopiña, Ana; Christian, Narvarez; Lady, Guanoliquin

Universidad San Francisco de Quito, Ecuador

Abstract:

Introduction: Bacterial adhesion represents the first step in the development of numerous infectious diseases, as it allows pathogens to establish contact and colonize both tissues and inert surfaces (Sarabia-Sainz et al., 2013). This process is mediated by adhesins, fimbriae, and other specialized structures that facilitate binding to glycoproteins and glycolipids on host cells or to artificial materials. Once initial adhesion is established, biofilm formation is triggered, leading to highly resistant structures that increase bacterial virulence and complicate eradication (Saldarriaga et al., 2023). Several studies have highlighted that preventing primary adhesion is an effective strategy to interrupt progression toward colonization and, consequently, to limit both infection development and surface deterioration. In this context, modulation of the physicochemical and topographic properties of materials emerges as an innovative alternative to reduce the initial interaction of bacteria with surfaces (Saldarriaga et al., 2023). The design of geometric patterns capable of decreasing the attachment of bacteria such as *Escherichia coli* ATCC and *Staphylococcus aureus* ATCC is particularly relevant, given the clinical and environmental importance of these species in device-associated infections and material contamination. Identifying surface configurations that hinder bacterial adhesion would not only contribute to improving safety in healthcare environments but also extend the lifespan of materials exposed to microbial colonization. Therefore, the study of geometric surface patterns stands out as a promising strategy for biofilm prevention and infection control.

Materials and Methods: The initial adhesion of *Escherichia coli* and *Staphylococcus aureus* was evaluated on polymers manufactured under different conditions: variation in manufacturing time, different fiber thicknesses, and different surface geometric patterns (square, circle, hexagon, and triangle). The same experimental protocol was applied to all tests. Initially, the polymers and six-well plates were sterilized under UV light while bacterial suspensions were prepared at a turbidity equivalent to McFarland 4, which were centrifuged for 30 minutes. The supernatant was discarded, and the cell pellet was resuspended in liquid Mueller-Hinton broth, ensuring homogeneity by vortex. Each plate included: (i) three wells with polymers submerged in medium with bacteria, (ii) a positive control (coverslip + medium with bacteria), (iii) a negative control (coverslip + medium without bacteria), and (iv) a material control (polymer + medium without bacteria). With this distribution, the plates were incubated for 30 minutes at 37°C with shaking at 120 rpm. Subsequently, PBS washes were performed to remove non-adherent cells. The polymers and coverslips were transferred to Falcon tubes with PBS and vortexed individually for 5 minutes to detach the adhered bacteria. A 100 µL aliquot was taken from each suspension, fixed on a slide with alcohol-acetone, and stained with crystal violet. Microscopic analysis involved counting bacteria in 15 fields per sample, and the resulting data were analyzed using the Wilcoxon statistical test to identify significant differences in adhesion between the different polymers evaluated.

Results, Discussion and Conclusions: Comparative tests identified significant differences in bacterial adhesion depending on the manufacturing conditions and surface design of the polymers. First, it was observed that polymers manufactured in less time and with thinner fibers had less adhered bacteria compared to those with thicker fibers or longer manufacturing times. This result suggests that finer and less consolidated surfaces difficult the initial attachment of *E. coli* and *S. aureus*. On the other hand, for geometric polymers, the first tests were performed with surfaces containing multiple identical shapes repeated within the cover slip area. Under these conditions, the triangular pattern

showed the lowest bacterial adhesion compared to the other geometries. To confirm that this effect depended on the orientation of the fibers, additional tests were performed using larger single geometric patterns, i.e., a single triangle, square, hexagon, or circle occupying the entire area of the coverslip. Consistently, polymers with a triangular pattern showed the lowest adhesion, followed by the square, the hexagon, and finally the circle, which showed the highest bacterial adhesion. It has been demonstrated that surface topography decisively influences bacterial adhesion, as structures such as fibers, pores, or grooves can guide cellular behavior, a phenomenon known as “contact guidance” (Cai et al., 2020). In this context, the modification of polymers through geometric patterns represents an innovative strategy to reduce bacterial attachment; this effect depends not only on the pattern but also on the intrinsic characteristics of the polymer, such as its micromorphological properties. Our results showed that polymers with triangular patterns were the most effective in decreasing bacterial adhesion. This finding helps to better understand how cells respond to these structures and opens a wide range of applications in research, particularly in tissue engineering, taking advantage of their adjustable mechanical properties and biocompatibility (Cai et al., 2020). Additionally, during observation of the contact angle in the membrane manufacturing process, it was noted that polymers with a triangular pattern tended to form more hydrophobic surfaces, as evidenced by a delay in polymer wetting compared to other patterns. This hydrophobic feature could help explain the lower bacterial adhesion on these surfaces too.

Notes:

Engineering Education and Artificial Intelligence at the National Science Foundation

Eric L. Miller

Division Director, Engineering Education and Centers (EEC), National Science Foundation, VA, USA

Abstract:

With a mission to promote the progress of science; advance the national health, prosperity, and welfare; and secure the national defense, the National Science Foundation (NSF) supports over 350 thousand researchers working across more than 1800 institutions. In support of the mission, NSF funds activities in areas ranging from the natural and material sciences, computing, and engineering to education, training, human behavior, and social dynamics. These activities take place within a broad range of universities, including those primarily serving undergraduates as well as emerging and developing research institutions, among others. This talk will provide an overview of the agency, with the objective of offering insight into opportunities available to students, early career researchers, as well as researchers coming from education-oriented institutions. Considering the impact artificial intelligence (AI) is having across all aspects of American society, the presentation will include a description of the recent NSF activities at the intersection of AI and engineering education.

Notes:

The Johns Hopkins Center for Bioengineering Innovation & Design (CBID)

Youseph Yazdi

Center Director, Johns Hopkins Center for Bioengineering Innovation & Design (CBID)
Associate Professor, Johns Hopkins School of Medicine
mPI and Innovation Core Director, NIH BluePrint Neurotech Harbor

Abstract:

The Johns Hopkins Center for Bioengineering Innovation & Design (CBID) represents a innovative model for healthcare innovation that incorporates learnings from experience and failure modes from industry, design, and academic programs. CBID's objective is to train healthcare innovators who can identify critical unmet clinical needs, rigorously de-risk them across technical, clinical, business, and execution domains, and advance solutions toward real-world impact. Students, mainly engineering, but also medicine, public health, design and business-work in teams embedded in clinical environments. Through immersive need-finding, structured opportunity assessment, iterative prototyping, stakeholder validation, regulatory strategy development, intellectual property positioning, and commercialization planning, teams progress from insight to implementation. CBID emphasizes experiential, team-based, and field-driven learning. Students engage directly with clinicians, patients, payers, regulators, and industry stakeholders to understand not only the technical problem but the full innovation ecosystem. The curriculum integrates engineering rigor with business modeling (including Business Model Canvas frameworks), regulatory pathways, reimbursement strategy, and operational execution planning. The program has produced numerous startup companies, licensed technologies, and industry partnerships. Outcomes demonstrate that structured innovation education-rooted in clinical immersion and systematic risk reduction can consistently generate high-impact healthcare ventures and leaders prepared to drive innovation across academia, industry, and global health systems.

Notes:

The Texas A&M School of Engineering Medicine (EnMed)

Lance Black

Sr. Associate Dean of Innovation & Strategic Projects
Harold J Haynes '46 EnMed Chair
School of Engineering Medicine, Texas A&M University, Houston, TX

Abstract:

The Texas A&M School of Engineering Medicine (EnMed) represents a bold reimagining of medical education designed to equip physician-innovators, “physicianeers”, with the clinical acumen of an MD and the problem-solving mindset of an engineer. EnMed’s objective is to train professionals who can simultaneously care for patients and invent solutions to unmet clinical needs. Over four years, students earn both a Doctor of Medicine and a Master of Engineering through an integrated curriculum that blends medical science, engineering design and Biodesign principles, anchored in real-world clinical contexts at Houston Methodist Hospital. EnMed’s pedagogy emphasizes team-based learning, project-based and experiential learning, and immersive innovation experiences that culminate in iterative prototype development and clinical translation. Dedicated facilities, including maker spaces, simulation labs, and industry engagement opportunities, support students in engineering solutions that address real clinical problems. Early cohorts have produced significant invention disclosures and filings, demonstrating that rigorous data collection, iterative refinement, and evidence-based curricular evolution can advance engineering-infused medical education.

Notes:

Electroconductive Hydrogels for Cardiovascular and Neuronal Tissue Regenerative Engineering

Anthony Guiseppi-Elie

Sr. Fellow and President, AIIMSEI
Sr. Dresden Fellow, TU Dresden
TEES Collaborator, Texas A&M University, USA

Abstract:

The convergence of bioelectronics and regenerative medicine has catalyzed the emergence of a new class of smart biomaterials - electroconductive hydrogels (ECHs) - capable of restoring the biophysical microenvironments essential for functional tissue regeneration. Nowhere is this convergence more consequential than in the context of excitable tissues such as cardiac and neuronal systems, where synchronized electrical signaling governs both physiology and pathology. This plenary lecture explores the rational design, synthesis, and functional deployment of ECHs - three-dimensional, water-swollen polymer networks incorporating inherently conductive moieties such as polypyrrole, polyaniline, PEDOT, and carbon-based nanostructures. I will present a unifying framework for tailoring electrical conductivity, mechanical compliance, and biochemical functionality, drawing from our contributions to the field that range from bio-interfacing at the cellular level to in vivo demonstrations of restored biofunctionality. Focusing on two critical regenerative targets - cardiac and neural tissue, I will present advances in scaffold integration, cell instructive interfaces, and electrotherapeutic modulation. Special attention is paid to i) the electrochemical properties of hybrid biomaterials that enable synchronization with endogenous signaling, ii) the role of conductivity gradients and anisotropy in mimicking native tissue architecture, and iii) the emerging paradigm of "living bioelectronics" in which hydrogel-based platforms are co-designed with stem or progenitor cell populations for dynamic, functional repair. Ultimately, this presentation will advocate for a convergence approach, blending materials science, bioengineering, and systems physiology to establish electroconductive hydrogels not merely as passive scaffolds, but as active mediators of healing, capable of interfacing, instructing, and integrating with complex tissue environments.

