CRS Israeli Local Chapter

ICRS 2025 CONFERENCE

The 14th meeting of the Israel Controlled Release Society

7-9 September, 2025
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Abstract book

KALEIDOSCOPE
Conferences | Events | Exhibitions

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Welcome words

It is a great pleasure to welcome you to the 14th Annual Meeting of the Israel Chapter of the Controlled Release Society (ICRS). Since 1996, the Chapter has been a driving force in promoting collaborations between academia and industry and advancing innovation in drug delivery research in Israel and worldwide.

This year's program highlights our main achievements and explores the opportunities that lie ahead. Topics will include:

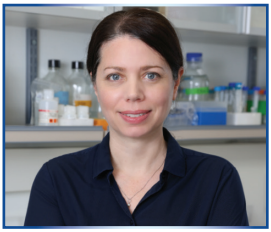
- Innovations and new technologies for improving targeting efficiency in drug delivery
- Development of long-acting drug delivery systems
- Integration of cutting-edge technologies such as machine learning and artificial intelligence into drug delivery platforms
- Advanced research in drug delivery, nanomedicine, and biomaterial sciences
- Translational research milestones and success stories from Israeli academia and industry collaborations

As the field of drug delivery continues to expand rapidly and gain global impact, ICRS remains dedicated to shaping its future in Israel and beyond. We look forward to inspiring talks, engaging discussions, and new collaborations that will contribute to improving patient care through innovative delivery strategies.

Prof. Ayelet David
Conference Chairperson
Ben-Gurion University of the Negev

Scientific Executive Committee

Prof. Avi Schroeder
Technion – Israel Institute of Technology



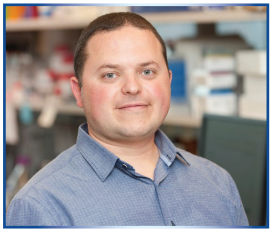
Dr. Ofra Benny
The Hebrew University of Jerusalem

Prof. Ronit Satchi-Fainaro
Tel-Aviv University

Prof. Dan Peer
Tel Aviv University

Prof. Rosa Azhari
Braude College of Engineering, Karmiel

Prof. Assaf Zinger
Technion – Israel Institute of Technology



Prof. Zvi Yaari
Hebrew University of Jerusalem, Israel

Prof. Yosi Shamay
Technion – Israel Institute of Technology

Prof. Aiman Abu Ammar
Azrieli College of Engineering

Prof. Boaz Mizrahi
Technion – Israel Institute of Technology

Dr. Dana Bar-On
Teva Pharmaceutical Industries Ltd

Prof. Marcelle Machluf
Technion – Israel Institute of Technology

Sunday, September 7th, 2025

13:00–14:00	**Registration & Light lunch, Exhibition & Poster set-up**
14:00–14:10	**Welcome and opening remarks** **Prof. Ayelet David,** *ICRS President, Ben-Gurion University of the Negev*
14:10–14:30	The Evolution of the Israeli Chapter of the Controlled Release Society **Prof. Abraham Rubinstein,** *The Hebrew University of Jerusalem*
14:30–15:15	Cellular Hitchhiking and Backpacking for Therapeutic Applications **Prof. Samir Mitragotri,** *John A. Paulson School of Engineering & Applied Sciences, Wyss Institute, Harvard University, USA* **[plenary speaker]**
15:15–17:45	**Session 1 | Advances in Targeted and Controlled Drug Delivery** ***Chairs : Prof. Ronit Satchi-Fainaro & Ofri Vizenblit***
15:15–15:35	Brain-Targeted Nanoparticles for Treating Parkinson's Disease **Prof. Avi Schroeder,** *Technion - Israel Institute of Technology*
15:35–15:55	Injectable Polymers for Local Delivery of Drugs **Prof. Avi Domb,** *The Hebrew University of Jerusalem*
15:55–16:25	**Coffee break & Exhibition & Poster set-up**
16:25–16:45	Q-Starch Carrier for Dermal Applications **Prof. Yosi (Joseph) Kost,** *Ben-Gurion University of the Negev*
16:45–17:05	Engineering Crystals and Polymers for Controlled Drug Delivery and Long-term Therapies: From Concept to Applications **Dr. Shady Farah,** *Technion - Israel Institute of Technology*
17:05–17:25	Nanoparticle Immunoimaging Reveals Metabolic Dysfunction Fueling CCR2-Dependent Inflammation in Infarcted Hearts" **Dr. Katrien Vandoorne,** *Technion- Israel Institute of Technology*
17:25–17:45	Noval Local Drug Delivery: From Platform Idea to a Successful Phase III Trial **Ms. Dalit Fellous Hazan,** *PolyPid Optimized Therapeutics*
17:45–18:05	Micron-Size Liposomes are Superior Drug-Products for Treatment of Local Pathologies Exemplified for Local Pain, Bone Modulation and Osteoarthritis **Prof. Chezy (Yechezkel) Barenholz,** *The Hebrew University of Jerusalem*

18:05–18:55	**Flash talks Block 1** (3 min talk + 2 min Q&A optional) ***Chair : Dr. Zvi Yaari***
18:05–18:10	Targeted Liposomes for Systemic Radiotherapy: Precision Delivery to Liver Metastases **PhD. Chen Tzror-Azankot**, *Bar-Ilan University*
18:10–18:15	Enzyme and Protein Modulated Cascade Mesophase Transitions of Polymeric Formulations **PhD. Keerthana Mulamukkil**, *Tel Aviv University*
18:15–18:20	DC-Targeted Nanoparticles Enhance Antitumor Immunity by Antigen Presentation Boost & PD-L1 Blockade **PhD. Marie Ruetter**, *Ben-Gurion University of the Negev*
18:20–18:25	Engineering Liposomes with Selectively Enriched Membrane Proteins for Targeted Delivery. **PhD. Sivan Arber Raviv**, *Technion – Israel Institute of Technology*
18:25–18:30	Nano-Ghosts: A Targeted Drug Delivery Platform for Cardiac Repair after Myocardial Infraction **PhD. Anastasia Brandis**, *Technion – Israel Institute of Technology*
18:30–18:35	Patient-Derived 3D Metastatic Melanoma Models for Target Discovery and Personalized Therapy **MSc. Anshika Katyal**, *Tel Aviv University*
18:35–18:40	Radiation-Guided Dual-Drug Nanoparticles Boost PARP Inhibitor Efficacy in BRCA1-Deficient Tumors **PhD. Giuseppe Longobardi**, *Tel Aviv University*
18:40–18:45	Soluble Mechanical Signaling as a Novel Regulator of Tumor Spheroid Mechanics **PhD. Katerina Tischenko**, *The Hebrew University of Jerusalem*
18:45–18:50	Size-Dependent Distribution and Retention of Biomimetic Nanoparticles in the Central Nervous System **MSc. Anat Lyubin Haimov**, *Technion – Israel Institute of Technology*
18:50–18:55	Bioinspired 4D-Printed Hydrogel Bioadhesives for Rapid, Trauma-free Tissue Repair and Potential Drug Delivery **PhD. Qi Wu**, *Technion-Israel Institute of Technology*
18:55–19:50	**Poster Session 1**
20:00	**Dinner at the Hotel Restaurant**
21:00	**Evening Social Program**

Monday, September 8th, 2025

08:30-09:00 — **Coffee, Exhibition & Poster set-up**

09:00-10:20 ▶ **Session 2 | Nanomedicines, Artificial intelligence and Predictive models**
Chairs : Dr. Assaf Zinger & Yulia Chulanova
Sponsored by ROYAL SOCIETY OF CHEMISTRY

09:00-09:20 — Decoding Tumor-Host Interactions: Engineering the Future of Personalized Oncology
Prof. Ronit Satchi-Fainaro, *Tel Aviv University*

09:20-09:40 — Biomechanical Aspects in Nano-Therapy and Diagnostics in Cancer
Prof. Ofra Benny, *The Hebrew University of Jerusalem*

09:40-10:00 — Data vs. Hypothesis Driven Drug Cocktail Design in Nanomedicine for Solid Tumors
Prof. Yosi Shamay, *Technion - Israel Institute of Technology*

10:00-10:20 — Cheminformatics and Machine Learning-Driven Optimization of Drug Delivery Systems
Prof. Alexander Tropsha, *Eshelman School of Pharmacy, University of North Carolina, Chapel Hill, USA*

10:20-10:40 — Decoding Delivery: Machine Learning-Driven Optimization of Targeting via Barcoded Nanoparticles
Ronen Eavri, *Barcode Diagnostics*

10:40-11:05 — **Coffee break & Exhibition & Poster set-up**

11:05-12:45 ▶ **Session 3 | Theranostics, Imaging, and Nanomaterials**
Chairs : Prof. Ofra Benny & Ron Kleiner

11:05-11:25 — Theranostic NanoGhost: Paving the Way from the Bench to the Clinic
Prof. Marcelle Machluf, *Technion - Israel Institute of Technolog*

11:25-11:45 — Developing Optical Nanosensors for Biomedical Applications
Dr. Zvi Yaari, *The Hebrew University of Jerusalem*

11:45-12:05 — Guiding Drugs with Sound: New Frontiers in Noninvasive Delivery
Prof. Tali Ilovitsh, *Tel-Aviv University*

12:05-12:25 — Desorption Electrospray Ionization Mass Spectrometry Imaging in Drug Delivery
Dr. Katy Margulis, *The Hebrew University of Jerusalem*

12:25-12:45 — Controlling Cell Functionality via Thermal Stimulation Using Magnetic Nano-Composites
Dr. Dekel Rosenfeld, *Tel-Aviv University*

12:45 — **Group Photo**

12:45-13:35 — **Lunch break & Exhibition & Poster set-up**

13:35-14:20 — From Lemons to Lemonade: Innovative Therapeutic Delivery Strategies
Prof. Molly Shoichet, *Chemical Engineering & Applied Chemistry, Donnelly Centre, University of Toronto, Canada* **[plenary speaker]**

14:20–16:00 ▶	**Session 4 | Biomaterials, Bioinspired Therapeutics and Next-Generation Immuno-Therapies** ***Chairs : Prof. Yosi Shamay & Marie Ruetter***
14:20–14:40	Our Body Knows Best: Unlocking the Secrets of Self-Targeting Therapies **Dr. Assaf Zinger,** *Technion – Israel Institute of Technology*
14:40–15:00	Advanced Materials for Tissue Engineering **Prof. Tal Dvir,** *Tel-Aviv University*
15:00–15:20	Bioinspired Functional Materials **Dr. Gali Fichman,** *The Hebrew University of Jerusalem*
15:20–15:40	Structural Modifications of the TNFα Inhibitor Enbrel Effect on its Therapeutic Efficacy in a Mouse Model of Rheumatoid Arthritis **Prof. Itay Benhar,** *Tel-Aviv University*
15:40–16:00	Bioactive Reinforcing Bioink for Hybrid Bioprinting of Implantable Tissues **Prof. Shulamit Levenberg,** *Technion – Israel Institute of Technology*
16:00–16:30	**Coffee break & Exhibition & Poster set-up ICRS President Election**
16:30–18:00	Patents and Innovations in Controlled Release Drug Delivery Workshop **Dr. Eyal Bressler** Topics: Patents 101 in Controlled Release | Reading Patents – Hands-On | Writing Patents – Practical Tips | Patents in R&D, Startups and Pharma
18:00–18:50 ▶	**Flash talks Block 2** (3 min talk + 2 min Q&A optional) ***Chair : Prof. Boaz Mizrahi***
18:00–18:05	Genome Editing Using Targeted Lipid Nanoparticles for Mantle Cell Lymphoma Therapy **PhD. Lior Stotsky,** *Tel Aviv University*
18:05–18:10	Brain-targeted mRNA-LNPs with Improved Neuronal Specificity Validated by AI **PhD. Haim Kadosh,** *Technion – Israel Institute of Technology*
18:10–18:15	CRISPR/Cas9 Genome Editing Using Lipid Nanoparticles for Hepatocellular Carcinoma Therapy **PhD. Dor Breier,** *Tel Aviv University*
18:15–18:20	High-Throughput 3D Microscopy Reveals Symmetric Spheroid-Fibroblast Organization **PhD. Maytal Avrashami,** *Technion – Israel Institute of Technology*
18:20–18:25	Long-Acting Liposomal Bupivacaine for Post-Operative Pain Relief **PhD. Keren Turjeman,** *The Hebrew University of Jerusalem*
18:25–18:30	3D Printing of Personalized Catheters with Smart pH-Responsive Coating for Improved Functionality for Long-Term Therapy Delivery **Dr. Nagham Moallem Safuri,** *Technion-Israel Institute of Technology*
18:30–18:35	DC-Targeted Nanovaccine Boosts Immunity and Efficacy of SoC and KRAS-Targeted Therapies in PDAC **MSc. Ron Kleiner,** *Tel Aviv University*
18:35–18:40	MILKOSOMES – Breast Milk Biomimetic Nano Particles as a Versatile, Non-Invasive, Oral Drug Delivery **PhD. Si Naftaly Kiros,** *Technion – Israel Institute of Technology*
18:40– 18:45	Double layer and Dual Drug Loaded Microneedle Patch for Comprehensive Skin Therapy **MSc. Gali Cohen,** *Technion – Israel Institute of Technology*
18:45– 18:50	Living Materials Approach for In-Situ Bio-Polymers Production Using Bacteria in Microneedles **PhD. Caroline Hali Alperovitz,** *Technion – Israel Institute of Technology*
18:50–19:40 ▶	**Poster Session 2**

19:40–20:40	**Dinner at the Hotel Restaurant**
20:45	**Awards & Dancing**

Tuesday, September 9th, 2025

08:30–09:15	**Coffee Exhibition & poster set- up | Committee Meeting**
09:15–10:00	Polyoxazolines for Micelles and Beyond **Prof. Alexander (Sasha) Kabanov,** *Center for Nanotechnology in Drug Delivery, University of North Carolina, Chapel Hill, USA* **[plenary speaker]**
10:00–10:45	**Round table: Bioconvergence in Health Care** **Topic: Leveraging omics-based profiling, AI, and advanced diagnostics to tailor treatments to individual patients** **Panel Members: Prof. Ofra Benny,** *The Hebrew University of Jerusalem,* **Prof. Ronit Satchi-Fainaro,** *Tel Aviv University,* **Prof. Avi Schroeder,** *Technion – Israel Institute of Technology,* **Prof. Yosi Shamay,** *Technion – Israel Institute of Technology,* **Dr. Ayelet Ofarim,** *Arad-Ophir , CAS* **Dr. Dalia Rivenzon-Segal,** *Reinhold Cohn Group*
10:45–11:15	**Coffee break & Exhibition & Poster set-up**
11:15–12:55	**Session 5 | Drug/Polymer Interactions, Controlled Cell Functionality and Medical Devices** ***Chairs : Prof. Avi Schroeder & Maytal Avrashami***
11:15–11:35	Polymeric Transformers: from Smart Fibers to Microneedles **Prof. Roey Amir,** *Tel-Aviv University*
11:35–11:55	Living Delivery System for the Treatment of Skin Infections **Prof. Boaz Mizrahi,** *Technion – Israel Institute of Technology*
11:55–12:15	Versatile Biodegradable Microneedle Arrays for Local and Systemic Drug Delivery **Prof. Aiman Abu Ammar,** *Azrieli College of Engineering Jerusalem*
12:15–12:35	Engineering Protein-Based Soft Actuators for Dynamic and Autonomous Catch-and-Release in Gastric and Intestinal Environments **Dr. Luai Khoury,** *Technion – Israel Institute of Technology*
12:35–12:55	Nano-Algae for Drug Delivery and Cancer Therapy Purposes **Dr. Aharon (Roni) Azagury,** *Ariel University*
13:00	**Closing Remarks** **Prof. Ayelet David,** *ICRS President*
13:20	**Light lunch**

Plenary Speakers

Prof. Samir Mitragotri
Wyss Institute, Harvard University, USA

Prof. Alexander Kabanov
University of North Carolina – Chapel Hill, USA

Prof. Molly Shoichet
University of Toronto, Canada

Guest Speaker

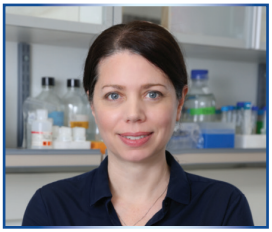
Prof. Alexander Tropsha
University of North Carolina – Chapel Hill, USA

Speakers

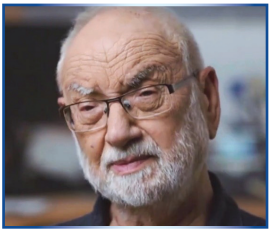
Dr. Luai R. Khoury
Technion – Israel Institute of Technology

Prof. Ronit Satchi-Fainaro
Tel-Aviv University

Dr. Zvi Yaari
The Hebrew University of Jerusalem



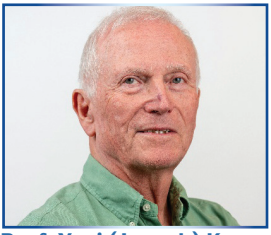
Prof. Ofra Benny
The Hebrew University of Jerusalem



Prof. Chezy (Yechezkel) Barenholz, *The Hebrew University of Jerusalem*

Dr. Aharon (Roni) Azagury
Ariel University

Prof. Tali Ilovitsh
Tel-Aviv University



Prof. Yosi (Joseph) Kost
Ben-Gurion University of the Negev

Dr. Gali Fichman
The Hebrew University of Jerusalem

Prof. Itai Benhar
Tel-Aviv University

Dr. Katy Margulis
The Hebrew University of Jerusalem

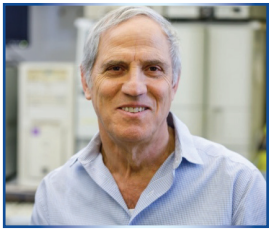
Dr. Assaf Zinger
Technion – Israel Institute of Technology

Prof. Shulamit Levenberg
Technion – Israel Institute of Technology

Prof. Avi Schroeder
Technion – Israel Institute of Technology

Prof. Boaz Mizrahi
Technion – Israel Institute of Technology

Dr. Shady Farah
Technion – Israel Institute of Technology



Prof. Avi Domb
The Hebrew University of Jerusalem

Prof. Aiman Abu Ammar
Azrieli College of Engineering Jerusalem

Prof. Abraham Rubinstein
The Hebrew University of Jerusalem

Dr. Dekel Rosenfeld
Tel Aviv University

Prof. Marcelle Machluf
Technion – Israel Institute of Technology

Prof. Yosi Shamay
Technion – Israel Institute of Technology

Prof. Roey Amir
Tel Aviv University

Prof. Tal Dvir
Tel Aviv University

Mr. Ronen Eavri
BarCode Nano

Ms. Dalit Fellous Hazan
PolyPid

Dr. Katrien Vandoorne
Technion – Israel Institute of Technology

Speakers abstracts

per appearance order in the program

The Evolution of the Israeli Chapter of the Controlled Release Society

Abraham Rubinstein

The Hebrew University of Jerusalem

In 1993, the Controlled Release Society (CRS) approached Prof. Yossi Kost of Ben-Gurion University of the Negev with the suggestion of establishing a local chapter of the society in Israel. At the time, beyond Kost's laboratory, several other research groups in Israel were engaged in the development of drug delivery systems. Major research activity was being conducted at the Hebrew University of Jerusalem, Tel Aviv University, and the Technion. The field of micro- and nano-carriers was explored by the groups of Chezy Barenholz, Simon Benita, and Elka Touitou at the Hebrew University; Rimona Margalit at Tel Aviv University; Smadar Cohen at Ben-Gurion University; and Noah Lotan at the Technion (focusing on agricultural applications). Indeed, the time had come to create a dedicated scientific framework for the field of drug delivery in Israel.

In 1996, the Israeli Chapter was formally established and registered as a non-profit organization. This milestone was celebrated at the CRS Annual Meeting in Stockholm, where Avri Rubinstein was elected as the first President of the chapter. That same summer, the Israeli Chapter organized its first scientific meeting on Controlled Delivery of Biomaterials, inviting Prof. Henry Kopecek of the University of Utah as a guest speaker. He was the first of many distinguished international scientists who would, in the years that followed, enrich the chapter's academic meetings.

Over time, the annual meetings of the Israeli Chapter gained a strong reputation for their high scientific quality. During the early years, these meetings were held modestly at Ort Braude College of Engineering in Karmiel, where participants stayed in student dormitories during the summer recess. Support from the pharmaceutical industry and academic institutions, along with the growing number of chapter members, enabled significant upgrades in meeting facilities, greater involvement of international guest speakers, and expanded financial support for students to attend the annual conferences.

Session 1:
Advanced in Targeted and Controlled Drug Delivery

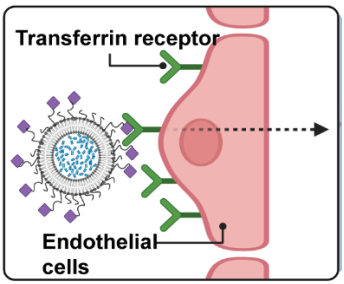
Brain-targeted drug delivery systems and synthetic cells

Avi Schroeder

Technion – Israel Institute of Technology

Nanotechnology holds numerous potential benefits for treating disease, including the ability to transport complex molecular cargoes, including RNA and proteins, as well as targeting specific tissues, including the brain. Brain-targeted nanoparticles enhance the delivery of monoclonal antibodies (mAbs) across the blood-brain-barrier (BBB) and into neurons, thereby allowing the intracellular and extracellular treatment of Parkinson's disease. 100-nm BTL cross human BBB models intact and are taken up by primary neurons. Within neurons, SynO4 is released from the nanoparticles and bound to its target – alpha-synuclein (AS), thereby reducing AS aggregation, and enhancing neuronal viability. In vivo, intravenous administration results in a seven-fold increase in mAbs in brain cells, decreasing AS aggregation and neuroinflammation and improving behavioral motor function and learning ability in mice. Targeted nanotechnologies offer a valuable platform for drug delivery to treat brain neurodegeneration.

The evolution of drug delivery systems into synthetic cells, programmed nanoparticles with an autonomous syn-bio capacity to synthesize diagnostic and therapeutic proteins inside the body, and their promise for treating disease, will be discussed.



BBB crossing

References:

1. Theranostic barcoded nanoparticles for personalized cancer medicine, Yaari et al. Nature Communications, 2016, 7, 13325
2. Synthetic cells with self-activating optogenetic proteins communicate with natural cells, Adir et al. Nature Communications, 2022, 13, 2328
3. Brain-Targeted Liposomes Loaded with Monoclonal Antibodies Reduce Alpha-Synuclein Aggregation and Improve Behavioral Symptoms in Parkinson's Disease, Advanced Materials, 2304654, 2023

Injectable polymers for local delivery of drugs

Prof. Abraham (Avi) J. Domb

The Hebrew University of Jerusalem

Biodegradable polymers have been used for absorbable sutures, orthopedic plates and clips, as well as drug carries and scaffolds for tissue engineering. Most biodegradable products are solid at room temperature, but some are injectable microspheres and pastes that have applications as drug carriers and tissue augmentation.

Injectable biodegradable pastes made from natural fatty acids have been used for the delivery of anticancer agents for treating head and neck cancer, as well as the delivery of gentamicin for eradicating bone bacterial infections. The synthesis and applications of absorbable polymers for medical use will be discussed.

Q-Starch carrier for dermal applications

Prof. Yosi (Joseph) Kost

Ben Gurion University of the Negev

High molecular weight hyaluronic acid (HMw-HA) is widely used in dermo-aesthetic treatments for skin rejuvenation and anti-aging. However, its rapid degradation and short residence time in the skin (<24 h) limit its therapeutic potential. To overcome these challenges, we developed a biocompatible nanocarrier system based on quaternized starch (Q-starch) nanoparticles (NPs) capable of binding HMw-HA. The resulting HMw-HA-NPs significantly improved HA stability and extended its skin residence time compared to commercially available HA, while preserving its biological function to stimulate collagen production in murine models. Furthermore, we employed low-frequency ultrasound (LFUS) to enable non-invasive transdermal delivery of HMw-HA-NPs. LFUS transiently enhances skin permeability, facilitating deeper and more uniform NP penetration. In vivo experiments confirmed enhanced delivery and retention of HMw-HA-NPs within skin layers without compromising HA activity. The combination of HMw-HA-NPs with LFUS addresses key limitations of current dermo-aesthetic therapies and supports the development of advanced, patient-friendly skin rejuvenation technologies.

Engineering Crystals and Polymers for Controlled Drug Delivery and Long-term Therapies: From Concept to Applications

Dr. Shady Farah

Technion – Israel Institute of Technology

Nanoparticle Immunoimaging Reveals Metabolic Dysfunction Fueling CCR2-Dependent Inflammation in Infarcted Hearts

Dr. Katrien Vandoorne

Technion- Israel Institute of Technology

Novel Local Prolonged Drug Delivery: From Platform Idea to a Successful Phase III Trial

Ms. Dalit Fellous Hazan

PolyPid

Objectives: Describes the design principles and innovative characteristics of the PLEX (Polymer-Lipid Encapsulation matriX) platform for local, prolonged, and controlled drug delivery, and its clinical translation when paired with doxycycline into effective surgical site infection (SSI) prophylaxis in major abdominal colorectal surgery.

Methods: The PLEX platform leverages a unique polymer-lipid based matrix, entrapping active drugs (small molecules, peptides and proteins) within protected reservoirs at the target site with control over both release rate and duration—enabling zero-order kinetics from days to months. PLEX technology addresses a crucial unmet need, overcoming the limitations of systemic delivery (enhances local drug concentrations, and minimizes systemic toxicity) and current local delivery approaches (such as initial burst, rapid clearance, or short drug exposure). Development of D-PLEX100, the doxycycline-based clinical candidate, involved formulation optimization for release kinetics and incision site retention, and preclinical validation for antimicrobial efficacy. Pivotal evidence was generated in the SHIELD II Phase 3 randomized prospective and controlled trial, enrolling 977 patients undergoing abdominal colorectal surgery. The primary endpoint encompassed incisional SSI, re-intervention, and all-cause mortality; key secondary endpoints included SSI rate.

Results: D-PLEX100 achieves prolonged and constant local doxycycline release, maintaining wound concentrations 3-5 mcg/mL for 30 days, well above the MIC of common susceptible and even some resistant SSI bacteria. In animal and clinical studies, D-PLEX100 demonstrated robust antibacterial activity (including >3-log reductions in MRSA and Gram-negatives), durable infection prophylaxis, and low resistance risk. The pivotal SHIELD II Phase 3 trial showed D-PLEX100 plus SoC antibiotics reduced primary endpoint

events by 38% (p=0.0039) and incisional SSIs by 58% (p=0.0013) versus SoC alone, with a safety profile comparable between groups.

Conclusions: The PLEX platform's unique design enables precisely engineered and prolonged local drug delivery. Its successful development, manufacturing and clinical translation as D-PLEX100 validates PLEX's promise for key clinical unmet needs, in SSI prevention and beyond.

Micron-Size Liposomes are Superior Drug-Products for Treatment of Local Pathologies Exemplified for Local Pain, Bone Modulation and Osteoarthritis

Prof. Chezy (Yechezkel) Barenholz

The Hebrew University of Jerusalem

Session 2 | Nanomedicines, Artificial intelligence and Predictive models

Decoding Tumor–Host Interactions: Engineering the Future of Personalized Oncology

Prof. Ronit Satchi-Fainaro

Tel Aviv University, Department of Physiology and Pharmacology, Gray School of Medical Sciences, Gray Faculty of Medical and Health Sciences, Tel Aviv University, Tel Aviv 6997801, Israel

Many drugs show promising results in laboratory research but eventually fail to show clinical benefit. One main reason for this translational gap is that the cancer models used are inadequate. Most models lack the complex tumor-stromal-immune cell interactions with their tumor microenvironment (TME) that are required for progression. Conventional 2D models, where cells grow on rigid plastic plates mainly as mono-cultures, fail to recapitulate these complex interactions. Hence, we developed a vascularized, hydrogel-based 3D-bioprinted tumor model consisting of patient-derived tumor, PBMCs, and TME cells. Our 3D models are based on our library of hydrogels as scaffolds for different tumor types according to the mechanical properties of the tissue of origin, which dictates the proteo-genomic signature and, hence, the response to different therapies. Using these unique high-throughput 3D models, we are currently validating their ability to mimic patient-specific tumors and TME, in order to serve as a tool to predict patient response to different treatments. To decide which therapies to test on our 3D platforms, we consider cancer-specific standard-of-care, investigational therapies that we develop in our lab, as well as therapies proposed by an AI-based algorithm that utilizes H&E slides to generate individual drug response scores for targeted and immune therapies. To validate the ability of our models to predict patient responses, we are currently conducting an 80-patient clinical trial at Sheba Medical Center, testing different treatments on samples covering 7 distinct cancer types. These unique 3D models have the potential to facilitate target discovery and drug development, as well as to serve as a reliable system for precision medicine.

Biomechanical Aspects in Nano-Therapy and Diagnostics in Cancer

Prof. Ofra Benny

The Hebrew University of Jerusalem

The integration of engineering, biology, and nanotechnology has revolutionized cancer therapy by enabling the development of next-generation drug delivery systems. Nanomedicine offers novel tools to improve the precision and efficacy of treatments, especially in oncology, where disease heterogeneity and the toxic nature of chemotherapy remain major challenges. Molecular biomarker-based targeting strategies are effective but often limited by the genetic instability of cancer cells. As an alternative, our team explores the use of biomechanical properties, both of cancer cells and nanocarriers, as a novel targeting paradigm. By employing advanced fabrication techniques and AI-driven design, the lab engineers nanoparticles with tunable mechanical features and also incorporates components for remote actuation via magnetic fields or thermal stimuli. These hybrid nanocarriers have demonstrated enhanced targeting and therapeutic synergy in preclinical cancer models. Furthermore, personalized evaluation of drug efficacy is achieved through the Tumor-on-a-Chip system, which models patient-derived tumor tissues in a physiologically relevant microenvironment. This integrated approach offers a powerful platform for personalized diagnostics and nano-therapeutics, grounded in the biomechanics of cancer.

Data vs. Hypothesis Driven Drug Cocktail Design in Nanomedicine for Solid Tumors

Prof. Yosi Shamay

Technion – Israel Institute of Technology

Cheminformatics and Machine Learning-Driven Optimization of Drug Delivery Systems

Prof. Alexander Tropsha

Eshelman School of Pharmacy, University of North Carolina, Chapel Hill, USA

Session 3 | Diagnostics, Imaging, and Nanomaterials

Developing Optical Nanosensors for Biomedical Applications

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The rapid advancement of biomedical technologies in recent decades has transformed patient care, yet challenges remain in achieving more precise, accessible, cost-effective, rapid, and automated diagnostic methods. Optical spectroscopic and imaging technologies present promising alternatives to current practices, offering benefits such as noninvasive, nondestructive probing, fast and robust signals, and compatibility with existing medical devices. Among these, single-walled carbon nanotubes (SWCNTs) have emerged as highly effective near-infrared (NIR) fluorescent nanosensors due to their exceptional stability, resistance to photobleaching, and high sensitivity in biological environments.

Beyond their demonstrated use in vitro and in vivo for detecting reactive oxygen species (ROS) and pH changes, SWCNT-based nanosensors show immense potential for additional biological and clinical applications. These include real-time monitoring of metabolic biomarkers and detecting tumor microenvironment changes.

Here, we will explore developing and optimizing SWCNT-based optical nanosensors for diverse biomedical applications, aiming to address existing challenges and integrate these innovative tools into clinical settings. By leveraging their unique properties, SWCNTs hold the potential to revolutionize diagnostics and therapeutic monitoring, fostering a new era of precision medicine and patient-centered care.

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Guiding Drugs with Sound: New Frontiers in Noninvasive Delivery

Prof. Tali Ilovitsh

Tel-Aviv University

Ultrasound is a noninvasive, clinically established modality with growing therapeutic potential, particularly when combined with gas-filled ultrasound contrast agents known as microbubbles. One promising application is the targeted delivery of lipid nanoparticles (LNPs), an FDA-approved platform for RNA therapeutics, to the brain, which is otherwise restricted by the blood-brain barrier (BBB). We optimized focused ultrasound parameters to safely open the BBB and enhance LNP delivery. Using low-frequency ultrasound and microbubble pre-injection, we demonstrated the delivery of siRNA- and mRNA-loaded LNPs into healthy and glioblastoma-bearing mouse brains, achieving up to a 12-fold increase in payload accumulation. Building on this success, we are now developing next-generation nanocarriers that unify ultrasound responsiveness and therapeutic payload into a single, hybrid particle. These drug-loaded nanodroplets, inspired by LNPs and fabricated via microfluidics, are sub-200 nm in size and remain stable in circulation. Upon ultrasound activation, they vaporize and collapse, releasing their cargo locally and enhancing treatment precision. In preliminary studies, we demonstrate the delivery of fluorescent tracers and chemotherapy to solid tumors using this single-step platform. Together, these approaches highlight the potential of ultrasound to noninvasively guide and trigger drug delivery. From LNPs for brain applications to novel hybrid nanodroplets for localized therapy, our vision is to overcome biological barriers and advance personalized treatment.

Desorption Electrospray Ionization Mass Spectrometry Imaging in Drug Delivery

Dr. Katy Margulis

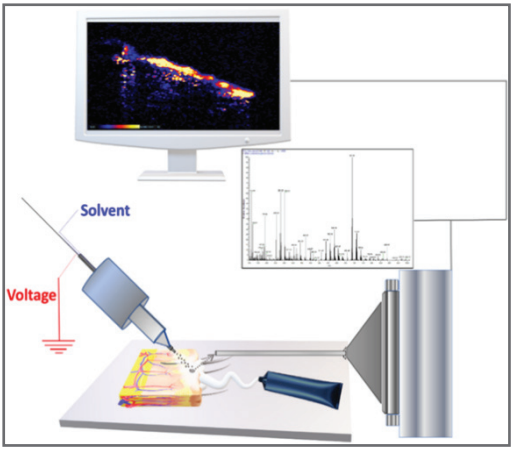
The Hebrew University of Jerusalem

We employ Desorption Electrospray Ionization Mass Spectrometry Imaging (DESI-MSI), an ambient mass spectrometry imaging technique, to advance drug delivery design, evaluate therapeutic effects, and uncover novel therapeutic targets across a broad spectrum of disorders.
DESI-MSI operates by directing a beam of charged solvent droplets onto tissue surface to desorb and ionize molecules (Fig.1). The tissue is moved at a controlled speed to record the mass spectra from different spatial coordinates, while the signals are subsequently converted into images of molecular ion distributions.

One major focus of our work is the development of drug delivery systems targeted to different skin strata. Using DESI-MSI, we directly visualize and quantify drug distribution across skin layers following dermal delivery without extraction or compound labeling. We developed a robust computational method combining DESI-MSI with automated XY-layer clustering of mass spectrometry data, enabling spatial visualization and quantification of APIs, carriers, and endogenous permeation enhancers. This approach was applied to evaluate three dermal formulations of the antifungal drug terbinafine, transfersomes, ethosomes, and liposomes, revealing distinct delivery profiles within the skin. We used a similar strategy to optimize cannabidiol skin delivery and to design formulations that confine chemical sunscreens to the stratum corneum.

Another focus of our work is intranasal drug delivery to the brain. We developed a system for delivering iron chelators to treat neurological disorders associated with brain iron accumulation. DESI-MSI provided real-time feedback on drug distribution and neurotransmitter modulation in brain tissue, supporting platform optimization and confirming physiological effects. Beyond drug delivery, we use DESI-MSI to investigate molecular changes

in several pathologies. MYC-driven neoplasms in conditional transgenic mouse models provide a platform for identifying cancer-specific molecular alterations and therapeutic targets. We have expanded this research to human clinical specimens, including oral squamous cell carcinoma, kidney, and liver cancers.



Controlling cell functionality via thermal stimulation using magnetic nanocomposites

Dr. Dekel Rosenfeld

Tel Aviv University

Bioelectronic medicine is an emerging field that utilizes external signaling to control cell activation and to identify novel therapeutic approaches. Recent advances use magnetic nanomaterials to control cell signaling, serving as transducers to convert external magnetic fields into biologically relevant signals. Iron oxide magnetic nanoparticles (MNPs) with a diameter of 20–30 nm dissipate heat when exposed to weak alternating magnetic fields (AMFs) with amplitudes <50 mT and frequencies of 100–600 kHz. This heat can be harnessed to activate cells with thermally sensitive ion channels on their membranes, a process known as magnetothermal modulation. The high penetration rate of AMF into deep tissues with no deleterious effects makes it an ideal signal for activating cells within deep organs in the body.

We exploit the magnetothermal approach to control calcium signaling in cells within deep organs. While the common approach of magnetothermal stimulation exploits MNPs in the form of ferrofluid, I will introduce novel approaches to achieve similar effects with three-dimensional magnetic nanocomposites. We utilize this model to demonstrate our approach for controlling calcium signaling and drug delivery.

Session 4 | Biomaterials, Bioinspired Therapeutics and Next-Generation Immuno-Therapies

Our Body Knows Best: Unlocking the Secrets of Self-Targeting Therapies

Dr. Assaf Zinger

Technion - Israel Institute of Technology

Biomimetic nanoparticles aim to emulate the behavior of either cells or exosomes effectively. For example, leukocyte-based biomimetic nanoparticles incorporate cell membrane proteins to transfer the natural tropism of leukocytes to the final delivery platform.

Here, I will demonstrate how tweaking the protein content improved the targeting of triple-negative breast cancer inflamed endothelium and describe The imaging challenges that arose in these projects. I will also discuss the reproducible production of two types of neuron-targeting biomimetic nanoparticles, each with a distinct lipid formulation backbone suited to potential therapeutic cargo (e.g., mRNA, small molecules, and protein), by integrating membrane proteins unbiasedly sourced from human pluripotent stemcell-derived neurons.

Our combined use of a microfluidic, bottom-up approach and tuning of key synthesis parameters enabled the synthesis of reproducible, enhanced biomimetic nanoparticles that have the potential to improve the treatment of inflammatory-based conditions and genetic disorders through targeted nano delivery.

Our Body Knows Best: Unlocking the Secrets of Self-Targeting Therapies

Marcelle Machluf, PhD

The Lab for Cancer Drug Delivery & Cell Based Technologies, Faculty of Biotechnology and Food Engineering, Technion, Haifa, Israel

Effective and targeted delivery remains one of the major challenges in drug delivery and particularely in RNA and gene-based therapeutics. NanoGhost is an innovative nano-delivery platform derived from the whole membrane of mesenchymal stem cells (MSCs), designed to combine the intrinsic tumor-homing and immunomodulatory properties of stem cells with a scalable, off-the-shelf nano-vesicle formulation.NanoGhost vesicles preserve key membrane proteins from parental MSCs, enabling selective targeting of pathological tissues, including tumors and inflamed microenvironments. The platform is engineered to encapsulate a variety of small molecules peptides, RNA cargo (e.g., siRNA, mRNA, microRNA) as well as gene-editing tools (e.g., CRISPR-Cas systems), ensuring efficient intracellular delivery with minimal off-target effects.We demonstrate that NanoGhost achieves high stability, biocompatibility, and loading efficiency, while bypassing common limitations of viral vectors and synthetic nanoparticles as well as bypasing the blood brein berriers. Preclinical studies show successful delivery of theraputics leading to GBM inhibition as well as RNA payloads delivery to other tumor sites in vivo. Unpublished data demonstrate that NGs can envelop LNPs thus adding to LNPs the inhernt taegeting ability of MSC to tumors opening the door for a safer nontoxic high loading capacity to the new biohybrid particles.

Advanced Materials for Tissue Engineering

Prof. Tal Dvir

Tel-Aviv University

Bioinspired Functional Materials

Dr. Gali Fichman

The Hebrew University of Jerusalem

Structural Modifications of the TNFα Inhibitor Enbrel Effect on its Therapeutic Efficacy in a Mouse Model of Rheumatoid Arthritis

Prof. Itay Benhar

Tel-Aviv University

Therapeutic blockade of proinflammatory cytokines has revolutionized the treatment of rheumatoid arthritis (RA), leading to the approval and widespread use of biologics for this pathology. A prominent target is tumor necrosis factor-alpha (TNFα), a proinflammatory cytokine. Etanercept (Enbrel™), a fusion protein consisting of the soluble portion of the p75-TNF receptor (TNFR) and the Fc fragment of human IgG1 (hinge, CH2 and CH3 domain) was the first TNF-specific biologic to make a substantial impact for the treatment of RA.

Enbrel (Etanercept) differs structurally and functionally from anti TNFα biologics monoclonal antibodies, mAbs, differences that may stem primarily from their structural differences. For example, regarding immune effector functions, the mAbs Infliximab and Adalimumab can induce complement-dependent cytotoxicity whereas Enbrel cannot. Such differences were attributed to Enbrel's lack of the CH1 domain of IgG1.

This study aimed to explore the effects of structural modifications of Enbrel on its therapeutic efficacy in a mouse model of RA, specifically focusing on isotype variation and the incorporation of the CH1 domain to the Fc constant region. We developed four murine versions of Enbrel: mEnbrel2a and mEnbrel1, with and without the CH1 domain. These versions were assessed for their ability to bind and neutralize TNFα in vitro, as well as their therapeutic effects in a mouse RA model in vivo. We found significant differences in efficacy that are dependent on antibody class of the Fc as well as presence or absence of a CH1 domain. These findings underscore the critical role of isotype and domain selection in optimizing the therapeutic potential of Fc-fusion proteins. These observations could provide valuable insights applicable to other Fc-fusion proteins and a broader range of pathologies.