Notes:

Fluid Dynamics and Biomechanics after Traumatic Neural Injury

Hoi Kwon [1], Sarah Tenney [2], Chris Streilein [2], **R. Chase Cornelison [1,2,3*]**

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Abstract:

Introduction: Each year approximately 100,000 people in the U.S. sustain permanent disability or paralysis due to a brain or spinal cord injury. While there are currently no therapies to regenerate damaged nervous tissue, a brief window of time after injury offers a therapeutic opportunity for intervention. Known as secondary injury, cascades of inflammatory and cytotoxic events progressively cause tissue adjacent to the original injury site to degenerate over 1-2 weeks. Therefore, halting this process could minimize tissue damage and the ensuing paralysis. The start of secondary injury coincides with accumulation of fluid edema, and the extent of edema strongly correlates with severity of functional deficits in both humans and animal models of spinal cord injury. While it is known that alleviating this pressure build-up decreases damage and improves function, how exactly fluid forces contribute to secondary spinal cord injury remains unclear. We conducted in silico, in vivo, and in vitro studies to address our revolutionary hypothesis that secondary neurodegeneration after spinal cord injury is driven by pathological interstitial fluid flow.

Materials and Methods: Computational modeling was performed using COMSOL Multiphysics. Animal procedures were conducted in accordance with the IACUC at the University of Massachusetts Amherst. Anesthetized Sprague-Dawley rats (8-12 weeks, Charles River) received a cervical laminectomy at C3–C5 followed by a C4 hemi-contusion at 150 kDynes using an Infinite Horizons spinal impactor (IH-0415, World Precision Instruments). Intramedullary pressure was measured using a catheter (ADinstrument®) for 30 min, recorded using PowerLab® software. Human neuroblastoma SH-SY5Y cells (ATCC) were differentiated into neuronal-like cells and cultured in 1:1 Dulbecco's Modified Eagle Medium (DMEM): F12 supplement +10% fetal bovine serum (FBS) and 1% non-essential amino acids. Human microglia (ABM) were cultured in DMEM +10% FBS. Human cortical astrocytes (Sciencell) were cultured in Astrocyte Medium +2% FBS and 1% growth supplement. Cells were serum-starved prior to shear, then 6-well plates were placed on an orbital shaker at 100 rpm to generate fluid shear (0.5-2 dynes/cm2).

Results, Discussion and Conclusions: We find interstitial pressure in the rat spinal cord increases within 1 hour of injury, peaks three days after injury, and relatively normalizes by seven days [5]. This timeline mirrors that of spinal edema and tracks with secondary injury cascades. A simulation of the injured rat cord predicts interstitial fluid velocities up to four-fold faster than normal flows and shear stresses ten-fold higher than normal at three days post-injury. These predictions are in-line with prior modeling in tumors, where high flow promotes disease progression. In a rat model of cervical (C4) hemi-contusion spinal cord injury, we find a strong correlation between regions of flow and expression of the apoptosis marker cleaved caspase-3. We also find that exogenously increasing flow 7 days after injury significantly increases lesion volume by four-fold compared to controls. We therefore conclude that high interstitial flow contributes to secondary injury and tissue damage. To understand the mechanisms, we used in vitro studies of astrocyte, microglia, and neuronal cell cultures under fluid shear. Direct exposure of human SH-SY5Y neuronal-like cells to a 'high' fluid shear significantly reduces neuronal cell survival and neurite length. Furthermore, shear-conditioned media from human astrocytes and microglia indirectly causes a similar reduction in neuronal outcomes. We identified that

this glial-neuronal signaling is mediated shear-induced purinergic signaling. Collectively, our results implicate pathological levels of fluid flow as an overlooked contribution to neurodegeneration after neural injury, which has potential to inform development of strategies to protect healthy nervous tissue and improve functional recovery.

Notes:

Cyclic Nanog Induction Reverses Senescence, Restores Metabolism and Improves the Function of Aged Skeletal Muscle through Partial Reprogramming

Stelios T. Andreadis

Director, Cell, Gene and Tissue Engineering (CGTE) Center, Department of Chemical and Biological Engineering, Department of Biomedical Engineering, and Center for Excellence in Bioinformatics and Life Sciences, University at Buffalo, The State University of New York, NY

Abstract:

Sarcopenia or age-related decline in muscle mass, strength, and regeneration limits mobility and quality of life in the elderly. Recent evidence underscores the potential of cellular reprogramming in mitigating age-associated cellular and tissue decline. Several studies from our laboratory reported that local expression of the key pluripotency transcription factor, Nanog can induce partial reprogramming, restoring the hallmarks of aging and enhancing muscle regeneration after injury in naturally aged mice. Here we explore whether systemic and cyclic Nanog administration can reverse aging and restore muscle function and regeneration capacity in naturally aged mice. We will also discuss some of the mechanisms of Nanog's action through metabolic reprogramming, especially amino acid and fatty acid metabolism. Taken together, our findings demonstrate that Nanog-induced partial reprogramming reverses molecular, metabolic, and functional hallmarks of aging in skeletal muscle without reprogramming to the pluripotent state.

Notes:

Ribocomputing: Leveraging RNA for Computation in the Cell

Jongmin Kim

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Abstract:

Introduction: Synthetic biology aims to develop engineering-driven approaches to the programming of cellular functions that could yield transformative technologies. Synthetic gene circuits that combine DNA, protein, and RNA components have demonstrated a range of functions such as bistability, oscillation, feedback, and logic capabilities. Despite many advances, technical challenges remain for scaling up the complexity of these networks due to the limited number of designable, orthogonal, high-performance parts, the empirical and often tedious composition rules, and substantial resource requirements for encoding and operation.

Materials and Methods: To capitalize on the predictable and programmable RNA interactions, we designed de-novo-designed RNA switches for constructing synthetic logic circuits in E. coli. These RNA switches and devices for complex circuit architectures were designed using NUPACK, a nucleic acid sequence and structure design program. These synthetic RNA circuit designs were then characterized in detail to evaluate performance in E. coli to validate the system functionality.

Results, Discussion and Conclusions: Here, we report a strategy for constructing RNA-only nanodevices to evaluate complex logic in living cells. Such 'ribocomputing' systems are composed of de-novo-designed parts and operate via predictable and designable base-pairing rules, allowing for effective in silico design of computing devices with prescribed configurations and functions in complex cellular environments. We demonstrate that these ribocomputing devices in E. coli can evaluate two-input logic expressions with dynamic range up to 900-fold and scale them to four-input AND, six-input OR, and a complex 12-input logic expression. By adopting an alternative RNA switch design framework, we then demonstrated a library of more than 100 repressors and 4-input NAND logic gates. The flexibility of RNA design could be used to program cellular morphology change with logical regulation of CRISPR guide RNAs, as well as translational coupling for multiplexed input and output signal processing in cells. The versatility of synthetic RNA-based circuits could be further extended by adopting aptamers for chemical and protein inputs together with RNA signals. Successful operation of ribocomputing devices based on programmable RNA interactions suggests that systems employing the same design principles could be implemented in other host organisms or in extracellular settings.

Notes:

Gut Gelectrode: Drug Delivery and Stimulation to the Gut via Conductive Hydrogel

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Abstract:

Introduction: The gastrointestinal tract (GI) regulates digestive, metabolic, neural, and endocrine systems. Dysregulation of GI pathways can lead to conditions including gastroparesis, intestinal bowel syndrome (IBS), and dysmotility. Therapies to date have primarily relied on pharmacological interventions, which may be limited in efficacy or associated with undesirable side effects. Electrical stimulation is an alternative and effective method of manipulating gut signaling and motility. Ingestible devices can deliver electrical stimuli acutely as they transit the gut, but cannot deliver longer-term intestinal stimulation for days or weeks. Implanted stimulation platforms utilize metal electrodes, which have a mechanical mismatch with soft tissue and inherently suffer from a trade-off between robust electrode-tissue contact and overcompression, which inhibits motility. Synthesized conductive hydrogels (CHs), which are cross-linked polymer matrices embedded with conductive nanoparticles or ionic liquids, have demonstrated excellent electrical conductivity, mechanical flexibility, and tissue-like softness, thereby facilitating seamless integration with gastrointestinal tissues. Here, we report the Gut Gelectrode, a hydrogel-based cuff electrode system for intestinal stimulation and drug delivery.

Methods: The Gelectrode integrates a ChiMA–ColMA conductive hydrogel into a flexible, removable cuff, enabling conformal contact with gut tissue for improved stimulation stability and comfort. The device's soft, adhesive interface reduces motioninduced artifacts while maintaining electrical efficiency over time. The Gelectrode, derived from naturally cross-linked biopolymers, exhibits tunable mechanical, electrical, and adhesive properties ideal for soft-tissue bioelectronics. We evaluate its performance through physical characterization, stability analysis, and biocompatibility testing in ex vivo and in vivo models.

Results: Following characterization studies, we find that the hydrogel remains in the abdomen of mouse models surrounding the upper GI, up to two weeks, in addition to showing evidence of biocompatibility. Overall, these findings establish the Gelectrode as a proof-of-concept multifunctional implant combining compliant materials, drug delivery capability, and localized therapy-demonstrating a novel strategy for chronic gut-brain axis modulation and next-generation gastrointestinal bioelectronic medicine.

Notes:

Formulation of Nanoliposomes Encapsulating Natural Bioactive Molecules Extracted by Enzymatic Hydrolysis

Louis Pruvost [1*], Jordane Jasniewski [1]

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Abstract:

Introduction: The sustainable valorization of alternative resources for the design of biomolecule carriers represents a major challenge in nanotechnology and biotechnology. In this context, our work explores the innovative use of two unconventional sources: salmon (*Salmo salar*) heads, a marine by-product, and the insect *Tenebrio molitor*. Through enzymatic hydrolysis, we extracted phospholipids and bioactive peptides capable of self-assembling into nanoliposomes thanks to a specific process. Phospholipids derived from salmon heads exhibit a composition favorable to the formation of stable nanostructures, while *T. molitor* peptides display antioxidant and anti-stress activities, highlighting their potential as functional molecules. In parallel, chondroitin sulfate isolated from salmon heads was successfully encapsulated within the liposomes, providing the system with strong anti-inflammatory properties on human inflamed chondrocytes. This synergy between lipid nanocarriers and encapsulated biomolecules offers a promising approach for the development of multifunctional therapeutic systems. Moreover, chitin extracted from the cuticle of *T. molitor* was transformed into a gel, serving as a matrix for the controlled release of liposomes. This original combination integrates the mechanical stability of a natural biopolymer with the progressive bioavailability of active compounds. Altogether, this study demonstrates the feasibility of an integrated concept that valorizes marine and insect resources to generate bioactive nanocarriers and innovative release matrices. The results open perspectives for applications in health, nutrition, and regenerative biomedicine, while aligning with principles of circular economy and sustainability.