Bioactive Reinforcing Bioink for Hybrid Bioprinting of Implantable Tissues

Prof. Shulamit Levenberg

Technion – Israel Institute of Technology

3D bioprinting is an emerging technology that offers promise for fabricating implantable tissues. Despite significant advancements, the field struggles to replicate the mechanical robustness and biological complexity of native tissues, particularly in applications requiring high mechanical strength such as bone. To overcome this limitation we introduced 'BioForceInk,' a bioactive reinforcing bioink designed for direct bioprinting alongside a cell-laden hydrogel within a cell-conductive environment. The bioink is based on thermosensitive microparticles. It is printable at room temperature and solidifies at 37°C, forming a stiff, porous scaffold within the construct. Our studies demonstrated its excellent printability, mechanical properties, and osteoinductive capabilities in a hybrid bioprinting context. To enhance vascularized bone differentiation in vitro and support bioprinted implant integration and bone recovery in vivo, the bioink is also enriched with osteogenic and angiogenic factors.

In this study we developed the growth factor-loaded BioForceInk and utilized it to create vascularized bone implants by hybrid bioprinting in tandem with cell-laden soft bioink. We evaluated the regenerative potential of the bioprinted vascularized bone implants in a critical-size bone loss model.

BioForceInk offers a unique combination of mechanical support and biological activity that facilitates the single-step fabrication of physiologically relevant bone implants. This study has the potential to advance bioprinting technology toward clinical application, contributing to the development of personalized, mechanically robust, and biologically functional bone implants. With its tunable properties, BioForceInk could be further adapted for the bioprinting of various tissues, reflecting its broad potential across the field.

Oral presentations abstracts

Flash talks Block 1

Targeted Liposomes for Systemic Radiotherapy: Precision Delivery to Liver Metastases

Chen Tzror-Azankot, Adi Anaki, Menachem Motiei, Tamar Sadan, Rachela Popovtzer

Bar Ilan University, Bar-Ilan University

Systemic radiotherapy presents a promising approach for treating both primary tumors and metastatic lesions by delivering β-radiation throughout the body. This strategy overcomes the limitations of traditional radiotherapy, which cannot safely target disseminated and microscopic disease. However, clinical translation has been limited by two major challenges: the lack of universal tumor-specific markers for targeted delivery and a mismatch between the long circulation time of delivery vehicles—particularly antibodies—and the short physical half-life of therapeutic radionuclides.

To overcome these barriers, we developed glucose-functionalized liposomes (GLPs) that enable broad, metabolism-based targeting of tumors. These nanoparticles are functionalized with a DOTA chelator on their surface, allowing precise conjugation of desired radionuclides. GLPs selectively accumulate in GLUT-1-overexpressing cancer cells and exhibit optimized circulation kinetics that align with radionuclide decay, ensuring efficient radiation delivery during peak tumor uptake.

In vivo studies in murine models bearing primary tumors demonstrated significantly higher accumulation of GLPs compared to non-glucose-coated liposomes, confirming GLUT-1-mediated specificity. In liver metastasis models, GLPs showed a threefold higher accumulation in metastatic lesions relative to healthy liver tissue. This targeting efficiency results from the combined effects of active targeting via GLUT-1 and passive targeting through the enhanced permeability and retention (EPR) effect.

These findings suggest that GLPs offer a novel and effective platform for systemic radiotherapy, capable of overcoming key limitations of current delivery methods. By integrating metabolic targeting, radionuclide conjugation, and pharmacokinetic optimization, this approach enhances therapeutic efficacy while minimizing off-target toxicity, presenting a promising path forward for treating aggressive and disseminated cancers. aggressive and disseminated cancers.

Enzyme and Protein Modulated Cascade Mesophase Transitions of Polymeric Formulations

Keerthana Mulamukkil, Orr Sarid, Shahar Tevet, Roey J. Amir

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Over the past few decades, stimuli-responsive polymeric assemblies have gained increasing interest as potential drug delivery systems owing to their ability to encapsulate/covalently bind hydrophobic drugs and release them upon specific stimuli. Among the various types of stimuli that have been explored (pH, temperature, light,...), enzyme-responsive systems hold great potential due to the observed overexpression of disease-associated enzymes such as proteases and lipases in tumor microenvironments, potentially enabling targeted payload release and enhanced therapeutic efficacy. While most reported systems undergo only a single mesophase transition, multi-step transitions could offer complex functionality. Recently, our group developed a modular strategy for enzyme-triggered cascade transitions using co-assembled diblock (DBA) and triblock amphiphiles (TBA) containing enzymatically cleavable dendrons. Upon exposure to an activating enzyme, the fast-exchanging DBA underwent selective degradation, destabilizing the TBA-enriched micelles and initiating a cascade transition to hydrogel micro-particles, which eventually form a bulk hydrogel. The TBA hydrogel network could be subsequently degraded at a slower rate.

To understand the potential of these enzyme-responsive mesophase shifting amphiphiles, it was important to examine the influence of non-specific protein-polymer interactions on its properties and function. For this, we systematically investigated the effects of varying concentrations of bovine serum albumin (BSA) and the activating porcine esterase (PLE) enzyme on the degradation of the DBA and the subsequent transition of the TBA into hydrogels. BSA was found to enhance DBA degradation by increasing unimer availability, thereby accelerating the micelle-to-hydrogel transition. Additionally, it was also observed that the presence of BSA could affect the hydrogel properties by altering its composition. Elevated PLE levels similarly boosted the degradation and transition kinetics. These findings

demonstrated that the timing and progression of each phase transition is affected by protein–polymer interactions, offering a deeper understanding on the structural transformations of this mixed copolymeric mesophase shifting formulation under biologically relevant environments.

DC-Targeted Nanoparticles Enhance Antitumor Immunity by Antigen Presentation Boost & PD-L1 Blockade

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Ben-Gurion University of the Negev

Introduction: Dendritic cells (DCs) within the tumor microenvironment (TME) have an insufficient capacity to activate T-cells via antigen presentation. Furthermore, PD-L1 expressed on tumor-associated DCs downregulates T-cell immune function by interacting with T-cell-expressed PD-1, as well as with co-stimulatory CD80 on the DC surface through cis-interaction, preventing its binding to CD28 on T-cells. Here, we present a strategy to simultaneously promote DC-mediated tumor-antigen presentation and block the inhibitory functions of DC-expressed PD-L1, which in synergy amplify the anti-tumor immune response.

Methods: We synthesized mesoporous silica nanoparticles (MSNPs) that were loaded with Clotrimazole (CLT) and surface-decorated with mannose (MaN) to target DCs and boost MHC II-mediated tumor antigen presentation and additionally conjugated a PD-L1-binding peptide (PDL1bp) to inhibit PD-L1 interactions. Under TME conditions, PDL1bp was cleaved and CLT was released. The MSNPs were tested for their ability to target DCs and to restore the T-cell activating capability of DCs in vitro and anti-tumor immunity in vivo by injection near tumor-draining lymph nodes of subcutaneous B16-F10 melanoma tumor-bearing mice.

Results: MSNP-MaN-PDL1bp/CLT blocked PD-L1 on DCs and increased cellular interactions between DC2.4 and EL4 T-cells and their subsequent IL-2 secretion. The particles were rapidly taken up by DC2.4 cells and promoted hen egg lysozyme (HEL) antigen presentation, as well as activation of HEL antigen-primed 3A9 T-cells. In vivo, the particles remarkably inhibited B16-F10 melanoma tumor growth compared to anti-PD-L1 antibody therapy, and upregulated levels of pro-inflammatory cytokines TNFα and IFNγ and effector molecule Granzyme B in the tumor tissue.

Conclusions: We successfully utilized MSNPs to restore and enhance DC-function via two separate pathways that act in synergy to stimulate T-cell activation in vitro and anti-tumor immunity in vivo. The strategy to trigger DCs to promote T-cell anti-tumor responses may be used to support T-cell-directed immunotherapies and represents a promising alternative to anti-PD-L1 immunotherapy.

Engineering Liposomes with Selectively Enriched Membrane Proteins for Targeted Delivery

Sivan Arber Raviv, Assaf Zinger

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Introduction/Background: Biomimetic nanoparticles (BNPs) are promising platforms for targeted drug delivery and diagnostic applications due to their ability to mimic natural cellular interactions. However, the undefined and variable membrane protein composition in current BNP formulations limits reproducibility and hinders clinical translation. To address this, we propose a bioinspired strategy to selectively enrich specific functional membrane proteins into liposomal membranes, generating enriched nanoparticles (ENPs) with enhanced biological targeting capabilities.

Methods/Materials: ENPs were engineered by incorporating the membrane proteins CD18, CD11a, and CD11b—key adhesion molecules involved in leukocyte migration to inflamed sites (100 kDa, 180 kDa, and 170 kDa, respectively)—into liposomal bilayers. Membrane proteins were fractionated by size using size-exclusion chromatography (SEC), and relevant fractions were validated by Western blot. ENPs were assembled using a microfluidics-based method. Protein incorporation was confirmed using proteomics and Western blot analysis, and the nanoparticle's size, charge, and stability were characterized. ENP accumulation was examined under both static and dynamic (flow) conditions and assessed using microscopy and flow-based methods.

Results: ENPs demonstrated high reproducibility and remained stable for 14 days. Enriching specific functional membrane proteins from the starting material by 3- to 5-fold. Under flow conditions, ENPs exhibited enhanced accumulation and uptake by LPS-activated human endothelial cells compared to liposomes and leukosomes (liposomes incorporating the entire leukocyte membrane protein extract). This suggests improved adhesion-mediated targeting and delivery efficiency.

Conclusions: Selective integration of enriched membrane proteins into liposomes provides a controllable and reproducible method for engineering functional ENPs. Our findings indicate that rationally designed ENPs significantly enhance biological targeting compared to conventional biomimetic platforms. This strategy holds strong translational potential for next-generation therapeutic nanoparticle design.

Nano-Ghosts: A Targeted Drug Delivery Platform for Cardiac Repair after Myocardial Infraction

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Myocardial infarction (MI) remains a leading cause of morbidity and mortality worldwide, highlighting the critical need for effective, non-invasive therapeutic strategies. One of the major clinical challenges is the lack of a systemic drug delivery platform that can selectively target injured cardiac tissue. To address this, our laboratory has developed membrane-derived nanovesicles—termed Nano-Ghosts (NGs)—produced from the plasma membranes of mesenchymal stem cells (MSCs). These nanoparticles retain the parent cells' surface markers, allowing them to home to sites of inflammation.

Objective: To develop a Nano-Ghost-based platform with enhanced cardiac targeting and therapeutic potential for modulating inflammation and promoting regeneration after MI.

Methods and Results: To improve cardiac targeting, we employed two strategies to modify MSCs prior to NG production. In the first, MSCs were transfected with a plasmid encoding Cardiac Homing Peptide (CHP), which preferentially binds to left ventricular cardiomyocytes, commonly affected during MI. In the second, MSCs were cultured under hypoxic conditions (2% O_2), inducing upregulation of migration and adhesion receptors. These two approaches address distinct aspects of MI pathology: targeted delivery to damaged cardiomyocytes and enhanced interaction with inflamed tissues. NGs were then generated from either CHP-expressing or hypoxia-conditioned MSCs. Both CHP-NGs and Hypoxic-NGs demonstrated selectivity toward cardiac cells in vitro and in a permanent MI rodent model. To evaluate therapeutic delivery, NGs were loaded with insulin-like growth factor-1 (IGF-1), known for its cardioprotective and regenerative effects. IGF-1-loaded NGs showed beneficial effects under oxidative stress and hypoxic conditions in vitro and will be further investigated in vivo.

Conclusion: Naive NGs displayed promising targeting and therapeutic potential, which was further enhanced through their surface modification, such as CHP expression and hypoxic conditioning of MSCs. These findings support the potential of NGs to serve as a targeted delivery platform for treating cardiac inflammation and promoting tissue regeneration following MI.

Patient-Derived 3D Metastatic Melanoma Models for Target Discovery and Personalized Therapy

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2 Sheba Medical Center

Objective: Advanced-stage melanoma remains a critical clinical challenge, with high mortality (~90%) and limited therapeutic success due to rapid progression and resistance. Although immunotherapies have revolutionized cancer care, their effectiveness is often limited as many patients develop resistance. Conventional 2D models fail to recapitulate the complexity of the tumor microenvironment (TME), limiting translational relevance. To address this, we developed 3D tumoroids and 3D-bioprinted melanoma models using patient-derived tumor and TME cells. Samples were obtained from an ongoing clinical trial involving 80 patients across seven cancer types. These models offer a robust platform for evaluating personalized therapies.

Methods: Tumor and blood samples were collected from patients enrolled in an ongoing clinical trial at Sheba Medical Center. Tumor tissues were enzymatically dissociated into single-cell suspensions, and PBMCs were isolated from blood samples. These cells were used to generate 3D tumoroids and 3D-bioprinted melanoma models. The 3D-bioprinted models employed two bioinks: one with tumor and TME cells, and another with endothelial cells and pericytes to form perfusable vasculature. Patient-specific H&E-stained slides were analyzed using an AI algorithm to generate tailored treatment recommendations, which were discussed with oncologists and tested in the models. Structural and functional validation was performed using confocal microscopy, multiplex flow cytometry, and viability assays.

Results: Our 3D models successfully predicted patient-specific treatment responses. In a mucosal melanoma case, standard therapies failed clinically

as well as in the tumoroid model. AI-guided screening identified regorafenib (Stivarga©) as a candidate; model testing confirmed efficacy, and subsequent compassionate treatment led to a partial response lasting nearly a year. The 3D-tumoroid models consistently mirrored clinical outcomes across different cancer indications.

Conclusion: Our 3D patient-derived tumoroid models accurately predict treatment responses and bridge the gap between preclinical studies and clinical outcomes. Our robust platform enables personalized drug screening, advancing precision oncology, and accelerating translational cancer research.

Radiation-Guided Dual-Drug Nanoparticles Boost PARP Inhibitor Efficacy in BRCA1-Deficient Tumors

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Objectives: Poly (ADP-ribose) polymerase inhibitors (PARPi) have transformed the treatment of BRCA1-mutated breast (BC) and ovarian cancers (OC), but their efficacy is short-lived. BRCA1-mutated tumors, which express high levels of programmed cell death protein-1 ligand (PD-L1), whose expression is further increased following PARPi treatment, could benefit from combining PARPi with immune checkpoint inhibitor. To address this, we developed P-selectin-targeting nanoparticles (sNPs) co-encapsulating niraparib and a small molecule of PD-L1i in a synergistic ratio which were evaluated on our unique 3D cancer-on-a-chip model.

Methods: sNPs were fabricated via microfluidics and fully characterized in terms of their physicochemical properties. Their stability and drug release were tested under physiological conditions, with efficacy evaluated in 2D and 3D cancer models. Using a 3D microfluidic tumoroid mode, wel assessed their ability to cross biological barriers. We further investigated the NPs' ability to target primary BC and OC as well as brain metastasis of BC in in vivo studies, following radiation as a strategy to enhance P-selectin expression, the ligand for the sulfate groups.

Results: The sNPs exhibited excellent colloidal properties, with a size of ~100 nm, a polydispersity index of 0.1 and a negative zeta potential. Drug encapsulation efficacy was high, approximately 53% for niraparib and 87% for PD-L1i, with a formulation yield of ~60%. NPs demonstrated

stability in biological environments, biocompatibility, hemocompatibility and sustained drug release. Radiation up-regulated P-selectin expression in BRCA1-deficient cancer cells and angiogenic endothelial cells, improving NP accumulation in primary tumors and brain metastases. A comprehensive evaluation using traditional 2D cell cultures, and advanced 3D tumoroids, tumor-on-a-chip platforms, and in vivo models confirmed the superior accumulation and efficacy of sNPs in BRCA1-deficient tumors.

Conclusion : We developed P-selectin-targeted NPs co-delivering niraparib and PD-L1i. Radiation enhanced NP accumulation in tumors, and synergistic drug release improved efficacy, offering a promising strategy against BRCA1-deficient cancers

Soluble Mechanical Signaling as a Novel Regulator of Tumor Spheroid Mechanics

Katerina Tischenko and Ofra Benny

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Solid tumors develop within complex microenvironments rich in mechanical stimuli. While much attention has been given to how cells respond to the stiffness of their extracellular matrix, emerging evidence suggests that mechanical information can also be transmitted through soluble cues, without direct physical contact. Understanding how such signals modulate tumor cell behavior is essential for uncovering new regulatory axes in cancer progression.

In this study, we explore how paracrine-derived mechanical signals—transferred through conditioned media—can regulate the mechanical properties of tumor spheroids. Using 3D culture models, we demonstrate that exposure to soluble factors secreted by mechanically primed or stromal-enriched tumor cultures can modulate the stiffness of naïve spheroids. Notably, this effect occurs independently of matrix adhesion, and is accompanied by cytoskeletal remodeling rather than classical focal adhesion reinforcement.

These findings support the existence of a non-canonical mechanotransduction mechanism in cancer, whereby cells interpret mechanical context through soluble messengers that influence their internal biomechanical state. The ability of tumor spheroids to adapt their mechanical phenotype in response to soluble signals highlights a previously underappreciated form of mechanical communication in the tumor microenvironment.

By revealing this ECM-independent pathway, our work contributes to a broader understanding of how tumors sense, integrate, and respond to their physical surroundings. This insight may have far-reaching implications for drug delivery, tissue penetration, and mechanically targeted therapies, as it

challenges the assumption that cell mechanics are regulated solely by solid-state interactions.

Our findings propose a new conceptual layer in cancer mechanobiology – one that views mechanical adaptation as a dynamic, soluble-mediated process, with potential significance for multiple aspects of tumor development and treatment response.

Size-Dependent Distribution and Retention of Biomimetic Nanoparticles in the Central Nervous System

Anat Lyubin Haimov, Tamar Gross Lev, Assaf Zinger

Technion- Israel institute of technology

Delivery of therapeutic and imaging agents to specific sites in the body – especially the brain – remains a major challenge. The blood-brain barrier (BBB) tightly regulates the passage of ions, cells, and molecules to preserve the neuronal microenvironment. Strategies to facilitate drug delivery across this barrier include modifying drug delivery systems (DDSs) to enhance permeability or utilizing alternative delivery routes that bypass it entirely. Intranasal administration offers a promising non-invasive route, but further optimization of the DDS is required to improve distribution and retention. Biomimetic nanoparticles – liposomes functionalized with membrane proteins – present a tailored approach by harnessing intrinsic cellular capabilities and mimicking extracellular interactions to facilitate targeted delivery.

Two formulations of Neurosomes – liposomes embedded with neuronal membrane proteins from SH-SY5Y cells – were fabricated at 100 nm and 200 nm and compared to size-matched empty liposomes. All nanoparticles were validated for physicochemical properties, including size, zeta potential, morphology (TEM), and protein presentation. In vivo experiments involved intranasal administration in awake mice. Particle distribution and retention were analyzed ex vivo using ChemiDoc MP fluorescent imaging and tracked dynamically using two-photon microscopy up to 3 hours post-delivery.

Small liposomes were rapidly cleared from the brain via both the olfactory and trigeminal pathways. Along the olfactory route, both small and large Neurosomes outperformed small liposomes. In the trigeminal pathway, large Neurosomes demonstrated the highest retention compared to all other formulations. These findings emphasize the role of size and membrane composition in determining the fate of nanoparticles in the CNS and suggest that larger biomimetic nanoparticles delivered intranasally offer a promising non-invasive strategy for drug delivery to the brain.

Bioinspired 4D-Printed Hydrogel Bioadhesives for Rapid, Trauma-free Tissue Repair and Potential Drug Delivery

Qi Wu, Shady Farah

Technion-Israel Institute of Technology

Conventional sutures and staples, common in surgery and wound care, often cause additional trauma, pain, and cost for patients. As alternatives, hydrogel bioadhesives with soft tissue-like features are capable of flexible tissue adhesion, promising for trauma-free tissue repair and healthcare. However, the majority of existing bioadhesives suffer from limited wet tissue adhesion, imprecise fabrication, and insufficient biological functionalities for effective wound management. This work proposes biomimetic hydrogel bioadhesives composed of modified natural tannic acid (TA), hyperbranched polylysine (HPL), and acrylic acid (AA), abbreviated PTLAs, to address such challenges as well as serve as a platform for drug delivery. These PTLAs are fabricated via 4D printing, enabling the precise and controlled production of bioadhesives that are customized in a personalized manner with great reproducibility. Thermal-induced shape memory property allows their applications via minimally invasive surgery. Inspired by molluscs, developed PTLAs exhibit robust tissue adhesion under wet conditions, outperforming many commercial and recently reported bioadhesives. Successful ex vivo lamb and in vivo rat models demonstrate ultrafast (5 seconds) and efficient sealing and hemostasis. Meanwhile, coupled with superior infection resistance, PTLAs ensure enhanced wound healthcare. Additionally, their self-gelling feature allows dry powder adhesion/sealing applications, supporting long-term storage and practical use in diverse healthcare settings. In addition to exceptional tissue adhesion, as-designed PTLAs could maintain their performance in extreme cold and high-pressure environments, making them suitable for promising emergency medicine, battlefield care, and harsh environmental applications. Overall, adaptive tissue-like PTLAs present transformative potential as bio-tapes, bio-bandages, bio-sealants, bio-carriers, etc., paving the way for next-generation bioadhesives design and enhanced drug delivery solutions.

Flash talks Block 2

Genome Editing Using Targeted Lipid Nanoparticles for Mantle Cell Lymphoma Therapy

PhD. Lior Stotsky, Lior Stotsky-Oterin, Dor Breier, Dana Tarab-Ravski, Meir Goldsmith, Inbal Hazan-Halevy, Anjaiah Aitha, Itai Benhar, Dan Peer

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Mantle Cell Lymphoma (MCL) is an aggressive rare B-cell malignancy, genetically characterized by the t(11;14) translocation that leads to overexpression of CyclinD1. Despite recent advances in chemotherapy and immunotherapy, all patients eventually relapse, rendering MCL incurable with current therapies. Therefore, new therapeutic strategies are most needed. SOX11 has emerged as a key transcription factor in the pathogenesis of MCL as it is highly expressed in ~90% of patients, while absent in normal B-cells. Its specific expression in aggressive MCL suggests that SOX11 may serve as a potential therapeutic target. CRISPR-Cas9 is a powerful tool for specific gene editing that holds great promise in treating various conditions, including hematological malignancies. We aim to harness CRISPR-Cas9 technology to specifically knockout SOX11 as a novel potential therapy for MCL. For this, we generated targeted lipid nanoparticles (LNPs) co-encapsulating Cas9 mRNA with sgRNA. To utilize the CRISPR-Cas9 system, we screened multiple sgRNAs and found an efficient candidate reaching ~80% editing in MCL cells. Next, we screened different LNP formulations, optimized composition, and identified a formulation that efficiently delivered CRISPR-Cas9 RNA into ~90% of the treated MCL cells. Combining both, SOX11-CRISPR LNPs led to significant gene editing and consequent cell death of MCL cell lines. To enhance target specificity, we developed an anti-CD38 lipidated single-chain variable fragment (scFv), which was then incorporated into the LNPs, enabling enhanced internalization and efficiency in MCL cells. Furthermore, to evaluate the therapeutic efficacy of our CRISPR-LNPs in-vivo, we established a novel xenograft MCL model that exhibits high engraftment levels of MCL cells in the bone marrow, as in most MCL cases.

Lastly, we performed biodistribution evaluations of the leading formulations, reaching the bone marrow of MCL-bearing mice. Our potential ability to disrupt essential gene expression, in-vivo, specifically in MCL cells, may open new avenues for treating this devastating disease.

Brain-targeted mRNA-LNPs with Improved Neuronal Specificity Validated by AI

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Delivering therapeutics to the brain remains a major challenge due to the restrictive nature of the blood-brain barrier (BBB), which limits the effectiveness of treatments for neurological conditions. Messenger RNA (mRNA)-based protein replacement therapy offers a powerful strategy by enabling the production of functional proteins within diseased brain cells. In this study, we designed brain-targeted lipid nanoparticles (BT-LNPs) to transport mRNA across the BBB with enhanced specificity at both the tissue and cellular levels. The nanoparticles were generated using microfluidic mixing and chemically modified with small molecules that engage BBB transport mechanisms.

Through in vivo screening, acetylcholine and nicotine emerged as leading targeting ligands, with acetylcholine-functionalized LNPs showing the highest brain transfection efficiency. To support these findings, we employed an artificial intelligence (AI) model trained to predict tissue-specific LNP activity. The model retrospectively identified acetylcholine as a top performer, validating the experimental results. Cellular-level analysis revealed that acetylcholine-LNPs predominantly targeted neurons and astrocytes, while nicotine-LNPs were more active in microglia. In addition, glucose-functionalized LNPs extended the duration of mRNA expression in the brain, indicating their potential for sustained therapeutic action.

Due to its strong neuronal targeting, acetylcholine was selected for mechanistic investigation. Results showed that these LNPs enter cells via receptor-mediated pathways in combination with lipid-driven endocytosis, resulting in enhanced mRNA delivery. Acetylcholine-LNPs also achieved efficient gene expression following in vitro BBB transit and in human induced pluripotent stem cell (iPSC)-derived cortical organoids.

Altogether, this study presents a predictive framework for designing CNS-targeted mRNA delivery systems and paves the way toward precision genetic therapies for brain disorders.

CRISPR/Cas9 Genome Editing Using Lipid Nanoparticles for Hepatocellular Carcinoma Therapy

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Hepatocellular Carcinoma (HCC) is the 6th most common cancer and one of the most lethal worldwide. The number of cases keep increasing yearly, and current predictions are that HCC mortality will reach 1 million annual deaths by 2030. As of today, HCC remains resistant to most therapies, including new immunotherapy regimens, which often achieve only a few months of progression-free survival. Therefore, new therapeutic approaches are necessary, with gene editing being a promising direction. Gene editing is a method in which engineered nucleases are utilized to induce double-stranded breaks at specific loci to introduce genomic modifications. One of the most common nucleases currently used in gene editing is the CRISPR/Cas9 system. In the case of cancer, CRISPR/Cas9 can be used to knock out a critical gene and lead to cancerous cells` death. In this work, multiple genes were tested as potential targets, with all sgRNAs leading to high levels of editing. The screening process highlighted that PLK1 is the best candidate as it showed ~65% reduction in viability following the editing process. Next, various lipid nanoparticle formulations were tested to determine the best one at delivering mRNA to the tumor cells via GFP measurements. The chosen formulation was then used to co-encapsulate Cas9 mRNA with PLK1-targeting sgRNA, showing above 90% editing and above 90% reduction in viability in HCC cells, highlighting the system's potential. Next, when testing LNPs' biodistribution in an orthotopic xenograft model, the LNPs showed ~12% penetration into the tumor. Finally, we are set to start a final efficacy experiment in an animal model to test both editing of the tumor and the effects on tumor development. It is our belief that this work may open up a new avenue of treatment for HCC, and potentially one day make the leap from the bench to the bedside.

High-Throughput 3D Microscopy Reveals Symmetric Spheroid-Fibroblast Organization

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Introduction: Multicellular tumor spheroids (MCTSs) are 3D culture models that better mimic in vivo tumor features than traditional 2D systems. Co-culturing these spheroids with fibroblasts enhances physiological relevance by enabling the study of tumor-stroma interactions, particularly the role of cancer-associated fibroblasts (CAFs) in tumor progression. However, imaging these 3D models remains challenging due to the need for z-stacks, long acquisition times, large data volumes, and phototoxicity. To address these limitations, we integrated a Tetrapod phase mask into a high-throughput microscope for depth-encoded imaging and developed unsupervised algorithms for 3D localization using minimal image input. This platform revealed distinct fibroblast-spheroid spatial interaction patterns and enabled efficient drug response analysis.

Methods: We incorporated point spread function (PSF) engineering into a high-throughput microscope using a Tetrapod phase mask, enabling depth encoding in single-plane images. We developed unsupervised algorithms for 3D localization of fluorescently labeled fibroblast aggregates interacting with tumor spheroids. The system was applied to co-culture spheroids of FaDu or SK-136 cancer cells with GFP-expressing 3T3 fibroblasts, imaged across multiple conditions and time points.

Results: Our method enabled low-phototoxicity, rapid 3D analysis of cell interactions using only two images per sample. We discovered a unique, spatially symmetrical fibroblast clustering pattern around spheroids, largely preserved across spheroid sizes and fibroblast concentrations.

Drug treatments altered this organization, allowing early detection and classification of responses. Additionally, fibroblast penetration patterns were found to depend on the cancer cell type, with distinct infiltration profiles observed between FaDu and SK-136 spheroids.

Conclusions: PSF-engineered high-throughput microscopy allows fast and efficient 3D imaging of tumor-fibroblast interactions. This platform enables large-scale screening of spatial cell behavior and drug responses, offering a powerful tool for studying interactions between tumor spheroids and invasive cell populations, such as fibroblasts, immune cells, etc., and for evaluating the therapeutic effects in physiologically relevant models.

30 Long-Acting Liposomal Bupivacaine for Post-Operative Pain Relief

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Objectives: Post-operative pain is often managed with systemic opioids, especially when treating moderate-severe pain. However, opioids carry well-documented risks, including dependence, respiratory depression, and other systemic adverse effects. Bupivacaine HCl provides pain relief for only a few hours, and Exparel, the current extended-release formulation, lasts up to three days. We aimed to develop LBL100, a long-acting liposomal bupivacaine formulation, designed to provide significantly longer postoperative analgesia than Exparel, while reducing bupivacaine HCl toxicity.

Methods: Drug-release kinetics were evaluated using a subcutaneous in vitro model. Analgesic efficacy and tolerability were assessed in Sprague-Dawley rats using a plantar-incision pain model and a maximum tolerated dose (MTD) study. Toxicokinetics of 2-dose subcutaneous injection of LBL100 (30-90 mg/kg) or bupivacaine HCl (9 mg/kg) with 1-week interval were assessed in beagle dogs.

Results: Bupivacaine HCl was cleared in vitro within 3-4 hours, while LBL100 provided sustained release over 3-4 days. In rats, a single dose of LBL100 produced analgesia lasting up to 7-days. It outperformed bupivacaine HCl (<8 h) and Exparel (<48 h), demonstrating a strong in vitro-in vivo correlation. In the rat MTD study, LBL100 was well tolerated up to 180 mg/kg

(4–6–fold the bupivacaine HCl dose), and the MTD was not reached, though mild sedation and local tissue responses were observed. In dogs, peak plasma concentrations (Cmax) for LBL100 were generally comparable to or slightly higher than those of bupivacaine HCl. Both formulations showed rapid absorption, with time to Cmax (Tmax) of approximately 0.5–hour. However, LBL100 resulted in prolonged drug exposure without significant accumulation. Tissue analysis confirmed retention for ≥2–weeks, consistent with depot–based release.

Conclusions: Results from preclinical models indicate that LBL100 drug–product achieved its objectives, resulting in longer and more effective analgesia than both bupivacaine HCL and Exparel, with favorable safety profile. These findings support clinical development for post–surgical pain control.

3D Printing of Personalized Catheters with Smart pH-Responsive Coating for Improved Functionality for Long-Term Therapy Delivery

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Hydrocephalus is a common brain disorder. The existing gold standard treatment method for hydrocephalus depends on surgical cerebrospinal fluid shunting using "one-size-fits-all" catheters, which are subjected to various complications, such as flow resistance, blockage, mechanical malfunctions, host-immune response, and microbial infection. Herein, we proposed implementing three-dimensional (3D) printing technology to develop the next generation of catheters with improved functionality and controlled liquid flowability, which can also be used as part of drug delivery systems. Our suggested technology is based on imaging data on the final destination in a personalized manner. In this work, we report for the first time, digital light processing (DLP) 3D printing of helical-shaped, flexible catheters using commercially available KeySplint soft resin. These catheters are fully customizable, where different parameters can be manipulated, such as diameter, the number and placement of drainage holes tailored to individual patient needs. The stability study of the 3D-printed KeySplint samples proved

the structural stability under physiological conditions for at least 3,240 hrs (135 days). Moreover, to further enhance the catheter's functionality, a pH-responsive smart surface chemistry was introduced on the catheter surface using two strategies (via plasma coating and by simply mixing with 3D printing resin). The coating can respond dynamically to tackle two critical challenges related to catheters: blockage of the catheters and infection/ biofilm prevention via chemical intramolecular rearrangement. Both CB-OH coated and 5% CB-OH mixed 3D-printed catheters significantly inhibited bacterial biofilm formation compared to the catheter control. Additionally, the CB-OH coated 3D-printed helical catheters showed a 37-folds reduction in particle deposition per unit volume relative to conventional 3D-printed linear catheters. Thus, the proposed surface-functionalized 3D-printed personalized catheters could provide a promising solution for many medical implants and treatments, as well as a methodology for long-term therapies and delivery of drugs.

DC-Targeted Nanovaccine Boosts Immunity and Efficacy of SoC and KRAS-Targeted Therapies inPDAC

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Objectives: Pancreatic ductal adenocarcinoma (PDAC) has a low survival rate due to its immunosuppressive nature and resistance to chemotherapy. To address this, we developed a dendritic cell (DC)-targeted nanovaccine (NV) to boost anti-cancer immunity.

Methods: The NV is composed of biodegradable polymers (PLGA/PLA) functionalized with mannose for targeted uptake by DCs and co-loaded with TLR agonists and PDAC-specific peptides derived from CEACAM5 protein, overexpressed in >90% PDAC cases. The NV efficacy was assessed on mice and patient-derived models, following physicochemical characterization, which demonstrated a diameter of 180 nm and preclinical safety.

Results: The NV induced significant changes in vivo in PDAC's TME, increased effector cells, including CD8 T cells, and decreased regulatory cells, such as Tregs and myeloid-derived suppressor cells. Combining the NV with chemotherapy (Gemcitabine/Nab-Paclitaxel) or targeted therapy (KRAS G12D inhibitor) further enhanced therapeutic outcomes compared to monotherapy. The combination therapy significantly repressed tumor growth and prolonged survival in an orthotopic model. From the proteomic analysis of the serum from NV-treated mice, we found five significant genes that participate in antigen processing and presentation, suggesting systemic activation of the immune system by the NV. Furthermore, we established a patient-derived ex vivo model using autologous PBMCs and 3D

tumor spheroids to evaluate NV efficacy. This unique 3D model enabled us to assess ex vivo the NV's effect on PDAC patient samples. We show that CECAM5 NV-activated T cells decrease 3D-spheroid size and increase IFN-γ secretion as well as Caspase-3 expression on cancer cells compared to untreated T cells.

Conclusions: Our NV induced a strong antigen-specific immune response and limited tumor growth while reshaping PDAC's immunosuppressive TME. Our 3D patient-derived model enables assessment of NV-driven immune responses and drug combinations in a clinically relevant context. This platform offers a strategy to generate robust immunity in cold tumors like PDAC.

MILKOSOMES – Breast Milk Biomimetic Nano Particles as a Versatile, Non-Invasive, Oral Drug Delivery

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Objectives: The main objective of this research is to develop an innovative approach for oral drug delivery by harnessing the unique properties of breast milk cells. The specific goals include identifying the cell populations from human breast milk that successfully traverse the gastrointestinal (GI) tract and engineering biomimetic phospho-lipid nanoparticles called "MILKOSOMES" for oral drug delivery.

Methods: To achieve these objectives, the research methodology involves several key steps. Initially, the study utilizes methods such as Fluorescence-Activated Cell Sorting (FACS) and RNA single cell sequencing to identify the maternal cell populations present in the blood circulation of nursing pups in-vivo. Subsequently, MILKOSOMES are engineered by a microfluidic technique using NanoAssembler. The MILKOSOMES are then characterized using dynamic light scattering (DLS) and transmission electron microscopy (TEM). The stability of MILKOSOMES in simulated gastric fluids is assessed, and their ability to cross the intestinal barrier is evaluated in-vitro using Caco2 cells (a human intestinal cell line) and ex-vivo using porcine intestine samples.

Results: The development of MILKOSOMES, incorporating membranal proteins from human breast milk cells and leukocytes, which are the main maternal cell populations crossing the GI tract during breastfeeding, has been successfully achieved. Furthermore, our in-vitro and ex- vivo studies have demonstrated the stability of MILKOSOMES in GI tract conditions and their enhanced capability to cross the intestinal barrier.

Conclusions: The findings obtained from this research establish a robust basis for future investigations and underscore the immense potential of MILKOSOMES as a transformative advancement in drug delivery platforms.

Significantly, the major medical impact of this research lies in its ability to make any large molecular drug orally bioavailability. This breakthrough has far-reaching implications, as it could revolutionize the administration of crucial medications such as insulin, chemotherapy agents, vaccines, and more, making them suitable for oral delivery

Double layer and Dual Drug Loaded Microneedle Patch for Comprehensive Skin Therapy

Gali Cohen, Adi Gross, Boaz Mizrahi

Technion

Microneedle-based drug delivery offers a minimally invasive approach for localized and controlled release of therapeutics. However, achieving precise temporal release of multiple drugs remains a major challenge, especially for clinical scenarios requiring both rapid and sustained pharmacological action. In this study, two novel microneedle (MN) designs were developed for the controlled co-delivery of bupivacaine (a local anesthetic) and ampicillin (an antibiotic), utilizing polymer matrices with distinct dissolution properties to modulate release kinetics. In the first model, a double-layered structure was constructed where the needle tip consisted of a hyaluronic acid (HA) and ampicillin mixture, designed for rapid dissolution, while the core and base were composed of chitosan loaded with bupivacaine, providing a slower, sustained release. In the second model, a chitosan-bupivacaine MN was coated with a layer of HA-ampicillin. Both MN designs exhibited uniform morphology and adequate mechanical strength suitable for skin insertion. Spinning Disk Confocal (SDC) microscopy confirmed the spatial distribution of the polymers within the MNs. In the double-layered model, HA was confined to the needle tips, with chitosan located at the base and minimal diffusion between layers. In the coated model, HA formed a distinct outer shell while chitosan remained distributed throughout the interior. In vitro drug release studies using Franz diffusion cells demonstrated that ampicillin was rapidly released, reaching complete (100%) release after 48 hours, while bupivacaine exhibited a more sustained release profile, reaching only 57% over the same period. These findings demonstrate that controlled dual-drug release can be achieved by leveraging the differential dissolution kinetics of HA and chitosan and the morphology of the MN. These platforms hold significant potential for clinical applications such as those requiring immediate antimicrobial protection and prolonged analgesia, such as in post-surgical care and wound management.

Living Materials Approach for In-Situ Bio-Polymers Production Using Bacteria in Microneedles

Caroline Hali Alperovitz, Noa Ben David, Adi Gross, Boaz Mizrahi

Technion

Living biomaterials, which integrate live organisms with traditional macromolecular scaffolds, function as "live manufacturers" capable of sensing their environment, synthesizing, and releasing biomolecules while remaining stable under physiological conditions. While systems that produce small biomolecules continue to advance, in situ production and secretion of high-molecular-weight biopolymers remain relatively underexplored. Here, we present a microneedle (MN) patch system encapsulating Bacillus paralicheniformis—a non-pathogenic, Gram-positive bacterium known for its production of γ-polyglutamic acid (γ-PGA). The MNs were designed to painlessly penetrate the stratum corneum and reach the dermis. Bacteria were uniformly distributed within the patch, and their presence had minimal impact on the microneedles' morphology and mechanical integrity. Upon application, B. paralicheniformis was released from the MNs and successfully produced γ-PGA, with molecular weights ranging from 64 to 563 kDa. Growth studies revealed that LB medium supports optimal bacterial proliferation, while E medium enhances γ-PGA biosynthesis. In vivo studies confirmed that B. paralicheniformis colonized mouse skin following MN administration and secreted γ-PGA without eliciting toxicity or inflammatory responses. Given the increasing therapeutic use of biopolymers and proteins for treating chronic and acute skin conditions, this living bacterial delivery system offers a promising platform for sustainable and symbiotic dermal therapies.