Methods: In the first step, the biomolecules of interest were obtained through enzymatic hydrolysis, controlled by the pH-stat method and by monitoring the degree of hydrolysis. A protease enabled the simultaneous release of lipids and peptides from salmon heads as well as from *Tenebrio molitor* larvae. The biomolecules (lipids, peptides, and chondroitin sulfate) were then purified through a combination of filtration, centrifugation, and the use of green solvents. For characterization, phospholipids were analyzed for fatty acid composition (GC-FID), lipid classes (TLC-FID), and phospholipid composition (LC-MS). The molecular size distribution of peptide extracts was determined by SEC-MALS, while chondroitin sulfate categories were identified by HPLC. Following characterization, liposomes were formulated using the lipid film hydration method, allowing the encapsulation of peptides or chondroitin sulfate. The resulting nanoliposomes were characterized in terms of particle size, zeta potential, and polydispersity index using dynamic light scattering (DLS) and NanoSight. Finally, the different liposomal dispersions were evaluated in various applications: the anti-inflammatory activity of salmon-derived chondroitin sulfate was tested on human chondrocytes (articular cells with osteoarthritis-induced inflammation); *T. molitor* peptides were assessed for anti-stress effects in murine behavioral models and for anti-inflammatory potential in human cardiac cells.

Results and Conclusion: The results demonstrated that lipids extracted from both natural sources exhibited highly valuable lipid profiles, with a high proportion of polyunsaturated fatty acids. In particular, salmon-derived lipids were rich in omega-3 fatty acids, including DHA and EPA. The extracted phospholipids were also enriched in phosphatidylcholine (PC), a key component for ensuring liposome stability. These high-quality lipid nanocarriers significantly enhanced the anti-inflammatory activity of chondroitin sulfate on human chondrocytes, notably through the inhibition of cartilage-degrading enzymes. In addition, insect-derived peptides were successfully encapsulated within

nanoliposomes. Their anti-stress properties were confirmed in murine behavioral assays, although further investigations are required to better elucidate their mechanisms of action. An anti-inflammatory effect was also observed in rat cardiac cells, and this activity was markedly improved when the peptides were delivered in liposomal form. Finally, an innovative hydrogel was developed from the insect cuticle (chitosan), providing a promising platform for the sustained release and delivery of these bioactive liposomal formulations.

Notes:

Cell-Derived Nanoparticles as Next-Generation Therapeutics: From Biomimetic Coatings to Scalable EV Platforms

Paula Maria Pincela Lins

Biomedical Research Institute, Hasselt University, Diepenbeek, Belgium

Abstract:

Introduction: Nanoparticle-based drug delivery systems have been widely explored due to their tunable physicochemical properties, high loading capacity, and potential to reduce the systemic toxicity of free drugs. Despite extensive development, conventional synthetic nanoparticles continue to face significant challenges, including rapid clearance and extensive adsorption of serum proteins, which decrease their targetability. Stealth coating strategies, such as PEGylation or polysaccharide capping, enhance circulation time but do not fully replicate the dynamic functions necessary for precise tissue targeting. Increasing evidence suggests that cell-derived nanoparticles (CNPs), including extracellular vesicles (EVs) or EV-like nanoparticles, have the ability to target tissue precisely. Such CNPs inherit complex biological properties from their parental cells, such as homotypic adhesion for cancer cells and deep-tissue penetration for macrophages and mesenchymal stem cells. This work investigates the advantages and limitations of CNPs as next-generation therapeutics, focusing CNP synthesis and characterization, cellular uptake pathways, homotypic targeting, and large-scale manufacturing. By comparing synthetic NP coatings and evaluating CNPs derived from different cell sources, this study aims to elucidate how biological complexity can be exploited to overcome longstanding challenges in nanomedicine.

Materials and Methods: Different CNP preparations were generated from cancer cells, macrophages, and dental pulp stem cells (DPSCs) and used either as coatings for synthetic materials or as intact vesicles. Gold nanorods (AuNRs) were coated with two types of macrophage-derived CNPs, while PLGA formulations were coated with cancer-cell–derived CNPs, with the overall goal of enhancing cancer-therapy performance. Cellular uptake studies were conducted using both parental cell lines and additional tumor-microenvironment-associated cells. Cytotoxicity assays were performed to evaluate anticancer efficacy. To improve the scalability of CNP production, particularly EVs from dental pulp stem cells (DPSC-EVs), we also examined whether hollow-fiber bioreactors (HFB) offer a viable upscaling strategy. DPSC-EVs were isolated by ultracentrifugation and characterized using nanoparticle tracking analysis, electron microscopy, and marker profiling. Functional assays included endothelial tube-formation assays to assess angiogenic potential and macrophage-based assays to evaluate immunomodulatory activity.

Results, Discussion and Conclusions: Cell-derived coatings, based on cancer and macrophage cell lines, demonstrated strong homotypic adhesion to target cells, supporting their potential for precision oncology. Macrophage-plasma-derived coatings promoted dynamin-dependent uptake in phagocytic cells, whereas EV-like-coated gold nanorods were internalized through macropinocytosis and microtubule-dependent pathways, underscoring the role of membrane asymmetry in biological recognition. The coated CNPs also exhibited improved anticancer activity. These coatings preserved complex features of tumormicroenvironment interactions, indicating that biomimetic systems can reproduce dynamic cellular behaviors that synthetic approaches cannot capture. During CNP manufacturing, HFB enhanced DPSCEV concentration while maintaining vesicle functionality, providing a viable strategy for scalable production. Overall, CNPs offer biological advantages that are unattainable with synthetic materials, enabling improved targeting, immunomodulation, and therapeutic signaling. Nevertheless, to facilitate translation, future efforts must address both coating heterogeneity and the current limitations of large-scale manufacturing.

A Biodegradable Nanofluidic Platform for Sustained Multidrug Cancer Immunotherapy

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Abstract:

Introduction: Effective cancer immunotherapy is frequently limited by inadequate intratumoral drug exposure, poor spatiotemporal control of immune activation, and dose-limiting systemic toxicity. Although combination immunotherapy can enhance efficacy by engaging complementary immune pathways, systemic co-administration of multiple agents presents substantial safety and delivery challenges. Engineering-based local delivery systems capable of sustained, spatially confined, and multi-agent release are therefore critically needed. Tumor-infiltrating lymphocytes (TILs) serve as key functional indicators of therapeutic immune activation within the tumor immune microenvironment (TIME). Here, we present a biodegradable nanofluidic drug-eluting seed (b-NDES) designed to provide controlled intratumoral delivery of multiple immunomodulators with minimal systemic exposure. By integrating nanofluidic transport control with biodegradable device architecture, this platform aims to enable sustained local immunomodulation, promote systemic antitumor immune responses, and establish durable immune memory while mitigating toxicity.

Materials and Methods: A fully implantable, biodegradable nanofluidic drug-eluting seed (b-NDES) was engineered to achieve sustained intratumoral release of α-CTLA4, a STING agonist, resiquimod (TLR7/8 agonist), IL-12, and α-CD40. Device performance and therapeutic efficacy were evaluated in murine models of triple-negative breast cancer (4T1), pancreatic cancer (KPC), and lung cancer (KLN205). Three- to five-drug configurations were compared to assess tumor control, systemic immune activation, and safety. For abscopal evaluation, bilateral KPC tumors were established with b-NDES implanted into a single lesion. Immune memory was assessed by tumor rechallenge and IFN-γ ELISpot assays. Tumor immune remodeling was characterized using Olink proteomics, CyTOF, and imaging mass cytometry (IMC).

Results, Discussion and Conclusions: The five-drug b-NDES configuration achieved complete tumor eradication in 5 of 6 mice in the 4T1 model and demonstrated robust tumor control in KPC and KLN205 models. In bilateral KPC tumors, localized b-NDES implantation induced regression of untreated contralateral tumors, indicating effective systemic immune engagement originating from a spatially confined delivery site. Rechallenged animals completely rejected secondary tumors and exhibited elevated IFN-γ-secreting splenocytes, confirming durable immune memory. High-dimensional immune profiling revealed increased intratumoral T-cell density, enhanced dendritic-cell activation, and polarization toward pro-inflammatory macrophage phenotypes in responding tumors. Proteomic and

cytokine analyses demonstrated a strong localized pro-inflammatory signature associated with effective tumor regression. Importantly, localized b-NDES delivery eliminated the weight loss, hypothermia, and liver toxicity observed with equivalent systemic administration, underscoring the safety advantage of controlled intratumoral release. Collectively, these findings demonstrate that b-NDES functions as a robust delivery platform enabling safe, sustained, and synergistic multidrug immunotherapy. This work establishes a scalable engineering strategy for localized immunomodulation with systemic therapeutic impact against aggressive solid tumors.

Notes:

Biodegradable Nanofluidic Drug-Eluting Seed for Sustained Intratumoral Drug Delivery of Immunotherapeutic Agents

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Abstract:

Introduction: Intratumoral immunotherapy offers a promising strategy to improve cancer treatment; however, heterogeneous drug distribution within the tumor and rapid drug leakage limit its therapeutic potential. To address these challenges, we developed the biodegradable Nanofluidic Drug-Eluting Seed (b-NDES), an implantable device designed to enhance intratumoral immunotherapy delivery, minimize systemic dissemination, and biodegrade over time, eliminating the need for surgical removal.

Material and Methods: Four formulations with varying ratios of polycaprolactone (PCL), poly (lactic-co-glycolic acid) (PLGA), and barium sulfate were electrospun to fabricate the implants. Surface modifications were implemented to tailor drug elution rates. Morphology, in vitro release of a CD40 agonist antibody, and degradation profiles were evaluated to identify the optimal formulation. Devices were then implanted intratumorally in a 4T1 triple-negative breast cancer (TNBC) murine model using a trocar-based procedure to assess CD40 agonist antibody biodistribution and therapeutic efficacy when co-delivered with a STING agonist and combined with radiotherapy.

Results, Discussion and Conclusions: The resulting devices featured a hollow cylindrical drug reservoir with a nanofibrous wall, where interconnected fibers formed fine pores enabling passive drug diffusion. Surface modification induced partial fusion of the nanofibers, reducing porosity and thereby regulating release kinetics. Among all tested formulations, the 1:4 PCL: PLGA with barium sulfate exhibited the most sustained and consistent in vitro release together with the fastest degradation rate, and was therefore designated as the final composition for b-NDES and selected for in vivo studies. In 4T1 TNBC murine models, b-NDES enabled localized and prolonged delivery of the CD40 agonist antibody, which remained confined within the tumor. Notably, complete tumor eradication was achieved when b-NDES-mediated delivery of the CD40 agonist antibody and the STING agonist was combined with radiotherapy, without evidence of systemic toxicity. These findings establish b-NDES as a minimally invasive intratumoral platform capable of localized, controlled, and sustained drug delivery, suitable for combination therapies in the treatment of aggressive tumors such as TNBC. Future work will focus on the use of this platform for immunotherapy-only approaches, enabling the

intratumoral delivery of immunotherapeutic drug cocktails to enhance therapeutic efficacy and promote tumor-specific immune memory while maintaining a favorable safety profile.