Poster Session 1 – September 7th

1	Ari	Levine	Sustained Drug Release: The Development of a Novel Liposomal Drug-Product Prototype for the Local AD
2	Yael	Shilo-Benjamini	Pharmacokinetics and tolerability of liposomal synthetic cannabidiol subcutaneous depot in calves
3	Yael	Shilo-Benjamini	Liposomal CBD injection in dogs: A randomized, blinded, placebo-controlled, crossover clinical trial
4	Michal	Brodsky	Programmable Formulation of Dual-Responsive Polymeric Micellar System that Undergoes Multi-Mesophase
5	Avichai	Srebrnik Gabbay	Tuning hydrophilicity and hydrophobicity to control enzyme-responsive amphiphile disassembly rate
6	Omer	Kfir	Automated Predictive Kinetic Modeling for Lipid Conjugation Synthesis
7	Ron	Kleiner	DC-Targeted Nanovaccine Boosts Immunity and Efficacy of SoC and KRAS-Targeted Therapies in PDAC
8	Anne	Krinsky	Revolutionizing Colorectal Cancer Treatment through 3D Models
9	Hala	Dawud	Programmable Mesophase Shifting Microneedles from Dendritic Tri-block Amphiphiles for Sustained Anti
10	Amartya	Sanyal	Activatable Dye and Dye-Conjugate Synthesis for Fluorescence Monitoring, PDT and SDT
11	Marina	Green	Antitumor activity of αHER2-topoisomerase I inhibitor conjugate via self-immolative dendritic linker
12	Ohad	Hasin	Optimized PLGA-PEG nanoparticles for targeted delivery and controlled release of small molecules
13	Ahuva	Cern	Prolonged release formulations of cannabidiol-protein complexes
14	Yulia	Chulanova	Using Lipid Nanoparticles to Deliver Genetic Medicine for Duchenne Muscular Dystrophy
15	Ester	Davis	Particle Uptake Patterns as a Treatment Tool of Bladder Cancer
16	Mor	Ozeri	Hypoxia-Induced Drug Sensitivity and Nanoparticle Uptake in Cancer Cells
17	Lipaz	David Glam	Magnetic Nanoparticles for Target Cell Capture: A Novel Diagnostic Approach for Endometriosis
18	Shiri	Katzir	Tiny Particles, Big Plans: Nanoparticles for Controlling Drug Transfer through the Placental Barrier
19	Yael	Fink	Delivery to synthetic cells using nanoparticles
20	Mohammad	Okkeh	Developing Optical Nanosensors for Monitoring Chemotherapy
21	Egor	Egorov	Robiochemistry: A Revolutionary Online Practical Education Platform

22	Yasmeen	Zahran	Developing Optical Nanosensors to Monitor Obesity
23	Noemie	Chekroune	Developing Optical Implantable Matrices for Clinical Monitoring
24	Riccardo	Rampado	Targeting mRNA Lipid Nanoparticles to inflammatory sites
25	Georgette	Maroukian	Nanoparticles with Sustained Release of L-NAC for Treating Primary Sclerosing Cholangitis
26	Keerthana	Mulamukkil	Enzyme and Protein Modulated Cascade Mesophase Transitions of Polymeric Formulations
27	Ajay	Gupta	Liposomal Formulation of Cyclometalated Iridium(III) complex as Anticancer Theranostic Agents
28	Yasmin	Habib	Multifunctional 2D Nanomaterials for Precision Cancer Therapy Triggered by Low-Energy X-Rays
29	Niv	Cohen	Nanomedicine and nanoscale formulations
30	America	Garcia Alvarado	TARGETED NANOPARTICLE DELIVERY IN PEDIATRIC BRAIN TUMORS USING A 3D MICROFLUIDIC TUMOROID-BBB MODEL
31	Eden	Freundlich	Functional microneedle for endotoxin removal directly from skin infection
32	Adi	Yona	Computer-Assisted Drug Design for the Discovery of Small Molecule Inhibitors for the TIGIT-PVR Axis
33	Anat	Glozman	Mechano-Profiling and Modulation of Red Blood Cell-Based Carriers
34	Tamar	Gross Lev	Resected Tumor Biomimetic Nanoparticles for Personalized Immunotherapy
35	Assaf	Bar	Exploring Cellular Tropism of mRNA-LNP Formulations for Treating Non-Alcoholic Fatty Liver Disease
36	Ofri	Vizenblit	Treating Triple-Negative Breast Cancer using Immunotherapeutic TAMs-mimicking Nanoparticles
37	Hila	Elbaz-Assor	Modulating the Metastatic Microenvironment of TNBC Using Biomimetic Nanoparticle
38	Mia	Albalak Menasherov	Developing Lipid Nanoparticle-Mediated Delivery of GRIN2B pDNA for Targeted Gene Therapy in GRIN2B-R
39	Suzan	Shehady	An Abdominal Aortic Aneurysm Micro-Physiological Model for the Study of Localized Nano-Therapeutics
40	Somu Naidu	Gonna	A Rational Design of Ionizable lipids for Lung-Specific mRNA delivery
41	Marie	Ruetter	DC-Targeted Nanoparticles Enhance Antitumor Immunity by Antigen Presentation Boost & PD-L1 Blockade
42	Sivan	Arber Raviv	Engineering Liposomes with Selectively Enriched Membrane Proteins for Targeted Delivery
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Poster Session 2 - September 8th

1	Orr	Bar Natan	Functional Personalized Complex Combination Nano Therapy for Osteosarcoma
2	Igal	Porat	Quantum Fertilizer for Agriculture: Enhancing Photosynthesis via Photocatalytic Ag2S Quantum Dots
3	Noga	Sharf-Pauker	Scaling Up Synthetic Cell Production Using Robotics and ML Toward Therapeutic Applications
4	Melad	Atrash	Rose Bengal Conjugated to Lectins for Targeted Antibacterial Photodynamic Treatment
5	Aviad	Elisha	P53 is a critical tumour suppressor protein that plays a key role in regulating the cell cycle and p
6	Ilana	Teboul	DIAGNOSTIC PROBE FOR SERUM RHEUMATIC HEART DISEASE BIOMARKERS DETECTION
7	Ilana	Elizarov	Biomimetic Microglia-Derived Nanoparticles for Reducing Traumatic Brain
8	Valeria	Rahamim	Noninvasive Drug Delivery: Leveraging the Power of Epithelial Cells
9	Amani	Zoabi	Stereoselective Interactions of Chiral Polyurea Nanocapsules with Albumins
10	Rotem	Menachem	BONE MARROW CXCR4-TARGETED LIPOSOMES LOADED WITH BORTEZOMIB OVERCOME MULTIPLE MYELOMA RESISTANCE
11	Keren	Turjeman	Long-Acting Liposomal Bupivacaine for Post-Operative Pain Relief
12	Adi	Anaki	Enhancing Therapeutic Efficacy and Immune Response with Bispecific Gold Nanoparticles in Cancer
13	Danielle	Nemcovsky	Shear Responsive Red Blood Cell-Based Carriers for Targeted Delivery
14	Roy	Goldraich	From Micro-Crystals To Nano-crystals for Enhanced Delivery and Biological Applications
15	Edwar	Odeh	Engineering and Formulating Long-Releasing Hollow-like or Condensed Progesterone Hormone Microcrystals with Controlled Polymorphism and Delivery Properties
16	Eid	Nassar-Marjiya	Development of Water-Soluble Functionalized Oligomers with Controlled Bleach Releasing Properties for Long-Term Antiviral Applications
17	Maya	Naim	Development of a High-Throughput Assay for Screening Platelet-Rich Clot Dissolution Using Automated
18	Or	Kandli	3D-Bioprinted Capsules for the Co-Delivery of Live Bacteria and Small Molecule Immunotherapies
19	Elissar	Ibraheem	Protein Crystallization for Drug Delivery Application
20	Krishanu	Ghosal	Precision 4D Printing of Multifunctional Olive Oil-Based Acrylate Photo-resin for Biomedical and drug delivery application
21	Mofeed	Elias	Synthesis of Multifunctional Biodegradable Polyesters for Drug delivery and Biomedical Applications
22	Haim	Kadosh	Brain-targeted mRNA-LNPs with Improved Neuronal Specificity Validated by AI
23	Dana	Nir	Enhancing Drug Permeability Into Solid Tumors Via Optoelectronic Silicon Nanowires-Mediated Electrop

24	**Viktor**	**Osmanov**	Mucoadhesive Chitosan-Polydopamine Hydrogels for Oral Delivery of Liposomes Targeting the Brain
25	**Nagham**	**Moallem Safuri**	3D Printing of Personalized Catheters with Smart pH-Responsive Coating for Improved Functionality for Long-Term Therapy Delivery
26	**Hadar**	**Lecker**	Targeted cell-derived NanoGhost as a platform for metastasis high resolution diagnostics
27	**Qi**	**Wu**	Bioinspired 4D-Printed Hydrogel Bioadhesives for Rapid, Trauma-free Tissue Repair and Potential Drug Delivery
28	**Simran**	**Jindal**	Ginger-derived biofilm antagonistic 3D-printable photoresins for complex implant designs for multifunctional biomedical and potential delivery applications
29	**Majd**	**Bisharat**	Engineering fully quaternized (Dimethylamino)ethyl methacrylate-based photoresins for 3D printing of biodegradable antimicrobial releasing polymers
30	**Nadine**	**Kana'an**	Formulating Multifunctional Bioactive Polymeric Hydrogels with Drug-Releasing Capabilities for Potential Wound Healing Management
31	**Noor**	**Wishahi**	Crystalline Formulations of Multiple Combined Drugs for Parallel Release Features
32	**Si**	**Naftaly Kiros**	MILKOSOMES – Breast Milk Biomimetic Nano Particles as a Versatile, Non-Invasive, Oral Drug Delivery
33	**Anat**	**Lyubin**	Size-Dependent Distribution and Retention of Biomimetic Nanoparticles in the Central Nervous System
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Posters Abstracts

Sustained Drug Release: The Development of a Novel Liposomal Drug- Product Prototype for the Local AD

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Introduction: Resolvin-D1 (RvD1) is a potent lipid mediator, known for its role in inflammation resolution and bone regeneration. Yet, despite its potency, RvD1 alone is cleared and metabolized by the body too quickly to have a sufficient duration of action. This study aims to develop an RvD1 drug-product prototype based on its encapsulation in large liposomes, as an effective RvD1 delivery system for local treatments. The long retention of these locally administered liposomes at the site of action, and the slow and controlled release of RvD1 there, can keep RvD1 above the therapeutic level for a prolonged period, enabling it to achieve a therapeutic effect.

Materials & Methods: Proprietary liposomal formulations were compared based on three variable parameters. Optimization was assessed based on in vitro evaluation, testing the encapsulation efficiency, release rate, and release duration of the active agent using ELISA analysis, as well as liposomal size, size distribution, and trapped volume.

Results: The optimized liposomal formulation showed a significant increase in its encapsulation efficiency of RvD1. Furthermore, following drug encapsulation, the optimized formulation significantly increased both the total amount of drug released as well as prolonged duration of significant drug release.

Conclusions: These results suggest that the optimized liposomal formulation will produce a drug-product prototype with the relevant optimal physicochemical characteristics necessary for sustained local drug release. Thus, this liposomal formulation is ready to be used in the relevant animal models of bone remodeling and modulation, to test for therapeutic efficacy as well as safety.

Pharmacokinetics and tolerability of liposomal synthetic cannabidiol subcutaneous depot in calves

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Prolonged pain is observed in neonatal calves undergoing husbandry procedures, such as disbudding, while the analgesics used have only a short-term effect. Cannabidiol (CBD) was reported to provide analgesia, however, first-pass liver metabolism results in low oral bioavailability. Liposomal encapsulation of CBD facilitates slow-drug-release, providing long-term plasma concentrations, increased bioavailability and consistent effects. Six Holstein calves (age 8-16 days; body weight 42.7-52.8 kg) were evaluated for pharmacokinetics and tolerability of a single SC injection of liposomal-synthetic-CBD (L-sCBD; 5 mg kg-1; 50 mg mL-1). Blood was sampled for CBD and metabolites plasma concentrations, complete blood count, serum chemistry and serum amyloid A (SAA) before and up to 6 weeks after injection. Physiologic parameters and adverse effects were monitored. Data overtime was compared with baseline using linear-regression mixed-effects (p-value < 0.05). Plasma CBD concentrations were detected for 4.5 (range 3-6) weeks; with median (range) peak plasma concentration (Cmax) of 44.1 (33.0-48.0) ng mL-1, time to Cmax 1 (0.25-1) day, and half-life 5.3 (3.8-11.6) days. The primary metabolite was 7-carboxy-CBD, which exceeded CBD exposure; the area under the concentration-time curve (AUC) ratio of 7-carboxy-CBD:CBD was 9.0 (4.2-16.1). A short-term significant increase in neutrophils was observed 2-days after injection. Several chemistry

parameters changed from baseline but were clinically insignificant. SAA decreased significantly from baseline. The main adverse reaction was a local swelling, cytologically characterized as a sterile granulomatous inflammation, which spontaneously resolved within 2-weeks. In conclusion, L-sCBD administered SC produced detectable CBD plasma concentrations for several weeks and was well tolerated by calves. The decrease in SAA, a positive acute-phase-protein, suggests that no systemic inflammatory response to injection occurred. Evaluation of L-sCBD as an additional long-term analgesic in calves undergoing routine painful husbandry management procedures (e.g., disbudding and castration) is therefore of interest.

Liposomal CBD injection in dogs: A randomized, blinded, placebo-controlled, crossover clinical trial

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Oral administration of cannabidiol (CBD) was reported to provide analgesia in dogs with osteoarthritis. Study objectives were to determine efficacy, pharmacokinetics and safety of large multilamellar vesicles of liposomal-synthetic-CBD (L-sCBD) injection compared with placebo in dogs with radiographically confirmed naturally-occurring osteoarthritis.

Eight dogs (4 males, 4 females; 8.5 [4.5-12.5] years-old; 34.9 [22.7-42.7] kg) were injected subcutaneously twice with 4-weeks interval; once with 7 mg/kg L-sCBD (50 mg/mL) and once with empty liposomes (placebo; equivalent volume) in a randomized, blinded, crossover design. Routine analgesics were continued. Before and 4-weeks after each injection, blood was sampled for CBD and metabolites concentrations, complete blood count and biochemistry. Efficacy was assessed via activity monitoring collar and scorings by owners and veterinary specialists. Adverse effects were monitored.

CBD plasma concentrations were detected up to 4-weeks in all dogs. Median (range) peak plasma concentration (Cmax) was 58.2 (35.1-141.0) ng/mL, time to Cmax was 3 (3-7) days and half-life 6.1 (4.6-9.5) days. The metabolites 6-hydroxy-CBD, 7-hydroxy-CBD and 7-carboxy-CBD were detected at low concentrations. Pain and lameness scores and behavior were significantly improved after L-sCBD treatment versus placebo. At 3-days after L-sCBD treatment, neutrophils and alkaline-phosphatase increased significantly,

while hematocrit and albumin decreased (all within reference interval, except neutrophils in 2/8 dogs). Adverse effects included 2-days fever and a minor-moderate local swelling, which resolved spontaneously.

In conclusion, subcutaneous L-sCBD provided long-term CBD plasma concentrations, improved analgesia and was tolerated by all dogs. A larger clinical cohort is required to further assess L-sCBD benefits and safety.

Programmable Formulation of Dual-Responsive Polymeric Micellar System that Undergoes Multi-Mesophase

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In recent years, stimuli-responsive nanostructures have attracted significant attention for their ability to selectively disassemble and release encapsulated cargo in response to external triggers. Such systems are particularly promising for drug delivery, as they can undergo changes in their chemical structure and physical properties upon exposure to specific stimuli, such as changes in pH, temperature, or the presence of enzymes. These triggers can induce morphological transitions between different self-assembled states, enabling dynamic control over structure and function. Tuning these transitions through precise chemical modifications of the amphiphilic building blocks provides a valuable step towards the design and performance of responsive delivery systems.

More complex systems, which are capable of undergoing multiple mesophase transitions, can potentially offer a more advanced platform for controlled drug delivery. For example, carriers in their micellar state have the potential to be injected and circulate rapidly in the body, accumulating at disease sites. Then, upon an enzymatic stimulus, the polymers can transition from stable micellar nanostructures to soft hydrogels, which can serve as a drug depot. After cargo release, the polymers can be further degraded into soluble polymers that can be readily cleared from the body. Our group recently reported a novel strategy for programming polymeric micelles to undergo sequential mesophase transitions into hydrogel and later into degraded soluble polymers, demonstrating how molecular architecture and enzyme specificity can be utilized to control these transitions.

In this work, we extended this approach to demonstrate the ability to molecularly program formulations to respond to two different types of stimuli by co-assembling di- and tri-block amphiphiles with two types of stimuli-responsive end-groups. We show the ability to tune the degradation rate by changing the ratio of the amphiphiles in the formulation. This tunability can be very beneficial for future programming of such mesophase shifting drug delivery systems.

Tuning hydrophilicity and hydrophobicity to control enzyme-responsive amphiphile disassembly rate

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Over the past few decades, there has been a significant interest in stimuli-responsive amphiphilic block copolymers that can self-assemble into various nano-sized structures in aqueous media due to their great potential as drug delivery systems. Among these polymeric assemblies, micelles show great potential due to their ability to encapsulate lipophilic drugs and thus enhance their solubility and decrease their toxicity and side effects. Moreover, stimuli-responsive polymeric micelles can be programmed to respond to specific cues, enabling the delivery and selective release of the drug at a controlled rate in the target site with little interference to healthy cells. Among the various types of stimuli-responsive polymeric assemblies, enzyme-responsive ones are particularly attractive since overexpression of various enzymes has frequently been observed in different diseases.

In this work, we developed a series of enzymatically degradable diblock amphiphiles with varying hydrophilic-to-hydrophobic ratios by altering either the hydrophilic block or the hydrophobic block. We characterized their self-assembly into micelles and studied the kinetics of their enzymatic degradation. The results shed light on the effects of the degree of hydrophobicity, the length of the hydrophilic block, and the hydrophilic-to-hydrophobic ratio on enzymatic degradation rates, demonstrating the ability to use precise molecular structure to design polymeric micelles with a broad range of degradation rates.

Automated Predictive Kinetic Modeling for Lipid Conjugation Synthesis

Omer Kfir

Designing and optimizing biochemical synthesis, such as the conjugation of lipids for advanced nanocarrier development, remains a complicated and resource-intensive endeavor, given the vast number of potentials lipids species and possible reactions, it's impractical to identify all relevant pathways and accurately estimate their kinetics or thermodynamics properties. A predictive kinetic model, forecasting reactions network and their dynamics, is a powerful tool addressing these needs, leading to a significant reduction in the number of required experiments during R&D, efficient utilization of resources and enabling improve products and synthesis processes. Computational modeling software programs have proven instrumental in various aspects of prediction and analysis in this field. However, a significant limitation persists: the lack of a single, fully automated framework capable of integrating these individual capabilities from minimal user inputs such as components, conditions and kinetic or thermodynamic libraries.

We aim to develop a platform that will need minimum data from the user and will be able to automate construct comprehensive predictive kinetic models, estimate missing kinetic or thermodynamic parameters and execute dynamic simulations of any lipid conjugation synthesis system. The platform employs a unique "core-edge" network generation algorithm, inspired by the Reaction Mechanism Generator (RMG) software for combustion reactions, which iteratively expands the reactions network by identifying high-flux edge species and adding them to the core. To address the scarcity of reliable kinetic parameters, the platform will integrate a hybrid approach combining database retrieval with machine learning approach (Graph Neural Network). Missing thermodynamic properties will be estimated using the Benson group additivity method. Missing ground truth data will be obtained from integration with high-throughput experimental data generation, allowing for dataset creation, model refinement and validation. This platform is expected to provide in-silico framework capable of creating a kinetic predictive model directly addressing the need for precise lipid conjugate synthesis.

DC-Targeted Nanovaccine Boosts Immunity and Efficacy of SoC and KRAS-Targeted Therapies in PDAC

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Objectives: Pancreatic ductal adenocarcinoma (PDAC) has a low survival rate due to its immunosuppressive nature and resistance to chemotherapy. To address this, we developed a dendritic cell (DC)-targeted nanovaccine (NV) to boost anti-cancer immunity.

Methods: The NV is composed of biodegradable polymers (PLGA/PLA) functionalized with mannose for targeted uptake by DCs and co-loaded with TLR agonists and PDAC-specific peptides derived from CEACAM5 protein, overexpressed in >90% PDAC cases. The NV efficacy was assessed on mice and patient-derived models, following physicochemical characterization, which demonstrated a diameter of 180 nm and preclinical safety.

Results: The NV induced significant changes in vivo in PDAC's TME, increased effector cells, including CD8 T cells, and decreased regulatory cells, such as Tregs and myeloid-derived suppressor cells. Combining the NV with chemotherapy (Gemcitabine/Nab-Paclitaxel) or targeted therapy (KRAS G12D inhibitor) further enhanced therapeutic outcomes compared to monotherapy. The combination therapy significantly repressed tumor growth and prolonged survival in an orthotopic model. From the proteomic analysis of the serum from NV-treated mice, we found five significant genes that participate in antigen processing and presentation, suggesting systemic activation of the immune system by the NV. Furthermore, we established a patient-derived ex vivo model using autologous PBMCs and 3D tumor spheroids to evaluate NV efficacy. This unique 3D model enabled us to assess

ex vivo the NV's effect on PDAC patient samples. We show that CECAM5 NV-activated T cells decrease 3D-spheroid size and increase IFN-γ secretion as well as Caspase-3 expression on cancer cells compared to untreated T cells.

Conclusions: Our NV induced a strong antigen-specific immune response and limited tumor growth while reshaping PDAC's immunosuppressive TME. Our 3D patient-derived model enables assessment of NV-driven immune responses and drug combinations in a clinically relevant context. This platform offers a strategy to generate robust immunity in cold tumors like PDAC.

Revolutionizing Colorectal Cancer Treatment through 3D Models

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Introduction: Gastrointestinal (GI) cancers, including colorectal, pancreatic ductal adenocarcinoma (PDAC), and gastric cancers, represent a third of cancer-related deaths worldwide and pose substantial therapeutic challenges. Despite advances in drug development, the standard of care (SoC) remains chemotherapies. Moreover, the survival rates for advanced-stage patients remain low.

Many drugs that show promise in laboratory settings fail in clinical trials, often due to inadequate models. Conventional preclinical models, like 2D-cell cultures and immunodeficient-mouse models, do not accurately reflect the complex tumor-stromal-immune cell interactions in the tumor microenvironment (TME). As a result, they fall short of replicating human tumors, hindering the translation of preclinical findings into clinical practice.

Materials and Methods: To address this gap, we are developing advanced 3D-models that closely replicate the TME of GI cancers: (1) 3D-Bioprinted model, (2) Tumor-on-a-Chip model, and (3) patient-derived organoids. These models will incorporate elements of the GI cancers' extracellular matrix, stromal cells, serum, and immune cells, accurately representing the clinical TME, including its cellular, molecular, and mechanical properties.

Results and discussion: As immunotherapies and targeted therapies

continue to show untapped potential, especially in GI cancers, we utilized our models as a platform for drug development. By accurately mimicking the TME, we evaluated the effects of novel therapies, including those developed within our laboratory, that will hopefully lead to new therapeutic options such as an anti-PD-1 antibody-attenuated IL2-fusion protein.

Conclusion: This research seeks to transform the preclinical landscape by developing 3D-models that connect laboratory research with clinical application, facilitating predictions of patient outcomes and innovative approaches to treating GI cancers.

Programmable Mesophase Shifting Microneedles from Dendritic Tri-block Amphiphiles for Sustained Anti

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Hydrogel forming microneedles (HFMNs) are solid MNs that transform into hydrogel upon absorption of skin interstitial fluid, whereas dissolving MNs (DMNs) dissolve upon insertion, releasing the encapsulated drug as a function of the polymer`s dissolution rate.

Using tri-block polymeric amphiphiles based on linear PEG, as the hydrophilic block, and dendrons with enzymatically cleavable end-groups, as the hydrophobic blocks, we developed a promising platform for a new type of MNs - mesophases shifting microneedles (MSMNs). The mesophase shifting mechanism is based on the tendency of these amphiphiles to form (i) hydrogels upon contact with water1,2, and subsequently undergo a transition into (ii) hydrogel microparticles, which can then be degraded into (iii) soluble hydrophilic polymers in the presence of target enzymes that cleave the hydrophobic end-groups of the dendrons. Exploring MSMNs made from dendritic tri-block amphiphiles with varying lengths of hydrophobic end-groups as a modular platform, we examined how structural changes affect the drug release kinetics, the integrity, and mechanical performance of the MNs. The developed MSMN arrays, were loaded with an antifungal agent and demonstrated high drug content, sufficient mechanical strength, and excellent insertion ability. By testing the MSMNs using full thickness porcine skin, we could show their ability to penetrate and undergo complete dissolution. To further study their therapeutic potential, these MSMNs were

tested against Candida albicans and exhibited significant, and prolonged inhibition of growth.

Our results show that the ability of these MSMNs to undergo mesophase transition combines advantages of both HFMNs and DMNs, potentially enabling localized and more effective treatment by increasing the residence time of the drug at the target site, by better penetration and sustainable delivery for an extended period

Activatable Dye and Dye-Conjugate Synthesis for Fluorescence Monitoring, PDT and SDT

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Long-wavelength dyes absorbing and emitting in the red and near-infrared (NIR) spectral region are beneficial as fluorescent reporters for drug delivery monitoring and as sensitizers for photodynamic (PDT) and sonodynamic (SDT) cancer treatment. Currently available long-wavelength dyes used for these applications suffer from insufficient brightness and limited photodynamic and sonodynamic efficacy. Additionally, these dyes require reactive groups for binding to target-specific molecules, such as antibodies. Incorporation of heavy atoms like iodine can enhance sensitizing activity; however, this often decreases water solubility, causing dye aggregation—especially upon antibody binding—and reducing brightness and efficacy. Synthesizing long-wavelength dyes that incorporate reactive groups, solubilizing sulfonic groups, and iodine atoms is therefore challenging.

This work developed a synthetic approach to a long-wavelength xanthene-cyanine dye, IXCy, containing iodine atoms along with reactive and sulfonated groups, as well as its dye-antibody conjugates, IXCy-Ab. Two synthetic routes were explored: Approach A involved retro-Knoevenagel condensation of presynthesized cyclohexane-cyanine with resorcinol; Approach B used direct condensation of a presynthesized xanthene-aldehyde derivative with indolenine. After synthesis, IXCy was activated with TSTU and DiPEA to form an NHS-ester (IXCy-NHS) and conjugated to the monoclonal antibody Trastuzumab, generating IXCy-Ab conjugates with dye-to-antibody ratios (DAR) between 0.5 and 2.0.

Approach A resulted in only 2% conversion with multiple unknown byproducts, and varying reaction conditions did not improve yield. In contrast, Approach B yielded IXCy at 15% with fewer impurities and a simpler synthetic process. The IXCy dye was successfully activated and conjugated

to Trastuzumab, producing IXCy–Ab conjugates with controllable DAR values. The study identified an effective synthetic route (Approach B) to obtain the xanthene–cyanine dye IXCy with iodine, reactive, and sulfonated groups in a 15% yield. The dye was successfully conjugated to Trastuzumab, forming IXCy–Ab conjugates that will be further investigated as environment-mediated activatable fluorescent reporters and sensitizers for PDT and SDT applications.

Antitumor activity of αHER2–topoisomerase I inhibitor conjugate via self-immolative dendritic linker

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Objectives: Antibody–drug conjugates (ADCs) are an expanding class of targeted anticancer therapies designed to selectively deliver cytotoxic agents to tumors while minimizing systemic toxicity. With 16 ADCs approved globally, they show promise in cancers (e.g. breast, lymphoma, and lung cancer). However, challenges in production, stability, and resistance require continued research and innovation. Here, we aimed to develop a dendritic ADC platform with enhanced stability, high payload capacity, and controlled-release mechanisms targeting HER2-positive tumors.

Methods: We developed unique linker technologies for bioconjugation of drug molecules for controlled-release applications. We synthesized cathepsin-cleavable ADCs based on a self-immolative dendritic scaffold, allowing for a high drug-antibody ratio (DAR) up to 16 payloads. This system increased stability in the circulation and enabled payload release at the targeted site. The anti-human epidermal growth factor receptor 2 (HER2) antibody, trastuzumab, was conjugated with topoisomerase I inhibitors, exatecan or belotecan. A maleimide moiety was introduced at the focal site for antibody attachment, and a short solubilizing moiety was added to increase the aqueous solubility.

Results: Our ADCs demonstrated high stability in serum while maintaining

intact HER2 binding ability. In vitro testing on human mammary carcinoma cells overexpressing HER2 demonstrated a substantial inhibitory effect on the proliferation of HER2-positive cells. Importantly, a single dose of our trastuzumab-based ADCs administered in vivo to mice bearing HER2-positive tumors, showed a dose-dependent inhibition of tumor growth and survival benefit, with the most potent antitumor effects observed at 10 mg/kg, which resulted in complete tumor regression and survival of 100% of the mice.

Conclusions: Our dendritic, protease-cleavable linker technology enables controlled release of two payloads per enzymatic cleavage, presenting a platform for highly potent and selective ADCs. This strategy holds promise for ADCs treatment for patients diagnosed with HER2-positive cancers and can be adapted for other malignancies and autoimmune diseases expressing alternative targets.

Optimized PLGA-PEG nanoparticles for targeted delivery and controlled release of small molecules

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Polymeric nanoparticles (NP) for drug delivery are a promising strategy to enhance therapeutic efficacy while reducing systemic toxicity. Here, we investigate the design and application of NP based on amphiphilic block copolymers composed of poly(lactic-co-glycolic acid) (PLGA) and polyethylene glycol (PEG) for the controlled release of small-molecule therapeutics. The hydrophobic PLGA enables drug loading, while hydrophilic PEG enhances colloidal stability and extends circulation time. Addition of terminal sulfate ($-OSO_3^-$) groups enabled targeting of P-selectin, which is overexpressed in the tumor microenvironment, and enhanced immune evasion to targeted areas. By systematically varying polymer composition, particle size and surface characteristics, we optimized encapsulation efficiency, release kinetics, and targeting capability. This work shows the versatility of PLGA-PEG NP for targeted delivery, supporting their use in precision medicine.

The allylation reaction of bifunctional PEG-OH was optimized to favor one hydroxyl terminus. The resulting HO-PEG-Allyl was polymerized with lactide and glycolide via ring-opening polymerization and catalyzed by ($Sn(Oct)_2$). The resulting PLGA-PEG-Allyl was acetylated on the PLGA terminus and then sulfated on the PEG terminus via thiolene reaction to obtain the final polymer AcO-PLGA-PEG-(OSO3)2. The synthesis process was thoroughly evaluated, the chemical structure was confirmed by 1H-NMR, polydispersity index (PDI) and molecular weight (MALDI-TOF) mass spectrometry, ensuring consistency

and reproducibility throughout the synthesis process.

PLGA-PEG synthesis was successfully scaled up while improving yields, allowing more control over the PLGA segment length, which improved polymer properties such as drug encapsulation capabilities. Using a series of targeted chemical washes and selective precipitation steps, we achieved precise polymer chain lengths, increased yields and better PDI values, compared to the commercially available polymer.

Polymeric NP were shown to be effective for both single-load encapsulation of a small bioactive molecule and dual-loading of a synergistic combination of Dabrafenib (DBF) and Trametinib (TRM) within a single NP for melanoma treatment.

Prolonged release formulations of cannabidiol-protein complexes

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Albumin is widely used as a nano-carrier for intravenous injections as exemplified by Abraxane, nanoparticle albumin-bound paclitaxel. However, the use of albumin as a drug delivery in the form of large particles of > 1 μm for extravascular administration, is not reported in the literature. Here we describe a formulation of CBD-albumin particles used for prolonged CBD release. CBD is highly lipophilic and therefore usually relies on its solubility in lipids for formulation development. The present approach suggests a non-lipid formulation approach for CBD.

Albumin solutions from several mammalian species were mixed with CBD and based on the mixing method and duration, homogenous particles were obtained. Homogenous particles were also obtained using intravenous immunoglobulins (IVIg). CBD-albumin and CBD-IVIg particles were injected intramuscularly to mice and resulted in a long pharmacokinetic profile with quantified plasma CBD concentration until the last time point tested (21 days). CBD-canine albumin particles were injected subcutaneously as a compassion therapy in two dogs suffering from pain (osteoarthritis and rectal stricture). The long pharmacokinetic profile obtained for the dogs was in agreement with the profile obtained in mice, showing quantifiable concentrations 28 days after a single administration. Additionally, decreased pain and improved quality of life was reported by the caregivers, suggesting prolonged analgesic effect.

The CBD-protein complexes provided prolonged CBD plasma profile of

several weeks following a single injection. The efficacy of this formulation in animal models should be investigated further. This protein-based formulation approach may present a novel solution for long-acting injectables.

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Using Lipid Nanoparticles to Deliver Genetic Medicine for Duchenne Muscular Dystrophy

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Objective: Duchenne Muscular Dystrophy (DMD) is a fatal genetic disorder affecting 1/5000 boys. DMD is caused by the lack of the dystrophin protein and is characterized by progressive muscle weakness. DMD eventually leads to death due to failure in both cardiac and diaphragm muscles, as they are unable to support normal functionality. Currently, DMD has a few available drugs with limited efficiency. The development of effective genetic treatment is greatly limited by the lack of an efficient delivery vehicle that would allow supplying the muscles with a full-length DMD gene, which, due to its significant size (11.5 kb), is unsuitable for viral delivery. In this project, we aim to leverage the recent progress in the lipid nanoparticle (LNP) field to develop a specific and efficient tool for DMD treatment.

Methods:
In this work, we first screened various LNP formulations on a myoblast cell line to select the best one based on measurements of luciferase mRNA delivery. Next, we evaluated the ability of those LNPs to deliver luciferase mRNA in vivo via an intramuscular injection in a healthy mouse and detected a relatively high signal. Separately, we explored the possibility of using circular RNA to prolong protein expression in vivo by injecting identical LNPs carrying either a linear or a circular mRNA and monitoring the expression over time.

Results: As a result, we observed that circular RNA sustains longer luciferase production of more than 72 hours when the linear mRNA product is

nondetectable. Therefore, in the next step, we explored targeting moieties to promote LNP-based delivery of circular RNA to muscle tissue, obtaining luciferase expression in the muscle fibres of a diseased mouse. In the future, we aim to evaluate the ability of targeted particles to systemically deliver to muscles and support therapeutic protein delivery.

Particle Uptake Patterns as a Treatment Tool of Bladder Cancer

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Objectives: This study explores particle uptake dynamics as a combined diagnostic and therapeutic platform for bladder cancer, focusing on tumor-specific uptake patterns associated with aggressiveness, heterogeneity, and disease progression. Bladder cancer is known for its high recurrence rates, requiring frequent invasive monitoring procedures. Our goal is to leverage these mechanobiological insights to develop size-optimized, drug-loaded microparticles that enable personalized treatment strategies, improve outcomes, and potentially complement or reduce reliance on invasive diagnostic methods.

Methods: Microparticles of various sizes were introduced into bladder cancer models, including monolayer cultures and three-dimensional spheroids, which better replicate tumor architecture. Uptake dynamics were systematically analyzed using Flow Cytometry to identify reproducible, size-dependent patterns across bladder cancer cell lines. Confocal microscopy visualized intracellular particle localization, while high-resolution scanning electron microscopy (SEM) provided detailed imaging of particle-cell interactions, surface morphology changes, and dynamic internalization events over incubation periods.

Results: Preliminary findings revealed consistent uptake profiles within individual cell lines, with subtle but significant differences among bladder cancer cell lines of varying aggressiveness and stages. Distinct size-dependent uptake trends were strongly correlated with tumor progression, phenotypic plasticity, and mechanical properties of the tumor microenvironment. Confocal and SEM imaging confirmed these uptake patterns as robust, quantifiable indicators of internalization, offering a window into tumor behavior and mechanical signatures.

Conclusions: These findings suggest that particle uptake analysis can form a foundation for future diagnostic strategies, enabling earlier detection of recurrence or tumor transformation through sensitive monitoring of uptake pattern shifts. Moreover, the results provide a framework for designing drug-loaded microparticles tailored to tumor-specific preferences, improving therapeutic precision and minimizing side effects. With further validation in bladder cancer mouse models, this approach holds promise for developing an integrative theranostic platform that combines real-time diagnostics with targeted therapy to reduce patient burden and enhance treatment outcomes.

Hypoxia-Induced Drug Sensitivity and Nanoparticle Uptake in Cancer Cells

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Objectives: Hypoxia, a hallmark of the tumor microenvironment, promotes cancer progression and therapy resistance by altering gene expression, metabolism, and cellular behavior. It also affects mechanical properties such as stiffness and elasticity, which influence disease development, metastasis, and drug response. These biomechanical changes can serve as diagnostic biomarkers and impact drug delivery by modulating interactions between cells and therapeutic agents. Understanding cell biomechanics may reveal novel therapeutic targets and support the design of more effective, personalized therapies, ultimately improving clinical outcomes.

Methods: Cells were cultured at 37°C with 5% CO_2. Hypoxia (1% O_2) was applied for 24–48 hours; controls remained in normoxia (21% O_2). Nanoparticle uptake was measured by flow cytometry following 24-hour incubation with fluorescent particles. Membrane fluidity was assessed via Laurdan staining and generalized polarization (GP) value calculation. Cholesterol levels were quantified after 24–48 hours using a commercial assay kit. PANC-1 spheroid elasticity was measured after 24 hours using MicroTester compression and analyzed with the Instantaneous Elastic model.

Results: Panc1 and H460 cells exposed to hypoxia and 2.5 Gy irradiation showed significantly increased uptake of 0.28 µm and 0.82 µm fluorescent nanoparticles. Cholesterol levels decreased after 24 and 48 hours of hypoxia in both cell lines. Treatment with methyl-beta-cyclodextrin (MβCD) at concentrations of 0–5 mg/ml under normoxic and hypoxic conditions reduced cell viability in a dose-dependent manner, consistent with cholesterol depletion effects. In 3D spheroids, hypoxia significantly increased mechanical stiffness, an effect not observed in 2D cultures.

Conclusion: Hypoxia and irradiation enhance nanoparticle uptake in Panc1 and H460 cells. Reduced cholesterol under hypoxia correlates with increased membrane fluidity and improved nanoparticle internalization. Hypoxia also induces increased stiffness in 3D spheroids. These findings highlight the potential of exploiting hypoxic tumor microenvironments to improve nanoparticle-based targeted drug delivery and enhance therapeutic efficacy.

Magnetic Nanoparticles for Target Cell Capture: A Novel Diagnostic Approach for Endometriosis

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Objective: Endometriosis is a chronic, estrogen-dependent disease affecting around 10% of women of reproductive age. Diagnosis is often delayed due to non-specific symptoms and reliance on invasive procedures like laparoscopy. This study proposes a non-invasive diagnostic approach using magnetic biomimetic liposomes to capture endometrial and endometriotic cells from menstrual fluid. The system combines superparamagnetic iron oxide nanoparticles (SPIONs) encapsulated in liposomes coated with membrane proteins from endometrial stromal cells. These liposomes are designed to selectively bind endometrial cells out of the menstrual fluid cells through homotypic adhesion and allow their isolation by magnetic force. We hypothesize that this method will enable specific isolation of endometrial cells from patient menstrual fluid samples for downstream proteomic and metabolomic analysis. The work includes liposome formulation, magnetic beads encapsulation, physicochemical characterization, in vitro targeting validation, and validation with menstrual samples from healthy donors and endometriosis patients.

Methods: Superparamagnetic iron oxide nanoparticles (SPIONs) were encapsulated in liposomes coated with membrane proteins from human endometrial stromal cells. These biomimetic liposomes are designed to selectively adhere to target cells via homotypic interactions. Liposomes were synthesized, characterized (size, PDI, zeta potential, TEM), and evaluated for targeting and cell capture efficiency in vitro. Menstrual samples from healthy and endometriosis patients will be analyzed using this system.

Conclusion: This platform could provide a novel, minimally invasive tool for early diagnosis and disease monitoring in endometriosis and may be adaptable for other diagnostic applications.

Tiny Particles, Big Plans: Nanoparticles for Controlling Drug Transfer through the Placental Barrier

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Conventional drug treatments during pregnancy can pose serious risks to the developing fetus, as many medications can freely cross the placenta and cause toxicity. Nanoparticles offer a promising strategy to overcome this challenge. When drugs are incorporated onto nanoparticles, their pharmacokinetics and biodistribution change dramatically. These engineered particles can be designed with "big plans" in mind – minimizing placental crossing to reduce fetal exposure or enhancing placental targeting to treat pregnancy complications (which mostly originate in the placenta). Understanding the design principles that govern nanoparticle behavior at the placental interface is essential for developing safe and effective pregnancy therapeutics.

In this research we examine how surface coating affects the bioditribution of 20nm GNPs. GNPs coated with mPEG, insulin, or glucose were injected to pregnant mice. Gold levels in maternal organs, placentas, fetuses, and extraembrionic tissues were quantified using ICP-OES 24 hours post injection. Our results show that surface functionalization of GNPs significantly influences biodistribution at the placental interface. Insulin- and glucose-coated GNPs showed significantly higher placental accumulation (50% and 30% increase vs. mPEG-GNPs) with minimal fetal exposure (<1%). Furthermore, Glucose-GNPs exhibited strong targeting to extaembrionic membrane, while insulin-GNPs favored uterine uptake. These findings highlight the potential of Insulin and glucose gold nanoparticles as a safe and effective platform for drug delivery during pregnancy.

Delivery to synthetic cells using nanoparticles

Yael Fink, MSc student , Avi Schroeder, Professor

Synthetic cells (SCs), created by encapsulating cell-free protein synthesis (CFPS) systems within giant unilamellar vesicles (GUVs), act as therapeutic bioreactors that mimic living cells and can produce proteins both in vitro and in vivo. While their membranes may become transiently permeable due to osmotic pressure, allowing small molecules such as amino acids and nutrients to enter, larger biomolecules like DNA are unable to pass through, limiting macromolecular exchange with the environment.

This study aims to develop a novel method for nanoparticle-mediated delivery into SCs via charge-based membrane fusion, overcoming limitations of synthetic membranes and internal encapsulation. The initial focus being on analyzing how various lipids influence the stability, fusogenicity, and charge of SCs and nanoparticles.

SCs are synthesized using water-in-oil emulsion transfer method, encapsulating CFPS components within GUVs while incorporating charged lipids on the SCs' membrane to promote fusion. Oppositely charged liposomes and LNPs are successfully prepared using the ethanol injection method and fusion efficiency assays was established based on Förster Resonance Energy Transfer (FRET)-based lipid mixing. Ongoing work include further characterization of the SCs and surface charge via Zeta potential and evaluation of functional delivery by monitoring protein expression inside SCs following delivery of DNA or RNA molecules using this system.

The approach is designed to demonstrate that oppositely charged liposomes or LNPs can successfully fuse with SCs membranes, enabling macromolecular delivery. Such capability could allow SCs to produce proteins from externally introduced DNA or RNA, enhancing their versatility and duration of protein synthesis. The ability to modify SCs contents post-fabrication holds significant promise for implications in synthetic biology and therapeutic delivery. This platform may also allow targeted control over SCs activation, expanding the potential for smart, responsive artificial cells in medicine.

Developing Optical Nanosensors for Monitoring Chemotherapy

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Hebrew university of Jerusalem - Zvi Yaari, Hebrew university of Jerusalem

Objectives: Triple-negative breast cancer (TNBC) is an aggressive form of breast cancer with significant treatment challenges due to its heterogeneity, lack of targeted therapies, and the presence of drug-resistant cancer stem cells. This often leads to suboptimal treatment choices, poor prognosis, high recurrence rates, and increased metastasis, causing severe side effects and reduced quality of life for patients. To address these issues, we are developing near-infrared (NIR) single-walled carbon nanotube-based optical nanosensors. Our objective is to enable real-time monitoring of tumor response to specific chemotherapy regimens, allowing oncologists to promptly adjust treatment strategies and directly report chemotherapy efficacy in TNBC patients.