Notes:

NanoLymph: An Implantable Immune-Engineering Platform for Transplantation Tolerance and Autoimmune Modulation

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Abstract:

Introduction: Immune rejection and autoimmune recurrence remain major barriers to durable cell therapy. We sought to engineer an implantable platform that locally recruits and programs regulatory immune networks to promote transplantation tolerance and enable antigen-specific immune modulation for future β-cell replacement in type 1 diabetes (T1D).

Materials and Methods: NanoLymph is an implantable device composed of 3D-printed biocompatible resin, a nylon mesh, a collagen scaffold, and a 30 nm polyethersulfone nanoporous membrane coupled to a drug reservoir. The device releases CCL22, IL-2/JES6 complexes, MR1, and αCD8 to recruit and expand regulatory T cells (Tregs) while suppressing effector T-cell activity. Device integration, drug release, biodistribution, histology, and flow cytometry were evaluated in a murine MHC-mismatched Leydig (TM3) cell transplantation model. A complementary strategy to generate Tregs was evaluated by recruiting immature dendritic cells (DCs) and inducing tolerogenic DCs (tolDCs) capable of converting naïve T cells into Tregs. Bone marrow–derived DCs (BMDCs) were harvested from femurs and tibias of NOD mice. Multiple tolerizing agents were tested in vitro to optimize tolDC induction, and a transmigration assay was used to identify optimal DC-recruiting chemokines. In vivo DC recruitment was evaluated following NanoLymph implantation in NOD mice.

Results, Discussion and Conclusion: NanoLymph integrated efficiently within subcutaneous tissue, demonstrating robust cellular infiltration, vascularization, and lymphangiogenesis. The device enabled sustained local drug release, and biodistribution analysis confirmed spatially restricted delivery. In the allogeneic transplant model, NanoLymph significantly prolonged TM3 cell survival compared with systemic immunosuppression alone. A second-generation NanoLymph variant was engineered to deliver a DC-recruiting and tolerizing cocktail. Dexamethasone was identified as the most effective tolerizing agent, and CCL21 was selected as the optimal chemokine for DC recruitment and was validated in vivo. NanoLymph creates a vascularized, immunoregulatory niche that protects transplanted cells from immune rejection through localized regulatory immune dominance. Incorporation of DC recruitment and tolerization establishes a foundation for antigen-specific tolerance induction, supporting future application to β-cell replacement and autoimmune diabetes without systemic immunosuppression.

Notes:

Computational Medicine for Sensing Health

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Abstract:

As new physiological sensing technologies become available for continuous monitoring of physiological signals, the dynamic response to external influences such as environmental inputs, medication, and surgery can be quantified. This research focuses on developing mathematical algorithms for dynamically tracking mental and physical health states in the presence of different interventions. (1) Mental Health Focus: We design algorithms for a closed-loop neural wearable architecture called MINDWATCH for mental and cognitive well-being. We first infer arousal-related autonomic nervous system (ANS) activations. Then, we model and decode cognitive arousal and performance brain states where the inferred ANS activations and behavioral data are used as cognitive arousal and performance observations, respectively. We use neurofeedback to close the loop and modulate cognitive arousal and performance. (2) Physical Health Focus: We investigate clinical data from patients to study inflammation, fatigue, and metabolism using cytokines, stress hormones, and metabolic hormones, respectively. We deconvolve biochemical signals (e.g., hormones) to obtain the secretory events underlying their pulsatile production. Then, utilizing the recovered secretory events, we decode hidden health states (e.g., energy) dynamically. The ultimate goal is to design toolsets that can provide clinically relevant information using biosensors to prevent, diagnose, and manage health conditions.

Notes:

Domain-Specific Foundational Models for Trustworthy Medical Imaging

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Abstract:

Introduction: Foundational models promise to transform medical imaging by enabling broad reuse of learned representations across tasks and institutions. However, directly transferring general-purpose foundational models into clinical imaging has proven insufficient. Medical data are high-resolution, heterogeneous, weakly labeled, and embedded within complex clinical workflows. In this setting, reliability depends not only on predictive accuracy, but also on robustness to dataset shift, efficient learning from limited annotations, and the ability to interpret and audit model behavior. This work argues that impactful foundational models for medical imaging must be domain-specific by construction. Rather than optimizing for scale alone, such models must integrate three capabilities essential for clinical deployment: (i) unified representations that support multiple clinical tasks without fragmenting data across separate models, (ii) mechanisms to identify and correct systematic model failures arising from hidden biases in data and preprocessing pipelines, and (iii) generative priors that respect anatomical structure and clinical semantics. We present a cohesive framework that demonstrates how these principles can be realized across diagnostic, prognostic, auditing, and generative settings in breast and lung imaging. By grounding large-scale learning in clinical language, anatomy, and evaluation protocols, this approach advances robustness, data efficiency, and interpretability - properties that are critical for building trustworthy AI systems in realworld medical practice.

Materials and Methods: Our approach combines large-scale multimodal representation learning, language-based model auditing, and anatomy-aware generative modeling within a unified, domain-aligned framework. High-resolution medical images are jointly learned with their accompanying clinical text to form shared representations that can be efficiently transferred to diverse diagnostic and prognostic tasks, even when labeled data are scarce. To improve reliability, model errors are analyzed by translating internal model behavior and associated clinical metadata into natural language, enabling automated reasoning to uncover systematic failure patterns and guide corrective updates—without requiring manual bias annotations. To complement discriminative modeling, we incorporate generative modeling strategies that synthesize realistic three-dimensional medical images guided by clinical descriptions and anatomical constraints. This combination ensures that generated data preserve structural plausibility while remaining controllable and interpretable. Across all components, language serves as a central interface linking images, clinical knowledge, and model behavior, enabling scalable learning while supporting transparency, robustness, and clinical auditability.

Results, Discussion, and Conclusions: Across multiple imaging modalities and clinical tasks, this domain-specific approach demonstrates consistent improvements in robustness, data efficiency, and interpretability compared to general-purpose models. Unified representations learned from paired images and clinical text enable strong performance across diagnosis, prognosis, localization, and reporting, while reducing reliance on large task-specific labeled datasets. Robustness to dataset shift is achieved through multi-institutional training and explicit mechanisms for identifying and correcting systematic model failures that would otherwise remain hidden in aggregate performance metrics. The incorporation of language-based auditing enables models to surface clinically meaningful error patterns, including those introduced by metadata and preprocessing choices, and to mitigate them without manual bias labels. Meanwhile, anatomy-aware generative modeling produces high-fidelity three-dimensional medical images that preserve critical structural features, supporting data

augmentation, simulation, and model analysis under controlled clinical conditions. Together, these results highlight that foundational models for medical imaging must be evaluated not only by accuracy but also by their ability to generalize, explain their behavior, and operate safely under real-world constraints. This work demonstrates that embedding clinical structure - through language, anatomy, and domain-aligned evaluation - provides a principled pathway toward trustworthy foundational models capable of meaningful clinical impact.

Notes:

Machine Learning Driven Optimization of Lipid Nanoparticles and RNA-based Cancer Therapeutics

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Abstract:

Introduction: With nearly annual approvals from 2018 – 2025, siRNA and mRNA-based therapeutics are rapidly changing modern medicine. While siRNA is promising for a diversity of conditions, ranging neurological, cardiovascular, endocrine, metabolic, and malignant diseases, extrahepatic delivery remains challenging. All FDA-approved siRNA therapeutics target hepatocytes. Lipid nanoparticles (LNPs) are the most clinically advanced RNA-delivery vector, protecting therapeutic RNA from degradation and targeting delivery in vivo. Two main design parameters (i) the molar ratios of lipids in the LNP and (ii) lipid chemical structures, determine encapsulation and transfection efficiency, immunogenicity, and biodistribution. Here, we combined design of experiments (DOE) and high throughput screening to train neural-boosted machine learning (ML) models to accurately predict optimal LNP formulation for targeted transfection of cancer cells or macrophages. A second challenge for RNA-LNP based cancer therapeutics is the penetration of LNPs into solid tumors. Cancer cell focal adhesions and their downstream SRC family kinase (SFK) signaling contribute to both tumor density and limited LNP penetration, as well as cancer invasiveness and chemoresistance. Here we show that siRNA-LNP mediated kinase silencing reduces the stiffness of ovarian cancer spheroids, and significantly improves LNP penetration. Collectively our data demonstrate that siRNA-LNP driven kinase silencing, simultaneously improves LNP penetration into solid tumors, reduces ovarian cancer proliferation and migration, halts tumor spheroid growth, and resensitizes drug-tolerant cells to chemotherapy.

Materials and Methods: Design of experiments was used to generate an LNP library (JMP software) by varying the molar ratios of 4 lipid components: ionizable lipid, cholesterol, PEG-lipid, and phospholipid. LNPs were used to encapsulate luciferase silencing siRNA, in order to allow for high throughput screening in luminescent cell lines. Robotic fluid handlers were used to formulate LNPs, and plate reader-based assays used to rapidly assess cell viability, LNP uptake (measured via a lipophilic fluorophore incorporated into the LNP), and silencing (via luminescence signal). Data was split into training and validation sets, used to train machine learning models. Neural-boosted machine learning demonstrated the most predictive power, and was used to optimize LNP formulations. siRNAs were developed to target either a unique region within a single kinase (si-unique), or a conserved domain across all Src family kinases (SFKs) (si-broad). RNA alignment was performed in silico with MAFTT v7, siRNA sequences followed Uy-Tei rules, and were blasted for off-targets. The region of highest overlap between SFKs was found to be within the ATP binding pocket. Notably, small molecule inhibitors including dasatinib bind to this conserved region. siRNAs were screened in vitro via RT-qPCR and western blot. LNP uptake and kinase silencing in ovarian cancer cells (OVCAR3, CAOV3) and spheroids were assessed via confocal microscopy and RT-qPCR. Atomic force microscopy (AFM) was used to assess mechanical properties of cancer spheroids. Therapeutic efficacy was assessed in 2D or spheroid cultures (hanging drop). Chemotherapy resistant ovarian cancer was generated by pulsed-step taxane dosing.