Methods: We synthesized and functionalized NIR single-walled carbon nanotube nanosensors with specific biomarker-targeting moieties. Comprehensive characterization studies were performed to confirm their successful synthesis and functionalization. In vitro assays were conducted to evaluate the nanosensors' ability to specifically and quantitatively detect designated biomarkers. This was evidenced by measurable changes in fluorescence intensity and/or wavelength upon exposure to varying biomarker concentrations. Stability tests were also performed to assess the nanosensors' integrity and functionality over time.

Results: Our characterization studies successfully confirmed the synthesis and functionalization of the nanosensors with specific biomarker-targeting moieties. In vitro assays demonstrated the nanosensors' capability to detect designated biomarkers specifically and quantitatively, as evidenced by measurable fluorescence intensity and/or wavelength changes upon exposure to varying biomarker concentrations. Furthermore, stability tests revealed that the nanosensors maintained their integrity and functionality for up to 60 days.

Conclusions: These results underscore the reliability of our nanosensor technology for precise biomarker detection in clinical settings. The developed NIR single-walled carbon nanotube-based optical nanosensors hold significant potential for future clinical applications, offering a promising approach to real-time monitoring of chemotherapy efficacy in TNBC patients and enabling more informed and timely treatment adjustments.

Robiochemistry: An Online Nanotechnology Platform for Remote Education

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Robiochemistry is a novel educational initiative designed to teach nanotechnology through direct interaction with automated laboratory equipment. Developed at the Technion – Israel Institute of Technology, this program enables students to remotely conduct advanced experiments in lipid nanoparticle (LNP) synthesis, characterization, and application using robotics and smart interfaces. The core of the course lies in its use of an automated liquid handling robot connected to an interactive user interface, allowing students to design, execute, and troubleshoot experiments in real time from any location in the world. Students synthesize lipid nanoparticles for RNA delivery, perform fluorescence-based characterization, and analyze their formulations using research-grade tools such as DLS and fluorescence microscopy. While remote access to nanotechnology experiments remains a rarity, Robiochemistry bridges this gap by digitizing hands-on processes without compromising experimental rigor. Students gain experience in critical techniques relevant to modern nanomedicine, including formulation optimization, protocol development, and data interpretation. Conducted over four weeks, the program admits top-performing students in chemistry, biology, and engineering from around the world. Teams are guided through experiment design and project management, culminating in academic posters that reflect their findings and methodologies. Beyond technical proficiency, the course fosters a deep understanding of nanoscale systems, interdisciplinary collaboration, and the translation of research into real-world applications. Robiochemistry not only equips students with nanotechnology expertise but also democratizes access to laboratory infrastructure, supporting talented individuals regardless of location or physical ability. As the global demand for nanomedicine grows, this model offers a scalable pathway to prepare the next generation of researchers through AI-integrated, remote experimentation.

Developing Optical Nanosensors to Monitor Obesity

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Obesity is a chronic metabolic condition characterized by excessive fat accumulation and altered adipose tissue function. It is associated with increased risk of cardiovascular disease, cancer, and metabolic dysfunction. Biomolecules secreted from adipose tissue reflect changes in metabolic states and are considered informative indicators of disease progression. Real-time, non-invasive monitoring of these signals may enable early detection and improved management of obesity-related complications. Optical nanosensors based on single-walled carbon nanotubes (SWCNTs) provide a promising platform for this task due to their deep tissue penetration, environmental sensitivity, and functional ability. SWCNTs transduce molecular interactions into optical signals, enabling precise detection of biomarker fluctuations. Developing such nanosensors could allow early detection of obesity-linked pathologies and improve clinical outcomes.

This study presents the development of an optical nanosensor platform utilizing SWCNTs, functionalized with molecular recognition elements to selectively interact with biological targets relevant to obesity. The optical signals produced upon target interaction were measured using near-infrared detection methods. Sensor characterization included physical and optical assessment, and biological testing was performed under controlled in vitro conditions simulating various metabolic states.

The developed nanosensors exhibited stable and reproducible optical responses corresponding to varying concentrations of specific secreted molecules. They were able to distinguish between environments with differing levels of metabolic activity. Sensor performance remained robust across multiple experimental conditions, with minimal interference from unrelated substances. Comparative biochemical analyses confirmed the correlation between optical signal intensity and biomarker concentration, supporting the sensitivity and specificity of the system.

The optical nanosensors demonstrated strong potential as real-time tools for monitoring obesity-associated biological signals. Their responsiveness and selectivity under physiological conditions suggest their future application in early detection, personalized tracking of metabolic changes, and non-invasive diagnostics. This platform may contribute to a better understanding of adipose tissue dynamics and support clinical strategies targeting obesity and its complications.

Developing Optical Implantable Matrices for Clinical Monitoring

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Introduction/Background: Single-walled carbon nanotubes (SWCNTs) emit in the near-infrared (NIR) region and exhibit high photostability, low tissue autofluorescence, and deep tissue penetration. Their fluorescence is highly sensitive to local environmental changes, enabling their use as label-free, optical biosensors. Embedding SWCNTs in biocompatible hydrogels can preserve these optical properties while allowing interaction with analytes. Hydrogels closely mimic biological tissues and offer tunable mechanical and structural properties, making them ideal matrices for in vivo sensing applications.

Methods/Materials: Various hydrogel formulations were synthesized with embedded SWCNTs. Physical characterization included swelling ratio measurements, compression testing, and frequency sweep rheology to assess mechanical and viscoelastic properties. NIR fluorescence spectroscopy was used to evaluate SWCNT emission and response to analytes. Fluorescence stability and SWCNT leakage were monitored over time. Gel morphology was examined via imaging to support physical findings.

Results: All tested hydrogels successfully encapsulated SWCNTs while preserving fluorescence. SWCNTs retained sensitivity to small analytes, displaying changes in intensity or wavelength upon exposure. Physical characterization revealed significant differences across formulations in swelling behavior, mechanical strength, and viscoelastic properties. These variations influenced both the stability and sensing performance of embedded SWCNTs, suggesting that the choice of hydrogel formulation can be tuned according to application-specific requirements, such as flexibility, diffusion, or durability.

Conclusions: This study demonstrates that hydrogel matrices can be optimized to support SWCNT-based optical sensing. The results establish a foundation for the development of implantable biosensors with tailored mechanical and optical properties. Ongoing work aims to expand this hydrogel library and refine sensor performance for specific clinical applications.

Targeting mRNA Lipid Nanoparticles to inflammatory sites

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Chronic inflammatory pathologies are an unmet clinical need because of limited treatment options. RNA therapeutics represent a new frontier to unlock novel therapies. In my work, I elucidated the effect of lipid nanoparticles (LNPs) composition in determining their tropism to the inflamed colon, resulting in LNPs with improved therapeutic efficacy in colitis-bearing mice. Herein, I test their application in other inflammatory settings and investigate mechanism behind their biological targeting, a knowledge that could aid in designing novel LNPs for different applications.

I investigate the contribution of circulating versus tissue leukocytes in mediating new fluorescent LNPs (n-LNPs) accumulation in the colon of dextran sodium sulphate (DSS) induced colitis mice, and in LPS-mediated lung inflammation, using flow cytometry analysis. Finally, I expanded the therapeutic application of the LNPs formulation by loading them with IL-10 mRNA and test them in colitis amelioration using multiple histological and molecular readouts.

n-LNPs demonstrated preferential uptake by leukocytes and endothelial cells that mediated their accumulation in the inflamed colon and lungs. Treatment with IL-10 mRNA-loaded LNPs resulted in a better colitis amelioration in DSS mice compared to benchmark (b) -LNPs, highlighting the importance of understanding the LNPs interaction with leukocytes to enable better improved LNPs design against inflammatory pathologies.

Nanoparticles with Sustained Release of L-NAC for Treating Primary Sclerosing Cholangitis

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Objectives: Primary Sclerosing Cholangitis (PSC) is a chronic liver disease marked by progressive bile duct scarring, inflammation, and fibrosis, often leading to liver failure. Current therapies are limited, with liver transplantation as the only definitive treatment. N-Acetyl-L-cysteine (L-NAC), a thiol-based antioxidant, has shown potential in repairing bile duct injury; however, its short systemic half-life limits therapeutic effectiveness. This study aims to develop L-NAC-loaded polymeric nanoparticles for sustained local delivery to the biliary system, offering a non-invasive, long-term treatment strategy for PSC.

Methods: Polymeric nanoparticles were fabricated using nanoprecipitation, microfluidics, and double emulsion techniques. Size distribution and polydispersity were analyzed via Dynamic Light Scattering (DLS), and morphology was assessed using Scanning and Transmission Electron Microscopy (SEM/TEM). L-NAC loading and release kinetics were quantified using High-Performance Liquid Chromatography (HPLC). Cellular uptake was evaluated by flow cytometry, and cytotoxicity was assessed with MTT assays. Anti-oxidative efficacy was tested in a reactive oxygen species (ROS)-induced model using tert-butyl hydroperoxide (TBHP).

Results: The double emulsion technique produced ~100 nm nanoparticles, ideal for bile duct penetration without obstruction. These nanoparticles exhibited high cellular uptake and sustained L-NAC release over several days. Compared to free L-NAC, the nanoparticle formulation significantly reduced intracellular ROS levels, indicating superior antioxidative activity in vitro.

Conclusions: L-NAC-loaded nanoparticles developed via double emulsion fabrication offer a promising therapeutic platform for PSC. Their optimal size

enables efficient bile duct targeting, and sustained release ensures prolonged anti-inflammatory and antioxidative action. This nanoparticle-based system may overcome current limitations of L-NAC therapy and represents a step forward in localized PSC treatment.

3D-Bioprinted Capsules for the Co-Delivery of Live Bacteria and Small Molecule Immunotherapies

Or Kandli, Marina Green Buzhor, Ronit Satchi-Fainaro

Tel Aviv university

Introduction: Immunotherapy has revolutionized cancer treatment; however, many patients remain unresponsive. Co-delivering live bacteria with computer-assisted drug-design (CADD) small molecule immunotherapeutics (SMi) offers a promising approach to overcoming therapeutic resistance. Certain gut bacteria have been shown to positively correlate with immunotherapy efficacy, and their targeted delivery may improve treatment outcomes.

Materials and Methods: We developed innovative 3D-bioprinted, enteric capsules that encapsulate live bacteria and SMi. The selected bacterial strains, both aerobic and anaerobic, include those reported to have a positive correlation with immunotherapy response. SMi were computationally designed to target PD-1/PD-L1, TIGIT-PVR, or JAG1-Notch pathways. Capsules were 3D-bioprinted using growth-promoting hydrogel bio-inks based on alginate and gelatine that support bacterial survival and improve printability. An additional enteric outer layer was 3D-printed to ensure gastric resistance and colon-targeted release. Capsules were evaluated for mechanical strength, release kinetics under simulated gastrointestinal conditions, and bacterial viability using fluorescent imaging and flow cytometry.

Results and Discussion: Our developed capsules were able to successfully encapsulate live bacteria and SMi, withstanding gastric conditions and maintaining the viability of anaerobic bacteria for over 15 days, while aerobic strains survived up to 3 days. We optimized the hydrogel formulations to promote bacterial proliferation. The 3D-bioprinted capsules' integrity remained intact under acidic conditions. These results confirm the feasibility of this delivery platform for maintaining viable bacteria and enabling precise colon-targeted delivery.

Conclusions: This 3D-bioprinted capsule represents a novel strategy to sensitize tumors to immunotherapy by combining live bacteria and SMi co-delivery. Incorporating bacteria associated with improved immunotherapy responses may enhance therapeutic efficacy and offer a personalized approach for patients who do not benefit from current treatments.

Liposomal Formulation of Cyclometalated Iridium(III) complex as Anticancer Theranostic Agents

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Despite advancements in therapeutic approaches and supportive care, cancer morbidity and mortality continue to rise globally. According to WHO and IARC reports, the number of cancer cases is predicted to nearly double by 2030, reaching 35 million. To combat this issue, researchers are exploring new solutions for precise cancer diagnostics and effective therapeutic strategies. One of the promising fields is the advancement of novel metal-based anticancer agents. In this study, we designed and synthesized a novel cyclometalated iridium (III) nanomaterial, which exhibits excellent photodynamic therapy (PDT) and bioimaging capabilities due to its high fluorescence quantum yield. Furthermore, to enhance the effectiveness of this agent, we encapsulated the complex into amphiphilic liposomal nanoparticles, which demonstrated robust tumor-targeting ability and biocompatibility. This encapsulation also enhanced its in vivo absorption and allowed for slow drug release, prolonging its action. This comprehensive approach could significantly reduce high mortality rates, particularly in individuals with advanced-stage cancers.

Multifunctional 2D Nanomaterials for Precision Cancer Therapy Triggered by Low-Energy X-Rays

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Cancer remains one of the leading causes of death worldwide, demanding new approaches that go beyond conventional treatments. Nanotechnology offers a powerful tool for precision medicine, enabling targeted drug delivery and trigger-controlled therapeutic activation.

As part of PERSEUS project, our approach leverages the unique properties of novel two-dimensional (2D) nanomaterials, specifically, tungsten disulfide (WS_2) nanocrystals were engineered into a multifunctional nano-system (NS) through functionalization with gold nanoparticles and organic photosensitizers. This planar nanomaterial possesses distinct physicochemical characteristics, including high surface area and anisotropic architecture, making it highly suitable for biomedical applications. Upon exposure to low-energy X-rays, the high Z-number components of the NS are expected to generate reactive oxygen species (ROS) via the photoelectric effect, thereby amplifying local cytotoxicity. In parallel, the radiation-triggered damage may promote immunogenic cell death (ICD), facilitating the release of tumor-associated antigens and initiating a systemic anti-tumor immune response.

We evaluated the radioenhancement potential of the NS in a pancreatic ductal adenocarcinoma (PDAC) model, both in vitro and in vivo. In vitro, Panc02 cells were treated with the NS, irradiated, and assessed for cell viability and clonogenic potential. The combined treatment significantly reduced metabolic activity and impaired colony formation, compared to irradiation

alone, indicating synergistic cytotoxicity. In vivo, C57BL/6 mice bearing flank PDAC tumors received intratumoral injections of NS followed by irradiation. Tumors were excised three days later and analyzed for histological markers of radiation damage. To explore active tumor targeting, the NS was successfully encapsulated within giant unilamellar vesicles. Encapsulation efficiency and structural integrity were validated using high-resolution scanning electron microscopy (HR-SEM).

This low-energy X-ray-activated amplification of oxidative stress using novel 2D materials paves the way for nanotechnology-based cancer therapies that can be clinically activated by standard imaging modalities, such as computed tomography (CT), enabling precise and non-invasive treatment.

Analysing the relationship between protein corona composition and LNPs biodistribution

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Lipid nanoparticles (LNPs) are versatile nanocarriers with demonstrated success in clinical applications.

Once LNPs enter a biological matrix, they encounter multiple biomolecules. These endogenous molecules interact with the surface of LNPs to form an additional layer – the protein corona. The protein corona has a significant effect on LNPs' fate in vivo. However, the mechanism behind endogenous targeting remains poorly understood. Clarifying these mechanisms holds great potential for improving LNP biodistribution by rational formulation design.

The biodistribution of LNPs can be precisely tuned by modifying their lipid composition. We have recently shown that by adjusting the lipid ratios, LNP delivery can be shifted from the liver towards organs beyond the liver – such as the gastrointestinal tract. This shift opens new avenues for treating inflammatory bowel diseases (IBDs).

Herein, we focus on the endogenous targeting mechanisms underlying the distinct biodistribution of LNPs. We aim to analyze the protein corona of different LNP formulations and to investigate the contribution of the identified proteins to LNP biodistribution.

Therefore, LNPs with different biodistributions were formulated by microfluidic mixing, and the physicochemical properties were measured. In vivo biodistribution was tested using LNPs encapsulating luciferase mRNA. To assess the protein corona composition, the LNPs were incubated with either serum or plasma. Following incubation, the LNP–protein corona complexes were separated from unbound biomolecules using monolithic column chromatography. The protein corona composition was subsequently analyzed by LC–MS.

All LNPs were associated with apolipoproteins, including ApoE, ApoA4, and ApoC2. ApoE was abundant in the corona of the liver-targeting formulation, in accordance with the literature. However, when comparing this formulation to LNPs with extrahepatic biodistribution, we observed a significant increase in various apolipoproteins.

While these results are preliminary, they suggest that in addition to ApoE, various apolipoproteins contribute to specific LNP biodistribution.

TARGETED NANOPARTICLE DELIVERY IN PEDIATRIC BRAIN TUMORS USING A 3D MICROFLUIDIC TUMOROID-BBB MODEL

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Pediatric brain tumors, such as medulloblastoma (MB), diffuse intrinsic pontine glioma (DIPG), and pediatric low-grade glioma (pLGG), present significant therapeutic challenges due to their aggressive nature, poor prognosis, and the lack of clinically relevant research models. The blood-brain barrier (BBB) limits the efficacy of treatments by hindering drug delivery to tumor sites. Targeted therapies, particularly those aimed at MAPK pathway mutations, have shown promise in pLGG, highlighting the need for advanced in vitro platforms to study and improve therapeutic strategies. This work aims to develop a clinically relevant 3D in vitro model to evaluate nanoparticle-based therapies targeting the MAPK pathway in pLGG.

We developed an in vitro 3D microfluidic chip model incorporating a multicellular tumoroid embedded in ECM-like hydrogel, surrounded by brain stromal cells and vascular structures to mimic the BBB. The model enables assessment of P-selectin-targeted poly(lactic-co-glycolic acid) (PLGA)-poly(ethylene glycol) (PEG) nanoparticles (NPs) co-loaded with BRAFi, Dabrafenib, and MEKi, Trametinib. Tumoroids were derived from both commercial cell lines and patient-derived tumor samples.

Our microfluidic model successfully mimicked the pediatric brain TME and enabled assessment of NPs extravasation across the BBB. P-selectin-targeted NPs demonstrated efficient penetration into the 3D tumoroid mass, reflecting

the overexpression of P-selectin in pediatric brain tumors compared to healthy brain tissue. The dual drug-loaded NPs showed enhanced potential for targeted therapy of dabrafenib and trametinib, particularly for LGG with MAPK pathway alterations. This approach underscores the importance of integrating targeted delivery systems with physiologically relevant models for optimizing therapeutic strategies.

This study presents a novel, clinically relevant 3D in-vitro platform for evaluating NP-mediated drug delivery to pediatric brain tumors. The combination of P-selectin-targeted NPs and a BBB-integrated tumoroid model supports the advancement of precision and personalized medicine. Our findings pave the way for preclinical validation of targeted therapies and rapid clinical translation for pediatric brain cancers.

Functional microneedle for endotoxin removal directly from skin infection

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Sepsis, resulting from dysregulated inflammatory response to infection, is a major clinical challenge due to its high mortality rates, increasing antibiotic resistance, and the absence of effective targeted therapies. In particular, skin and soft tissue infections caused by antibiotic-resistant Gram-negative bacteria such as Pseudomonas aeruginosa, which can rapidly progress to systemic sepsis. This escalation is largely driven by the release of bacterial endotoxins and associated pro-inflammatory cytokines. To address this unmet clinical need, we developed a minimally invasive microneedle (MN) patch designed for locally adsorbtion and removal of endotoxins directly from the infected wounds. The MN device was fabricated using the micromoulding technique followed by functionalization with polymyxin B, an endotoxin-binding ligand. Patches were characterized to ensure sufficient mechanical properties including needle strength allowing effective penetration into wounded surface. Adsorption of lipopolysaccharides (LPS) by the MN patch was visualized using fluorescence microscopy, confirming efficient endotoxin capture on the needle surfaces. The interaction between LPS and polymyxin B was demonstrated by quartz crystal microbalance (QCM) analysis, providing evidence of specific binding affinity. Beyond endotoxin removal, the antibacterial performance of the functionalized MN patch was evaluated against Escherichia coli, showing a significant inhibitory effect and further supporting the therapeutic potential of the device. These findings highlight the MN patch as a promising platform for easy-to-administer, localized intervention in infected wounds, with the potential to reduce systemic inflammation and prevent the onset of sepsis.

Computer-Assisted Drug Design for the Discovery of Small Molecule Inhibitors for the TIGIT-PVR Axis

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Computer-assisted drug design (CADD) is a powerful approach employing computational tools to enhance the development of new drugs. By simulating molecular interactions between proteins and ligands, CADD allows chemists to identify promising drug candidates. Here, CADD was utilized to design novel small molecule (SM) inhibitors for the immune checkpoint (IC) target T-cell immunoglobulin and ITIM domain (TIGIT). ICs play important roles in immune suppression within the tumor microenvironment (TME) and have been highly investigated in the past decade in combination therapies to enhance anti-tumor responses. The main tool for blocking these targets has been monoclonal antibodies. SM's offer advantages such as simpler manufacturing, compliant administration, improved tumor infiltration, and blood-brain barrier (BBB) penetration.