Results, Discussion and Conclusions: Machine learning modeling yielded LNP formulations that outperformed the FDA-approved Onpattro formulation. Optimized LNPs yielded ~80 – 90% gene silencing in a range of cell lines including colorectal cancer, ovarian cancer, and human macrophages, following optimization for each cell type. siRNA allows for targeted silencing of a single kinase, or broad SFK silencing. Both si-unique and si- broad demonstrated on-target IC50 < 4mM; with si-unique demonstrating minimal off-target kinase silencing in ovarian cancer lines. siRNA-driven SFK silencing decreases ovarian cancer proliferation and migration, and resensitizes tolerant ovarian cancer to chemotherapy. Both broad and unique kinase-silencing siRNAs reduced ovarian cancer migration by 75% and proliferation by 73%. In chemotherapy-tolerant cells, broad kinase silencing siRNA significantly reduced cancer proliferation and migration by 56%, outperforming both the unique kinase-silencing siRNA and small molecule kinase inhibitors. Unique kinase silencing siRNAs reduced ovarian cancer spheroid growth 2-fold. Unlike the cytostatic responses found clinically with small molecule tyrosine kinase inhibitors, our siRNAs resulted in spheroid shrinkage, highlighting its therapeutic advantage in a complex 3D environment. Furthermore, our siRNAs were able to restore chemotherapeutic sensitivity in drug-tolerant models, outperforming small molecule kinase inhibitors. This effect may be attributed to a prolonged effect (days) compared to small molecules (hours). siRNA-driven kinase silencing improves LNP penetration into cancer spheroids. DOE optimization of LNP formulation ultimately increased silencing in OVCAR3 from 51% to 88%. To determine the effects of optimized siRNA-LNPs on the mechanical properties of tumor spheroids, AFM was used. Both si-unique and si-broad significantly reduced tumor stiffness by 100Pa, compared to empty LNP controls. Consistent with AFM data, confocal microscopy demonstrated significantly increased LNP-tumor penetration with broad kinase silencing siRNA, compared to si-unique or empty-LNP controls. This data demonstrates that siRNA-driven silencing of kinases involved in focal adhesions can improve LNP-penetration into solid tumors. Our multi-kinase targeting siRNA-LNP acts as both a therapeutic, shrinking tumor size, while also aiding the delivery of encapsulated therapeutics, offering a promising strategy for overcoming chemoresistance and improving solid tumor RNA-LNP delivery.

Notes:

Rapid Detection of Deterioration in Pediatric Oncology Patients for Sepsis Prevention

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Abstract:

Introduction: Pediatric oncology patients are often immunocompromised. Their rates of hospitalization and death are higher than those of the general pediatric population (281.5/1,000 vs. 6.2/1,000 and 40.7/1,000 vs.0.15/1,000 person-years, respectively). They also require more extensive resources, with 40% expected to need Pediatric Intensive Care Unit (PICU) care compared to 12.8% of all pediatric patients. Their immunocompromised state places them at high risk for secondary complications, including bacterial sepsis. Sepsis is a life-threatening, dysregulated host response to infection that is fatal if untreated. It can progress to septic shock, characterized by severe circulatory and metabolic abnormalities. Mortality from sepsis and septic shock is higher in pediatric oncology patients (12.9%) than in the general pediatric population (9%). Early signs of sepsis are often non-specific, though subtle changes in vital signs or serum biomarkers may indicate impending deterioration before overt clinical decline. These vulnerabilities underscore the need for rapid, reliable detection of deterioration in pediatric oncology patients. The primary objective of this study was to identify deterioration after PICU admission and assess the potential for application in home or ambulatory settings via wearable monitoring.

Materials and Methods: We included 2,144 pediatric oncology patients, using hospital data prior to PICU admission. The data for pediatric oncology patients was obtained from Ann & Robert H. Lurie Children's Hospital of Chicago's electronic health records (EHR). The data only included patients that had suspected sepsis. We trained a multivariable logistic regression model with 5-fold cross-validation to predict deterioration. Our model trained on the following features to predict deterioration: heart rate, respiratory rate, mean arterial pressure taken from the blood pressure cuff, blood oxygen saturation, temperature, race, sex, ethnicity, and gender. The deterioration outcomes predicted by our model was the receipt of vasoactive/inotrope drip or death. Performance was evaluated by comparing the AUC of our model to the standard of care based on the Pediatric Early Warning Score (PEWS).

Results, Discussion and Conclusions: Our model demonstrates fair performance in determining which pediatric oncology patients will deteriorate as measured by death (AUC 0.743) and vasoactive/inotrope drip (AUC = 0.712). When comparing our results to the standard of care (the PEWS scoring system), the performance of our model is slightly below the standard of care (AUC = 0.79) [6]. However, it is important to remember that PEWS is primarily used in an in-patient setting, and there are currently limited options for detecting deterioration outside of this setting. The fact that our results are comparable to the standard of care demonstrates promise that more advanced modeling will move our solution towards being able to effectively detect deterioration in ambulatory settings. We also examined the feature importance of our models, or the features that contributed the most to the performance of our models. What is interesting to note is that sex and ethnicity tended to be among the top three most important features. This indicated that these features may have potentially predictive capabilities in determining if a pediatric oncology patient will experience deterioration, although not found to be statistically significant. This also illustrates the importance of considering the inclusion of these features in models to predict health outcomes, as they may have an impact on the risk of developing a particular outcome particularly when considering potential class imbalances in the dataset.

Biomedical Materials Science

Sara Ceci

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Abstract:

Introduction: Biomedical materials research is evolving rapidly, driven by advances in nanotechnology, biofabrication, smart biomaterials, regenerative medicine, and bioelectronic interfaces. As interdisciplinary collaboration accelerates, there is a growing need for dedicated platforms that bridge fundamental materials science with translational biomedical applications. Biomedical Materials Science is a newly launched, fully open-access journal committed to publishing high-quality research spanning biomaterials design, characterization, biointerfaces, tissue engineering, drug delivery systems, biosensing materials, and clinical translation. The journal aims to foster collaboration between engineers, materials scientists, clinicians, and industry innovators. This poster introduces the journal's scope, editorial vision, peer review model, and opportunities for community engagement, including article collections and editorial board participation. The goal is to connect with researchers presenting at BEBI 2026 whose work aligns with emerging themes in bioelectronics and biomolecular engineering.

Materials and Methods: This poster presents an overview of the journal's structure and development strategy, including:

- Defined thematic sections covering biomaterials synthesis, regenerative biomaterials, bioelectronic materials, and translational applications
- A rigorous, transparent peer review workflow supported by an international editorial board
- Open-access publishing model to maximize visibility and citation impact
- Targeted article collections aligned with major conferences and emerging research areas

Engagement strategies include editorial board expansion, community-driven special issues, and partnerships with leading research networks. The journal development plan focuses on scientific quality, rapid decision timelines, and global author representation.

Results, Discussion and Conclusions: Since its launch, Biomedical Materials Science has initiated publications of original research articles and commissioned contributions that reflect strong interest in bioactive scaffolds, nanostructured materials for sensing applications, smart polymers, and regenerative interfaces. The journal uses a single-anonymous peer review model, where reviewers know the authors' names and affiliations but provide anonymous reports based on scientific robustness, originality, and clarity; ensuring constructive, fair evaluation while maintaining review integrity. In alignment with Springer Nature's open science principles and BMC's editorial standards (which similarly emphasize rigorous peer review and transparent ethics policies across their portfolio of open-access journals), Biomedical Materials Science adheres to published policies that enhance reproducibility, reviewer independence, and author support.

The journal addresses several community needs:

1. A focused venue dedicated specifically to biomedical materials innovation.
2. An inclusive, open-access platform for global dissemination.
3. Editorial leadership spanning engineering, life sciences, and clinical translation.

By engaging directly with researchers at BEBI 2026, the journal aims to expand its editorial board, invite high-impact submissions, and develop thematic collections aligned with cutting-edge conference topics. In conclusion, Biomedical Materials Science provides a dedicated platform for advancing interdisciplinary research at the interface of materials science and biomedicine. Researchers are invited to contribute original research, reviews, and participate in shaping the journal's scientific direction.

Notes:

Biogenic Carbon Quantum Dots as Neoteric Inducers for Directing Chondrogenic Differentiation

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Abstract:

Introduction: Mesenchymal stem cells (MSCs are central to regenerative medicine owing to their self-renewal capacity, multilineage differentiation potential, and ability to restore tissue function. Their differentiation into osteocytes, adipocytes, chondrocytes, neuroblasts, and fibroblasts enables therapeutic applications in bone and muscle repair, wound healing, and neurodegenerative disorders. However, clinical translation of MSC-based therapies is limited by challenges such as noninvasive administration with long-term cell tracking and the lack of biocompatible, cost-effective, and eco-friendly strategies for lineage-specific differentiation. Furthermore, efficient stem cell differentiation, migration, and in situ imaging remain essential for regenerative success. In this context, materiobiology has increasingly explored carbon-based nanomaterials as modulators of MSC fate. Graphene quantum dots and carbon dots regulate osteogenic and adipogenic differentiation through pathways including BMP, TGF-β, MAPK, Wnt, and Notch, while enabling intrinsic optical tracking. Nevertheless, carbon-mediated chondrogenesis without exogenous growth factors remains underexplored. Herein, we report biogenic carbon quantum dots (CQDs) synthesized from garlic peel waste as multifunctional nanomachines that direct chondrogenesis, enhance MSC migration, and enable simultaneous cell tracking. These eco-friendly CQDs exhibit strong photoluminescence, mitochondrial localization, and reactive oxygen species–mediated signaling, enabling growth factor–free chondrogenic differentiation and rapid wound closure. This waste-to-resource strategy highlights biogenic CQDs as promising chondrogenic inducers for regenerative medicine.

Materials and Methods: Garlic peel agrowaste was collected from vegetable vendors in Uttar Pradesh, India, and used for carbon quantum dot (CQD) synthesis. All animal studies were approved by the Institutional Animal Ethics Committee (CPCSEA/AIP/2015/03/005) and conducted according to CPCSEA guidelines. Immortalized human feeder fibroblast (IHF) cells were obtained from Prof. Anis Feki (Geneva University Hospital, Switzerland). Human Wharton's jelly-derived mesenchymal stem cells (hWJ-MSCs) were cultured in low-glucose DMEM supplemented with fetal bovine serum and antibiotics following ICSCR approval (ICSCR/114/20(o)). CQDs were synthesized via a hydrothermal process using garlic peel powder at 180 °C for 4 h and purified thereafter. Structural and optical characterization was performed using XRD, TEM/HRTEM, AFM, FTIR, XPS, Raman spectroscopy, UV–vis, photoluminescence, and TCSPC. Cytocompatibility, cellular uptake, ROS generation, migration, stemness, and chondrogenic differentiation were evaluated using standard cell-based assays, flow cytometry, microscopy, qRT-PCR, and histology. Hemocompatibility and histocompatibility were assessed in Wistar rats. Statistical analysis was performed using ANOVA.

Results, Discussion and Conclusions: Biogenic carbon quantum dots (CQDs) were successfully synthesized from garlic peel agrowaste via a hydrothermal route, yielding uniformly dispersed, spherical nanoparticles with an average size of ~5–6 nm. Structural and chemical characterization confirmed their polycrystalline carbon framework enriched with oxygen-, nitrogen-, and sulfur-containing functional groups, imparting excellent aqueous dispersibility and excitation-dependent photoluminescence. These optical properties enabled efficient intracellular imaging of human Wharton's jelly–derived mesenchymal stem cells (hWJ-MSCs) without compromising cell viability.

Cytocompatibility studies demonstrated that CQDs were well tolerated by both immortalized human fibroblasts and hWJ-MSCs at biologically relevant concentrations, while preserving MSC surface markers and stemness-associated gene expression. Notably, CQD internalization led to controlled intracellular reactive oxygen species (ROS) generation, which played a pivotal signaling role rather than inducing oxidative stress. This ROS modulation significantly enhanced MSC migration, as evidenced by accelerated wound closure in scratch assays. Most importantly, CQDs robustly directed chondrogenic differentiation of hWJ-MSCs in the absence of conventional growth factors. Enhanced deposition of sulfated glycosaminoglycans and collagen, along with upregulated expression of key chondrogenic markers (COL II, COL X, and ACAN), confirmed effective lineage commitment comparable to chemically induced controls. Histological analyses further corroborated mature cartilage-like extracellular matrix formation. In conclusion, garlic peel–derived CQDs function as a multifunctional, biocompatible nanoplatform capable of simultaneous stem cell imaging, migration enhancement, and growth factor–free chondrogenic induction. This waste-to-wealth strategy offers a sustainable and translationally promising approach in materiobiology and regenerative medicine, addressing critical limitations associated with conventional differentiation cues.

Notes:

A Smart and Highly Porous Hydrogel for Diabetic Wound Healing

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Abstract:

Introduction: Wound healing is a complex, multi-stage biological process involving hemostasis, inflammation, proliferation, and tissue remodeling. In diabetic wounds, this process is often impaired due to persistent inflammation, excessive exudate, poor vascularization, and increased susceptibility to infection. These challenges necessitate advanced wound dressings capable of dynamically adapting to the changing wound microenvironment. Hydrogels have emerged as promising wound care materials because of their high-water content, flexibility, and ability to maintain a moist environment that supports tissue regeneration. However, conventional hydrogels frequently suffer from weak mechanical strength, limited bioactivity, lack of intrinsic antimicrobial properties, and uncontrolled therapeutic release. To address these limitations, we developed a multifunctional dual-crosslinked hydrogel composed of Poly(N-isopropylacrylamide) (PNIPAM) and Gum Arabic (GA). PNIPAM provides thermoresponsive behavior near physiological temperature, enabling temperature-triggered modulation of bioactive release. Gum Arabic, a natural biopolymer rich in glycoproteins and polysaccharides, enhances mechanical stability through hydrogen bonding and hydrophobic interactions while contributing intrinsic anti-inflammatory and antimicrobial properties. The synergistic integration of PNIPAM and GA results in a mechanically robust, biocompatible, and smart hydrogel designed for controlled bioactive release and improved diabetic wound healing outcomes.

Materials and Methods: PNIPAM–Gum Arabic (GA) hydrogels were synthesized via UV-initiated free radical polymerization. N-isopropylacrylamide (NIPAM) and GA were separately dissolved in deionized water, followed by the addition of nanoclay (Laponite XLG) as a physical crosslinker and 2,2'-diethoxyacetophenone as a photoinitiator. The mixture was exposed to UV irradiation (365 nm, 10 mW/cm^2) for 45 minutes to form dual-crosslinked hydrogels with varying GA concentrations. The hydrogels were characterized using scanning electron microscopy (SEM), Fourier-transform infrared spectroscopy (FTIR), differential scanning calorimetry (DSC), mechanical tensile testing, rheological analysis, swelling studies, contact angle measurements, and HPLC-RID for release profiling. Biocompatibility was evaluated using human dermal fibroblasts (HDF) through alamarBlue and flow cytometry assays. Antibacterial activity was assessed using agar diffusion against E. coli, S. aureus, E. faecalis, and A. junii. Wound healing efficacy was examined via in vitro scratch assays and an in vivo full-thickness diabetic rat wound model, followed by histological and immunofluorescence analyses.

Results, Discussion and Conclusions: The fabricated PNIPAM–Gum Arabic (GA) hydrogels exhibited a highly porous and homogeneous microstructure, as confirmed by SEM analysis, enabling efficient fluid

absorption and oxygen diffusion critical factors for diabetic wound healing. FTIR spectra verified successful polymerization and the formation of a dual-crosslinked network mediated by hydrogen bonding and hydrophobic interactions. Increasing GA content significantly enhanced mechanical performance, with PNIPAM-GA-200 demonstrating superior tensile strength, elasticity (up to 1600% strain), and improved Young's modulus, indicating reinforced structural integrity. Rheological studies confirmed dominant elastic behavior (G' > G''), supporting long-term dressing stability. The hydrogel displayed thermoresponsive behavior with a lower critical solution temperature near physiological range (~32–34 °C). At 37 °C, the network underwent hydrophobic contraction, triggering accelerated GA release compared to room temperature, following Fickian diffusion kinetics. This temperature-responsive release is advantageous for on-demand therapeutic delivery in wound environments. Biocompatibility studies using human dermal fibroblasts demonstrated significantly improved cell viability in GA-containing formulations compared to PNIPAM alone. The PNIPAM-GA-200 hydrogel maintained high viability over 14 days. In vitro scratch assays confirm enhanced cell migration and wound closure. In vivo studies in full-thickness diabetic rat wounds showed accelerated re-epithelialization, increased collagen deposition, and reduced inflammatory markers, particularly IL-1β expression. Furthermore, the hydrogel exhibited notable antibacterial activity against both Gram-positive and Gram-negative strains. Collectively, these findings highlight the synergistic integration of thermoresponsive behavior, mechanical reinforcement, and intrinsic bioactivity, positioning PNIPAM-GA hydrogel as a promising smart platform for advanced diabetic wound care.

Notes:

Agarose Stamped Device for Standardized Zebrafish Larvae Immobilization

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Abstract:

Introduction: Reliable and standardized immobilization of zebrafish larvae is essential for quantitative behavioral assays and high-resolution imaging, yet commonly used agarose embedding methods are time-consuming, variable, and can restrict access to important sensory or motor structures. More advanced microfluidic strategies improve positioning precision but often require specialized fabrication expertise and are not easily customizable. To provide a simple and accessible alternative, we developed the Agarose Stamped Device (ASD), a customizable, low-cost platform that uses 3D-printed stamps to create larva-sized cavities in agarose. These stamped wells enable rapid, reproducible positioning of multiple larvae while allowing selective freedom of movement for specific body regions when needed. The ASD aims to improve throughput, reduce handling variability, and expand behavioral and imaging capabilities in zebrafish research.

Materials and Methods: Custom stamp designs were created using CAD software and fabricated via 3D printing. Stamps were used to mold agarose into standardized cavities with tunable geometry. We evaluated device performance by systematically varying agarose concentration, cavity depth, and width to identify configurations that maximize positioning stability while preserving targeted behavioral freedom. Eye area symmetry and eye coordinate variability were used as quantitative alignment metrics. The ASD was tested across multiple behavioral paradigms, including optokinetic response, optomotor response, and suction-feeding assays, along with fluorescence-based screening of transgenic larvae. Imaging and behavior were recorded using established tracking tools and custom software.

Results, Discussion, and Conclusions: Optimized ASD cavities (approximately 0.525 mm width, 0.5 mm depth, 1.5% agarose) provided highly reproducible larval alignment with reduced drift during imaging. Free-tail and free-eye configurations preserved natural visuomotor behaviors, enabling simultaneous tracking of eye rotations and tail movements in optokinetic and optomotor assays. Free-mouth designs supported suction-feeding experiments, where particle image velocimetry revealed distinct suction events and quantifiable feeding dynamics. The ASD also improved the efficiency of large-scale fluorescence-based screening, allowing rapid identification and gentle retrieval of transgenic larvae with higher survival compared to conventional embedding. The device is inexpensive, easy to fabricate, and customizable for diverse experimental needs. Collectively, the ASD enhances precision, reproducibility, and throughput in zebrafish larval experiments while maintaining behavioral relevance. Its accessibility and adaptability make it a valuable tool for biomedical engineering, neuroengineering, and behavioral neuroscience applications.

Notes:

Polydopamine and Antifouling Polymer Brushes: Toward a Substrate-Independent Coating Strategy

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Abstract:

Introduction: Poly (carboxybetaine acrylamide) (PCBAA) is one of the most effective materials for preventing non-specific adsorption from complex biological media (biofouling). To achieve these antifouling capabilities, PCBAA must be synthesized in a way that allows it to form a brush-like structure with high grafting density. PCBAA in this form thus belongs amongst so-called polymer brushes (PBs), named after the conformation largely responsible for the superb antifouling capabilities. PBs are typically synthesized via surface-initiated atom transfer radical polymerization (SI-ATRP) from initiator-bearing self-assembled monolayers (SAMs), and this approach works exceptionally well with alkanethiolates on gold, where strong thiol-gold affinity ensures robust monolayer anchoring. Reliance on thiol-gold chemistry for dependable PB synthesis limits broader applicability in areas like biosensing, as many sensing platforms do not readily accommodate gold. Although alternative approaches to achieving antifouling PBs have been reported, they largely remain substrate-specific, so the search for a more universal strategy is ongoing. In this search, polydopamine represents a promising option. First described as a nature-inspired candidate for surface-material-independent coating by Lee et al., dopamine self-polymerizes under mild conditions, forming a robust adhesive layer. While polydopamine has been extensively used for direct surface modification via Schiff base and Michael addition reactions with amines and thiols, relatively few studies have explored growing antifouling PBs from polydopamine-modified surfaces.

Materials and Methods: We synthesized PCBAA brushes via SI-ATRP from gold, glass, and silicon nitride surfaces pretreated with polydopamine and ω-mercaptoundecyl bromoisobutyrate. The resulting brushes were characterized using infrared spectroscopy (IR), X-ray photoelectron spectroscopy (XPS) and spectroscopic ellipsometry. Antibody immobilization and antifouling performance against diluted and undiluted human blood plasma were evaluated by quartz crystal microbalance (QCM), surface plasmon resonance (SPR) and chirped guided mode resonance (GMR).

Results, Discussion and Conclusions: Our results demonstrate that this polydopamine-based strategy successfully produces PBs on planar gold surfaces, with IR and ellipsometry consistent with brush formation. SPR showed successful antibody immobilization and resistance to biofouling from undiluted human blood plasma. However, achieving comparable results on glass and silicon nitride proved more challenging, as both the mechanism of polydopamine polymerization and this polymer's resulting structure differ substantially on chemically distinct substrates, suggesting that longer deposition times and, likely, modified brush polymerization approaches are needed for non-gold surfaces.

Notes:

DNA-Based Biosensors for the Detection of miRNA Cancer Biomarkers

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Abstract:

Introduction: Chronic lymphocytic leukemia (CLL) is the most common form of leukemia among adults in Western countries, with a steadily increasing global incidence. This trend highlights the urgent need for advanced diagnostic and monitoring tools that enable early detection and support more effective therapeutic interventions. In recent years, microRNAs (miRNAs) have emerged as promising cancer biomarkers due to their high stability in body fluids, tumor-specific expression profiles, and central roles in regulating pathways associated with tumor development and progression. Accurate and sensitive detection of miRNAs can therefore provide critical insights for early diagnosis and real-time monitoring of cancer dynamics. Currently, miRNA analysis relies mainly on techniques such as quantitative polymerase chain reaction (qPCR), reverse transcription-PCR (RT-PCR), and next-generation sequencing. While these approaches offer high sensitivity and quantification accuracy, they are limited by complex sample preparation, long assay times, contamination risk, and the need for specialized laboratory equipment. Moreover, PCR-based platforms often struggle with sequence specificity when distinguishing miRNAs that differ by only a single nucleotide, leading to potential false positives. To overcome these challenges, we developed a novel biosensing platform that combines antifouling polymer brushes with DNA nanostructures for label-free, highly specific, and rapid detection (<30 min) of miRNAs in buffer and human plasma. This system eliminates the need for sample pretreatment and significantly enhances detection performance through molecular nanostructure engineering.

Materials and Methods: The biosensor is designed by combining antifouling polymer brushes with DNA nanostructures. Polymer brushes were synthesized via surface-initiated atom transfer radical polymerization (SI-ATRP) of carboxybetaine acrylamide (CBAA), a zwitterionic monomer known for its strong resistance to nonspecific interactions.4 These brushes formed a dense, hydrated layer on gold-coated sensor chips. In proof-of-concept experiments, short capture strands were immobilized on the surface and subsequently coated with the pCBAA brush layer. Complementary, fluorescently labeled miRNAs (miR16, miR-155, miR-150) were then hybridized to the capture strands. Successful hybridization, visualized by fluorescence microscopy, confirmed that RNA could penetrate the polymer brush and bind to surface bound probes. To further validate specificity and antifouling performance, hybridization was tested in untreated human plasma using surface plasmon resonance (SPR). To improve detection sensitivity, six-helix bundle DNA origami nanostructures were designed using caDNAno, visualized with oxView, and structurally validated via oxDNA simulations5. These nanostructures were functionalized with multiple capture strands and immobilized on the polymer coated surface. The nanoscale precision of DNA origami allowed controlled spatial arrangement of probes, enhancing hybridization efficiency and specificity. Detection was performed using label-free SPR and quartz crystal microbalance (QCM), enabling realtime monitoring of miRNA binding. Kinetic parameters, association and dissociation rate constants, were extracted using global fitting models. Additionally, melting temperature (T_m) shifts of surface bound duplexes were analyzed to assess duplex stabilization by the polymer environment. All measurements were performed without any sample pretreatment, highlighting the platform's simplicity and robustness.

Results, Discussion and Conclusions: Fluorescence microscopy confirmed successful hybridization of miRNA with complementary oligonucleotides immobilized on polymer brush-coated surfaces. The

zwitterionic coating effectively suppressed nonspecific interactions, even in complex matrices like human plasma, demonstrating strong antifouling performance. SPR measurements revealed clear and reproducible sensorgrams for miRNA hybridization events. The obtained kinetic parameters-association constants around 10^5 $M^{-1}s^{-1}$ and dissociation constants near 10^{-3} s^{-1}- indicated high-affinity interactions. Notably, the presence of polymer brushes resulted in a measurable increase in the DNA melting temperature, suggesting enhanced duplex stability due to favorable electrostatic interactions with the zwitterionic matrix. This stabilization may improve hybridization efficiency under physiologically relevant conditions. Incorporation of six-helix bundle DNA origami further improved detection sensitivity. The DNA nanostructures increased the number of available miRNA capture sites in a well-defined nanoscale geometry, leading to an order of magnitude increase in measurement sensitivity compared to surfaces with randomly immobilized oligonucleotides. Most notably, the biosensor enabled miRNA detection in under 30 minutes without the need for RNA extraction, purification, or amplification. This significant simplification of the workflow positions our platform as a viable tool for rapid diagnostics and near-patient testing. In conclusion, our study demonstrates a novel biosensing strategy that leverages DNA nanotechnology and antifouling chemistry to enable label-free, highly sensitive, and specific detection of miRNAs in complex biological media. The integration of programmable DNA origami with polymer brush functionalized surfaces holds strong potential for next-generation biosensors in cancer diagnostics.

Notes:

Polymer Brush-Engineered Upconversion Nanoparticles as Next-Generation Labels for Biomarker and Pathogen Detection

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Abstract:

Introduction: Upconversion nanoparticles (UCNPs) have attracted increasing attention as advanced labels for bioanalytical applications. Unlike conventional fluorophores, UCNPs emit visible light through a non-linear photon-upconversion process, in which two or more near-infrared photons are absorbed and converted into a single photon of higher energy. This anti-Stokes emission does not occur in natural biological materials, enabling background-free luminescence detection. In addition, UCNPs offer high photostability, narrow emission bands, and the possibility of multiplexed detection, making them excellent candidates for ultrasensitive assays. In biosensing, UCNP-based assays have demonstrated significantly improved analytical sensitivity compared to conventional fluorescence labels. They are particularly promising in digital formats, where single-nanoparticle counting allows the detection of extremely low biomarker concentrations. Nevertheless, important challenges persist, particularly those affecting assay robustness in complex samples. Surface engineering of UCNPs, for example, through PEG coating, improves colloidal stability and reduces non-specific interactions; however, it is not sufficient to fully eliminate off-target binding. Therefore, advanced strategies are still necessary to ensure that nanoparticles bind specifically to their intended targets. To assess the potential of UCNP-based bioassays in clinically and environmentally relevant scenarios, we apply this approach to two distinct targets: prostate-specific antigen (PSA), a key biomarker for prostate cancer diagnostics, and *Legionella pneumophila*, a pathogen responsible for severe pneumonia outbreaks. Detection of both analytes is demanding, since ultra-high sensitivity and robustness against complex sample backgrounds are essential for accurate analysis. We therefore compare the performance of upconversion readout with that of quartz crystal microbalance (QCM) and surface plasmon resonance (SPR) sensors.

Materials and Methods: UCNPs with an average size of 21 nm were used as luminescent labels and synthesized according to a previously published protocol. The host matrix consisted of $NaYF_4$ doped with Yb^{3+} and Er^{3+}, providing efficient upconversion luminescence under near-infrared excitation. For surface functionalization, a bifunctional linker containing a bisphosphonate group was attached to the UCNP surface. The terminal bromide group of the linker served as an initiator for subsequent surface-initiated atom transfer radical polymerization (SI-ATRP). Two types of antifouling polymer coatings were synthesized directly on the nanoparticle surface: (i) fully zwitterionic poly (carboxybetaine methacrylamide) (pCBMAA, 100%), and (ii) a copolymer system consisting of zwitterionic pCBMAA and non-ionic poly(N-(2-hydroxypropyl) methacrylamide) (pHPMAA) in a 20:80 molar ratio. The performance of the modified UCNPs was evaluated using a combination of quartz crystal microbalance with dissipation monitoring (QCM-D), SPR, and an upconversion laser scanner (Labrox Upcon S-Pro). To benchmark the performance of the UCNP-based assays, measurements were compared with assays employing fluorescence-based labels. Key sensing parameters included: 980 nm NIR excitation, with emission collected at 540/655 nm using a 50 ms integration per spot on the upconversion scanner; QCM-D operated at 5 MHz with simultaneous resonant frequency (Δf) and dissipation (ΔD) tracking, and SPR in angle-scanning mode, performed at two wavelengths (785 and 670 nm).

Results, Discussion and Conclusions: The SI-ATRP modification of UCNPs was successfully achieved for both antifouling coatings. Infrared (IR) spectroscopy, specifically ATR-FTIR and FT-IRRAS spectra, confirmed the presence of polymer layers on the nanoparticle surface. The homopolymer pCBMAA exhibited stronger IR signals than the copolymer system, which can be mainly attributed to polymerization kinetics. In the case of the homopolymer, the propagation of monomer units proceeds more efficiently, leading to a thicker layer and thus higher IR intensity. In contrast, copolymerization of pCBMAA with pHPMAA results in a slower growth process and correspondingly weaker spectral response. In addition, digital immunoassay experiments were carried out for the detection of PSA. We investigate whether UCNPs coated with polymer brushes provide improved performance, specifically, a lower limit of detection, relative to conventional PEG-coated nanoparticles by mitigating nonspecific interactions. The resulting limits of detection and overall sensitivity are evaluated within the digital format and compared with those obtained using label-free SPR. In both cases, the digital UCNP format reached a lower LoD than PEG-coated nanoparticles and by more than one order of magnitude versus label-free SPR, with comparable selectivity; as SPR was label-free, amplification could further narrow this gap. Furthermore, in subsequent experiments, the detection strategy was validated for Legionella pneumophila. Here, the sensitivity of secondary amplification of the QCM signal was compared using commercially available fluorescence-labeled antibodies and UCNPs functionalized with an antifouling polymer brush carrying specific antibodies against *L. pneumophila*. The UCNP-based approach provided superior signal amplification and sensitivity, resulting in increased QCM sensor response and fluorescence readout. The relative advantages and limitations of the UCNP-based approach, including its implications for QCM sensor response and fluorescence readout, are discussed. These results underline the potential of polymer-coated UCNPs as advanced labels for pathogen detection in complex matrices. In both approaches, performance was evaluated via shifts in resonant frequency (Δf), with selectivity ensured by the primary capture step and not compromised by subsequent signal amplification. In QCM, direct (label-free) detection yielded an LoD on the order of ~10^4 CFU·mL^{-1}, which improved by >1 order with UCNP amplification (~10^3 CFU·mL^{-1}) and by a further ~2–3× in the fluorescence readout; the use of a commercially available fluorescent label did not afford comparable improvement.

Notes:

Effect of Membrane Polymer Surface Patterns on Initial Bacterial Adhesion

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Abstract:

Introduction: Bacterial adhesion represents the first step in the development of numerous infectious diseases, as it allows pathogens to establish contact and colonize both tissues and inert surfaces (Sarabia-Sainz et al., 2013). This process is mediated by adhesins, fimbriae, and other specialized structures that facilitate binding to glycoproteins and glycolipids on host cells or to artificial materials. Once initial adhesion is established, biofilm formation is triggered, leading to highly resistant structures that increase bacterial virulence and complicate eradication (Saldarriaga et al., 2023). Several studies have highlighted that preventing primary adhesion is an effective strategy to interrupt progression toward colonization and, consequently, to limit both infection development and surface deterioration. In this context, modulation of the physicochemical and topographic properties of materials emerges as an innovative alternative to reduce the initial interaction of bacteria with surfaces (Saldarriaga et al., 2023). The design of geometric patterns capable of decreasing the attachment of bacteria such as *Escherichia coli* ATCC and *Staphylococcus aureus* ATCC is particularly relevant, given the clinical and environmental importance of these species in device associated infections and material contamination. Identifying surface configurations that hinder bacterial adhesion would not only contribute to improving safety in healthcare environments but also extend the lifespan of materials exposed to microbial colonization. Therefore, the study of geometric surface patterns stands out as a promising strategy for biofilm prevention and infection control.

Materials and Methods: The initial adhesion of *Escherichia coli* and *Staphylococcus aureus* was evaluated on polymers manufactured under different conditions: variation in manufacturing time, different fiber thicknesses, and different surface geometric patterns (square, circle, hexagon, and triangle). The same experimental protocol was applied to all tests. Initially, the polymers and six-well plates were sterilized under UV light while bacterial suspensions were prepared at a turbidity equivalent to McFarland 4, which were centrifuged for 30 minutes. The supernatant was discarded, and the cell pellet was resuspended in liquid Mueller-Hinton broth, ensuring homogeneity by vortex. Each plate included: (i) three wells with polymers submerged in medium with bacteria, (ii) a positive control (coverslip + medium with bacteria), (iii) a negative control (coverslip + medium without bacteria), and (iv) a material control (polymer + medium without bacteria). With this distribution, the plates were incubated for 30 minutes at 37°C with shaking at 120 rpm. Subsequently, PBS washes were performed to remove non-adherent cells. The polymers and coverslips were transferred to Falcon tubes with PBS and vortexed individually for 5 minutes to detach the adhered bacteria. A 100 µL aliquot was taken from each suspension, fixed on a slide with alcohol-acetone, and stained with crystal violet. Microscopic analysis involved counting bacteria in 15 fields per sample, and the resulting data were analyzed using the Wilcoxon statistical test to identify significant differences in adhesion between the different polymers evaluated.

Results, Discussion and Conclusions: Comparative tests identified significant differences in bacterial adhesion depending on the manufacturing conditions and surface design of the polymers. First, it was observed that polymers manufactured in less time and with thinner fibers had less adhered bacteria compared to those with thicker fibers or longer manufacturing times. This result suggests that finer and less consolidated surfaces difficult the initial attachment of *E. coli* and *S. aureus*. On the other hand, for geometric polymers, the first tests were performed with surfaces containing multiple identical shapes repeated within the cover slip area. Under these conditions, the triangular pattern

showed the lowest bacterial adhesion compared to the other geometries. To confirm that this effect depended on the orientation of the fibers, additional tests were performed using larger single geometric patterns, i.e., a single triangle, square, hexagon, or circle occupying the entire area of the coverslip. Consistently, polymers with a triangular pattern showed the lowest adhesion, followed by the square, the hexagon, and finally the circle, which showed the highest bacterial adhesion. It has been demonstrated that surface topography decisively influences bacterial adhesion, as structures such as fibers, pores, or grooves can guide cellular behavior, a phenomenon known as “contact guidance” (Cai et al., 2020). In this context, the modification of polymers through geometric patterns represents an innovative strategy to reduce bacterial attachment; this effect depends not only on the pattern but also on the intrinsic characteristics of the polymer, such as its micromorphological properties. Our results showed that polymers with triangular patterns were the most effective in decreasing bacterial adhesion. This finding helps to better understand how cells respond to these structures and opens a wide range of applications in research, particularly in tissue engineering, taking advantage of their adjustable mechanical properties and biocompatibility (Cai et al., 2020). Additionally, during observation of the contact angle in the membrane manufacturing process, it was noted that polymers with a triangular pattern tended to form more hydrophobic surfaces, as evidenced by a delay in polymer wetting compared to other patterns. This hydrophobic feature could help explain the lower bacterial adhesion on these surfaces too.

Notes:

Dual-Targeted Antibody-Drug Conjugate for Improved Treatment of Colorectal Cancer

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Abstract:

Colorectal cancer (CRC) remains the second leading cause of cancer-related mortality in the United States, indicating a need for improved therapeutic options. Antibody-drug conjugates (ADCs), a rapidly growing class of targeted cancer therapeutics, deliver cytotoxic payloads to tumors using antibodies recognizing overexpressed surface proteins, thereby sparing normal tissues. Epidermal growth factor receptor (EGFR) is a well-established CRC therapeutic target; however, EGFR-directed therapies are limited by recurrence, acquired resistance, and KRAS mutations. The failure to eliminate cancer stem cell (CSC) subpopulations within tumors is recognized as a driver of CRC relapse, deeming the targeting of CSCs an attractive therapeutic approach. Leucine-rich repeat-containing G protein-coupled receptor 5 (LGR5) is a CSC marker overexpressed in CRC that is associated with metastasis, resistance, and poor prognosis. Furthermore, LGR5 has been shown to be upregulated following EGFR inhibition regardless of KRAS mutational status (High et al., Cell Reports Medicine 2025). EGFR-targeting therapies have been shown to enhance the efficacy of LGR5-targeting ADCs in CRC xenograft models, but tumors still relapse. This supports dual-targeting of EGFR and LGR5 for CRC, but warrants investigation into alternative dual-targeting strategies, such as bispecific ADCs (bsADCs), which can target two different proteins simultaneously and may enhance tumor specificity, limit the emergence of resistance, and overcome key limitations of current therapies. We developed an EGFR:LGR5 bispecific antibody (bsAb) by transient expression of a common light chain as well as anti-EGFR and anti-LGR5 heavy chains with oppositely-charged amino acid mutations to promote heterodimerization. BsAb binding, internalization, and lysosomal trafficking were assessed using immunocytochemistry. Time-course experiments were used to evaluate receptor expression following bsAb treatment. The cytotoxic payload CPT2 was conjugated to EGFR:LGR5 bsAb in a site-specific manner to generate an EGFR:LGR5 bsADC with a drug-to-antibody ratio of eight. Cytotoxicity assays were used to compare bsADC cytotoxicity to LGR5 monospecific ADC with identical linker-payload. The EGFR:LGR5 bsAb demonstrated efficient internalization and delivery to the lysosome and reduced expression of both target receptors. EGFR:LGR5 bsADC exhibited dramatically enhanced cytotoxicity relative to LGR5-targeted ADC. These findings support dual EGFR and LGR5 targeting as a strategy to improve CRC cell-killing and potentially reduce resistance and recurrence. Further research can compare bsADCs to EGFR- and LGR5-targeted ADCs in vivo, evaluate ADC resistance mechanisms, and define bsADC tolerability profiles.

Notes:

EMR-Based Machine Learning Prediction of Cholangiocarcinoma in Northeast Thailand

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Abstract:

Introduction: Cholangiocarcinoma is a bile duct cancer with a poor prognosis and is a significant public health problem in Northeast Thailand. The incidence rate of cholangiocarcinoma in this region is among the highest in the world and is strongly related to Opisthorchis viverrini or liver fluke infection and long-standing hepatobiliary disease. In Khon Kaen province, the age-standardized incidence rate of cholangiocarcinoma is about 13.4 per 100,000 person-years, more than twice the national average. Most patients are diagnosed at an advanced stage, when treatment options are limited, and survival is low. In routine practice, electronic medical records (EMR) store information on liver fluke infection, praziquantel treatment, comorbidities, and laboratory tests, but these data are not routinely used to support risk assessment. Machine learning methods can use complex patterns in EMR data to identify people at high risk of developing cholangiocarcinoma before clinical presentation. This study aimed to develop and internally validate machine learning models using 10 years of EMR data from a tertiary hospital in Northeast Thailand to predict incident cholangiocarcinoma, and to explore which routinely collected clinical factors contribute most to the prediction models.

Materials and Methods: We conducted a matched case–control study using electronic medical records from Srinagarind Hospital in Northeast Thailand, linked to the Khon Kaen Cancer Registry, from November 2014 to February 2025. Cholangiocarcinoma cases aged 18 years or older were identified from the registry and hospital records. Controls without cholangiocarcinoma were matched 1:1 to cases by sex, age, and residential province. Predictors included demographics, Opisthorchis viverrini infection status, history of praziquantel treatment, chronic liver and biliary disease, comorbidities, and liver function tests. The matched dataset of 5,079 cases and 5,079 controls was split into training (70%) and testing (30%) sets. We developed three prediction models: logistic regression, Elastic Net, and Random Forest. Model performance on the test set was evaluated using area under the receiver operating characteristic curve (AUC), sensitivity, specificity, and F1 score. Boruta and SHAP values were used to examine feature importance.

Results, Discussion and Conclusions: We included 5,079 incident cases of cholangiocarcinoma and 5,079 matched controls. In this high-burden setting, many participants had documented or unknown Opisthorchis viverrini infection, a history of praziquantel treatment, and chronic hepatobiliary disease. All three prediction models showed high discrimination in the test set, with areas under the receiver operating characteristic curves of around 0.96. The Random Forest model had the best overall performance, with a sensitivity of about 0.90, specificity above 0.99, and an F1 score around 0.95, while logistic regression and Elastic Net performed similarly. Feature importance analyses using Boruta and SHAP values showed that Opisthorchis viverrini infection status, especially the unknown infection status category, history of praziquantel treatment, and chronic liver and biliary disease contributed most to the predicted risk. In contrast, single-timepoint liver function test results contributed less. The strong contribution of the unknown infection category likely reflects missing or undocumented infection information in the electronic medical records and testing patterns, rather than a direct biological effect. These findings indicate that machine learning models using routinely collected electronic medical records can accurately predict cholangiocarcinoma risk in Northeast Thailand and may support risk-based selection of individuals for further diagnostic workup or closer imaging-based surveillance. External validation across other hospitals and a prospective assessment of how these models could be integrated into clinical workflows are needed before implementation in routine care.

Notes:

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