We exploit in silico studies with the aim of interfering with two lock-and-key interactions facilitating the TIGIT-PVR ligation. For virtual screening, three chemical libraries were selected: (i) a dataset of 1400 FDA-approved drugs for repurposing, (ii) an Enamine dataset consisting of 6.8 million synthetically feasible and drug-like compounds, and (iii) a ChEMBL dataset of 1.5 million compounds molar mass up to 1000 g/mol. Fingerprint clustering and molecular dynamics simulations were used to evaluate in silico hits. Furthermore, to investigate combination therapies for cancer cells and angiogenic endothelium overexpressing P-selectin, targeted polymeric nanoparticles (pNPs) have been designed.

The three datasets have been docked to the TIGIT-PVR interface and resulted in 30 potential TIGIT binders which will be tested in vitro on 3D cancer models mimicking the tumor microenvironment. pNPs with P-selectin-targeting sulphate groups were synthesized and formulated achieving NP's of approximately 100 nm in diameter.

CADD was used to identify potential SM inhibitors for the TIGIT-PVR ligation. pNPs decorated with P-selectin-targeting sulphate groups were prepared to assess combination therapies and enhance accumulation of the encapsulated drugs at the TME to increase efficacy and reduce off-target effects.

Mechano-Profiling and Modulation of Red Blood Cell-Based Carriers

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Introduction: Red blood cells (RBCs) are naturally long-circulating carriers, surviving up to 120 days in the bloodstream, making them promising vehicles for drug delivery. Their flexible membrane allows them to navigate even the smallest capillaries. Drugs can be loaded into RBCs using techniques like hypotonic loading or electroporation, and membrane modifications, such as cholesterol enrichment to enhance stability or glutaraldehyde treatment to adjust rigidity, can be used to optimize membrane stability and release mechanism. This controlled release capability allows for localized therapy, such as treating vasoconstriction that may occur post aneurysm rupture, while minimizing systemic side effects. Better understanding of the biomechanical properties of RBC carriers and modulating these properties can be valuable for developing improved RBC based therapeutics.

Methods/Materials: RBCs were loaded with Dextran-FITC via hypotonic dialysis and compared to native cells. Mechanical properties were tuned using agents like glutaraldehyde, and heat treatment to control cell stiffness and potential drug release behavior. Mechanical profiling of RBC properties was preformed via static shape deformation using aqueous liquid crystals and elongation measurements while dynamic perfusion through a microfluidic flow model that mimics the capillary networks in the lungs allowed to study their navigability and transport dynamic as observed via high-speed microscopy. Additionally, drug release was examined by FACS analysis.

Results: Preliminary results demonstrated similarities between native and carriers RBCs loaded via the hypotonic dialysis method. Measurements showed neglectable differences in deformation index in the liquid crystals' solution, and similar flow behavior have been recorded in both cell types. While high-speed imaging and computational simulation show significant deformation of the RBC carriers flowing the microfluidic capillary model, no

significant drug leakage was measured.

Conclusions: Studying and tuning the mechanical properties of RBCs based carriers may be valuable to improve their function as a versatile and controllable platform for targeted drug delivery.

Resected Tumor Biomimetic Nanoparticles for Personalized Immunotherapy

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Triple-negative breast cancer (TNBC) remains one of the most aggressive breast cancer subtypes, lacking targeted therapies and necessitating the development of innovative treatment strategies. Here, we introduce EPISOMES—epitope-presenting liposomes derived from resected TNBC tissue—as a biomimetic nanoparticle platform designed to induce tumor-specific immunotherapy. Using a microfluidic assembly process, tumor-derived membrane proteins were integrated into liposomal nanoparticles, resulting in EPISOMES with extended stability for up to 21 days at 4°C. Comprehensive physicochemical characterization revealed that EPISOMES present a diverse repertoire of tumor-associated antigens capable of eliciting potent immune responses. In a 4T1 murine TNBC model, intramuscular vaccination with EPISOMES significantly suppressed tumor growth and reduced splenomegaly, indicative of systemic anti-tumor effects. Mechanistically, EPISOMES treatment enhanced leukocyte infiltration into the tumor microenvironment, specifically CD19+ B cells and CD4+ helper T cells. Ex vivo recall assays with subiliac lymph node cells demonstrated antigen-specific proliferation of CD4+, CD8+ and CD19+ cells, accompanied by increased secretion of IL-2 and TNF-α, further supporting the immunostimulatory capacity of EPISOMES. These findings highlight EPISOMES as a promising platform for personalized cancer immunotherapy, leveraging patient-specific tumor-derived proteins to mount targeted immune responses against TNBC.

Exploring Cellular Tropism of mRNA-LNP Formulations for Treating Non-Alcoholic Fatty Liver Disease

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Background: Non-alcoholic fatty liver disease (NAFLD) is the most prevalent chronic liver condition worldwide, encompassing a spectrum from simple steatosis to non-alcoholic steatohepatitis (NASH). Although NAFLD primarily arises from hepatic lipid accumulation, increasing evidence highlights the role of extrahepatic organ systems—particularly the gut and spleen—in disease progression. Ionizable lipid-based nanoparticles (LNPs) have emerged as promising platforms for RNA delivery, with the identity of ionizable lipids affecting cell type-specific and extrahepatic delivery of mRNA therapeutics.

Methods: A panel of seven ionizable lipids was synthesized, and corresponding mRNA-LNPs were formulated using a luciferase-encoding mRNA payload. The formulations underwent physicochemical characterization to ensure proper size, mRNA encapsulation and integrity. In vitro luciferase expression assays were conducted in murine hepatocyte and macrophage cell lines. Based on these results, selected LNPs were further assessed in vivo in mice, examining biodistribution, inflammatory response, and cellular expression across major organs.

Results: All LNP formulations met physicochemical criteria. In vitro, lipid A2 and lipid A2R showed higher luciferase expression than SM-102-based controls. In vivo, these formulations demonstrated superior mRNA delivery following intravenous administration, with notable passive targeting of the spleen and intestine. Cytotoxicity studies showed no adverse inflammatory responses at 6 hours post-injection. Cellular biodistribution studies further revealed enhanced delivery of mRNA to macrophages in both the liver and spleen using lipids A2 and A2 R.

Conclusions: Ionizable lipids A2 and A2R enable improved extrahepatic

mRNA delivery, particularly to macrophage populations in the spleen. Targeting macrophage populations across multiple organs may provide a strategic advantage in attenuating the progression of NAFLD using mRNA-LNP therapeutics.

Treating Triple-Negative Breast Cancer using Immunotherapeutic TAMs-mimicking Nanoparticles

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Objectives: Tumor-associated macrophages (TAM) are pivotal contributors to tumor progression, metastasis, and immune evasion in triple-negative breast cancer (TNBC). Despite their critical role, most therapeutic strategies primarily target tumor cells, overlooking the immunosuppressive tumor microenvironment (TME). This study aims to develop an innovative, drug-free therapeutic platform called MPsomes, macrophage biomimetic nanoparticles, designed to modulate TAM recruitment in TNBC.

Methods: MPsomes were fabricated using a microfluidic-assisted approach by integrating macrophage-derived membrane proteins into lipid-based nanoparticles. Their functionality was assessed in-vitro through adhesion assays using inflamed endothelial monolayers, tumor vessels-mimicking flow chamber assays, and transwell migration assays. In-vivo efficacy was evaluated in TNBC mouse models by examining TAM infiltration and tumor progression following systemic MPsomes administration, compared to conventional liposomes.

Results: In-vitro, MPsomes demonstrated selective adhesion to inflamed endothelium and effectively reduced macrophage recruitment across endothelial barriers. In-vivo, treatment with MPsomes led to a significant reduction in intratumoral TAM populations and resulted in a considerable slowdown of tumor growth, compared to liposome control.

Conclusions: MPsomes offer a drug-free immunotherapeutic strategy capable of modulating the tumor microenvironment by targeting and disrupting TAM dynamics. These findings underscore the therapeutic potential of biomimetic nanoparticles in reshaping immune landscapes and slowing down tumor progression in TNBC.

Modulating the Metastatic Microenvironment of TNBC Using Biomimetic Nanoparticle

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Metastatic Triple-negative breast cancer (TNBC) is characterized by a high risk of mortality. The common organs for the development of metastatic TNBC are lungs, bones and brain. The metastatic microenvironment of triple-negative breast cancer (TNBC) is highly immunosuppressive and promote tumor cell extravasation, survival, and colonization at distant sites. Metastasis-associated macrophages (MAMs) are known to promote tumor progression by secrete vascular endothelial growth factor A (VEGFA), enhancing vascular permeability and suppressing immune responses. In this study, we will develop biomimetic lipid nanoparticles coated with membranes from polarized J774 macrophages (M2 phenotype) to competitively inhibit MAMs at inflamed endothelial sites- Macrophage-Based Nanoparticles M2 (MPsomes2.0).

We will characterize MPsomes2.0 in terms of membrane protein composition, stability, and their targeting capability toward inflamed endothelial cells. Their therapeutic potential will be evaluated through in vitro assays of inflamed endothelial cells and in vivo using murine model of TNBC lung metastasis. We hypothesize that MPsomes2.0 will reduce cancer cell extravasation and modulate the metastatic microenvironment.

This drug-free, macrophage-inspired approach may offer a novel immunomodulatory strategy for managing TNBC metastasis and improving therapeutic outcomes.

Developing Lipid Nanoparticle-Mediated Delivery of GRIN2B pDNA for Targeted Gene Therapy in GRIN2B-R

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GRIN2B-related neurodevelopmental disorders also result from heterozygous loss-of-function mutations in the GRIN2B gene, which encodes the GluN2B subunit of the NMDA receptor. These mutations impair excitatory neurotransmission and early brain development, leading to cognitive and behavioral impairments. Although the genetic basis is well understood, no current therapies address the underlying molecular cause.

To address this need, we developed a non-viral gene delivery system using brain-targeted lipid nanoparticles (LNPs) encapsulating plasmid DNA (pDNA) encoding GRIN2B. The LNPs were optimized for efficient central nervous system (CNS) delivery, and we validated their performance in primary neuronal cultures, demonstrating effective uptake and GluN2B protein expression via molecular and fluorescence-based assays. This provides an essential step toward evaluating the functional effects of gene restoration in neurons. In ongoing studies, we aim to assess how GluN2B expression alters neuronal excitability and synaptic activity using electrophysiological recordings. These experiments will be complemented by high-content imaging and molecular assays to track neuronal activity and synaptic integration following transfection.

For in vivo evaluation, we employed intranasal administration of LNPs to bypass the blood-brain barrier via olfactory and trigeminal pathways. Following both mRNA and pDNA LNPs delivery through this route, we detected reporter protein expression in the brain, with lower expression levels in peripheral organs, highlighting the selectivity of this non-invasive approach. We are currently mapping brain regions and cell types that internalize the LNPs and express the delivered genetic material, with a focus on achieving neuronal specificity and minimizing off-target expression through promoter optimization.

Our findings represent a proof-of-concept for a novel LNP-based gene replacement approach for GRIN2B haploinsufficiency. Beyond GRIN2B, this platform may be extended to other monogenic neurodevelopmental disorders, offering a versatile and clinically relevant framework for CNS-targeted gene therapy.

An Abdominal Aortic Aneurysm Micro-Physiological Model for the Study of Localized Nano-Therapeutics

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Introduction: Abdominal Aortic Aneurysm (AAA) is a life-threatening vascular condition characterized by chronic inflammation, oxidative stress, smooth muscle cell (SMC) apoptosis, and extracellular matrix degradation by matrix metalloproteinases (MMPs). Despite its severity, no pharmacological treatments are currently approved. Nanoparticle-based systems delivering agents such as MMP inhibitors and anti-inflammatory drugs have shown promise in animal studies but still require validation in human-relevant models. This highlights the need for advanced micro-physiological platforms for reliable preclinical drug assessment.

Methods/Materials: We are developing a human micro-physiological "organ-on-chip" model of AAA , which features a lower microfluidic channel lined with human endothelial cells (ECs) under flow, and an upper chamber containing human aortic smooth muscle cells (HAoSMCs), separated by a semi-permeable polyethylene terephthalate (PET) / poly(dimethylsiloxane) (PDMS) membrane. To induce AAA-like conditions, pathological stimuli such as H_2O_2, Angiotensin II, and elastase are applied. The model is then evaluated using assays for apoptosis, reactive oxygen species (ROS), MMP activity, elastin degradation, and calcification.

In parallel, fluorescent poly(lactic-co-glycolic acid) (PLGA) nanoparticles loaded with Nile Red are first synthesized and functionalized with vascular adhesion molecules for targeted delivery. Then, therapeutic PLGA nanoparticles encapsulating doxycycline, rapamycin, or pentagalloyl glucose, each of which has shown anti-inflammatory, antioxidant, or aneurysm-suppressing effects in previous AAA studies, will be tested for their efficacy in the model.

Results: Preliminary results demonstrate successful attachment of ECs under flow, forming a near-continuous monolayer. Cells were seeded at ~10,000 cells/µL, with flow maintained under perfusion at 30 µL/hour for 72 hours. Nile Red-loaded PLGA nanoparticles displayed a uniform size distribution with an average size of approximately 200 nm. Pathological response assays and synthesis of drug-loaded nanoparticles for therapeutic testing are ongoing.

Conclusions: This innovative AAA model can serve as a robust preclinical platform for evaluating nanoparticle-based therapies, potentially guiding future vascular disease treatments.

A Rational Design of Ionizable lipids for Lung-Specific mRNA delivery

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Introduction / Background: Nucleic acid-based therapeutics, such as siRNA, mRNA, and CRISPR-Cas systems, have shown immense potential for treating cancer, viral infections, and genetic disorders. However, nucleic acids are unable to cross the cell membrane on their own due to their inherent instability and poly-anionic nature. Lipid nanoparticles (LNPs) have emerged as the most successful delivery systems, as evidenced by their clinical use in COVID-19 and RSV mRNA vaccines. Among the LNP components, ionizable lipids play a pivotal role in RNA encapsulation and intracellular delivery. Despite the success of mRNA-LNPs, extra-hepatic delivery, especially to the lungs, remains a significant challenge.

Methods / Materials: We designed and synthesized a focused library of ionizable lipids featuring biodegradable linkers, including ester, carbonate, amide, and urea functionalities. These lipids were formulated into LNPs using standard helper lipids and tested for their physicochemical properties, RNA encapsulation efficiency, and in vitro transfection efficiency. We conducted in vivo biodistribution studies using luciferase mRNA and CRE mRNA in mice to evaluate organ and cell-specific expression, respectively, and identify lipids with lung-targeting potential.

Results: Our results demonstrate that subtle changes in the linker chemistry of ionizable lipids significantly influence the physicochemical properties,

pKa, and organ-selectivity of LNPs. Lipids incorporating amide and urea linkers exhibited a favorable pKa range (>7.0), enhancing lung-specific mRNA delivery. One lead candidate, Lipid 35, showed pronounced mRNA expression in the lungs. When formulated with mRNA encoding a bacterial toxin (Pseudomonas exotoxin A, mmPE), Lipid 35-LNPs significantly reduced lung tumor burden and prolonged survival in a metastatic lung cancer mouse model.

Conclusions: Our study highlights the importance of rational design in ionizable lipid chemistry to achieve targeted mRNA delivery. The use of biodegradable linkers, particularly amide and urea moieties, enabled the development of lung-specific LNPs with therapeutic efficacy, offering a promising strategy for extra-hepatic RNA delivery.

Functional Personalized Complex Combination Nano Therapy for Osteosarcoma

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Osteosarcoma, the most common primary bone cancer in adolescents, remains a major challenge, with survival rates below 20% for metastatic cases and no significant therapeutic progress in over 40 years. Current treatments face systemic toxicity and resistance. Functional personalized therapy using drug sensitivity profiling and synergistic drug combinations, offers a promising path forward. This study explores polydopamine-stabilized nanoparticles for precision-targeted kinase inhibitor(KI) delivery, addressing OS heterogeneity and treatment gaps. A panel of 17 drugs, including chemotherapeutics and KI, was screened across four osteosarcoma cell lines. Promising drug pairings, trametinib-ponatinib and rapamycin-ganetespib, were encapsulated into polydopamine-stabilized nanoparticles (< 150 nm) and characterized for stability and encapsulation efficiency. In vitro efficacy was evaluated in 2D and 3D models, with synergy quantified using computational tools. In vivo studies using K7M2 xenografts assessed tumor volume reduction, survival, biodistribution, and toxicity. Each result of the drug sensitivity assays was compared to predictions made by frontier LLM models, to evaluate if the results are based on known hypotheses and are somewhat predictable. Functional profiling revealed distinct drug sensitivities across cell lines, demonstrating the necessity of personalized approaches. Nanoparticle formulations achieved superior stability and encapsulation, enhancing drug delivery and synergy in vitro, particularly in spheroids, where traditional therapies showed reduced efficacy. In vivo studies using K7M2 xenografts, nanoparticle combinations significantly reduced tumor volume and improved survival compared to standard-of-care treatments. The alternating administration strategy further minimized systemic toxicity while maintaining efficacy. Histological analysis confirmed reduced off-target effects and better preservation of healthy tissue in the alternating group. In addition, we show that the vast majority of the results could not have been predicted by all LLMs, emphasizing the need for experimental data-driven personalization vs

hypothesis-driven. This study demonstrates that combining synergistic drugs with nanoparticle delivery offers an effective and safe strategy to address osteosarcoma heterogeneity and resistance.

Quantum Fertilizer for Agriculture: Enhancing Photosynthesis via Photocatalytic Ag2S Quantum Dots

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Climate change presents unprecedented challenges to global agriculture, with rising temperatures, extreme weather, and increased abiotic stress threatening crop yields. As food demand grows with population growth, improving photosynthetic efficiency offers a promising way to increase crop yields. Here we show that silver sulfide (Ag_2S) quantum dots (QDs), semiconductor nanoparticles 3–12 nm in size, can enhance photosynthesis and improve biomass accumulation by expanding the usable light spectrum. These QDs are water soluble, low in cytotoxicity and possess unique photoelectric and fluorescent properties. Upon exposure to ultraviolet and near-infrared light, electrons in the QDs' metallic lattice become excited and can be transferred to proteins in the photosynthetic electron transport chain, including Photosystem II, as show in Figure 1. The additional electrons may enhance ATP production, resulting in increased biomass accumulation.

In this research we evaluate the impact of Ag_2S QDs on plant growth and photosynthetic efficiency. Ni doped Ag2S QDs are synthesized in ethylene glycol within an inert system. 7 QD sizes were applied Nicotiana tabacum via foliar spraying, and the plants were assessed for dry weight, chlorophyll concentration, leaf area and root length. The treatment with 6.0 ± 0.5 nm QDs showed a significant increase in plant dry weight (55%), leaf area (33%) and root length (30%), and no significant change in chlorophyll concentration, compared to non-treated plants. The QDs significantly increased tobacco biomass and growth parameters under in a growth chamber (sterile, LED as light source). Future experiments will focus on the effect of the QDs in greenhouse conditions (non-sterile, sun as light source). Our findings suggest that nanomaterial-assisted photosynthesis could support sustainable agriculture and improve food security in a changing climate.

Scaling Up Synthetic Cell Production Using Robotics and ML Toward Therapeutic Applications

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Objectives: Synthetic cells (SCs), developed through bottom-up synthetic biology, hold great potential for biomedical applications, with the promise of replacing malfunctioning natural cells and treating diseases with spatiotemporal control. Currently, most SC synthesis and characterization processes are manual, limiting scalability and efficiency, which hinders clinical translation. In this study, we developed an automated method for large-scale production of protein-producing SCs for therapeutic applications.

Methods: We integrated a robotic liquid handling system (LiHa) for automated solution assembly and employed a tissue dissociator-based emulsification method to scale up SC production. Machine learning (ML)-based image analysis was employed to assess SC quality and protein synthesis, enabling automated, high-throughput and accurate SC characterization. Large-scale luciferase-expressing SCs from a single homogeneous batch, produced via this automated method, were administered to mice, allowing for real-time monitoring of protein expression and reducing experimental variability.

Results: Automating stock solution preparation reduced manual labor and variability and reduced production time by 50%. Tissue dissociator-based emulsification achieved a 30-fold increase in batch size while preserving SC characteristics. Convolutional neural network (CNN)-based analysis outperformed traditional methods by accurately distinguishing SCs from oil droplets, enhancing quality control. In vivo, SCs produced using the automated pipeline exhibited consistent protein expression and significantly lower variability between test subjects compared to manually produced SCs.

Conclusions: The developed automated methods markedly improved the scalability, consistency, and quality of SC production, paving the way for preclinical and clinical applications. Machine learning–enabled characterization further enhanced quality assurance. Together, these advancements represent critical steps toward the clinical translation of SC-based therapies.

Reference

Sharf-Pauker, N., et al. Scaling Up Synthetic Cell Production Using Robotics and Machine Learning Toward Therapeutic Applications, Adv. Biology, 2025, 10.1002/adbi.202400671.

Rose Bengal Conjugated to Lectins for Targeted Antibacterial Photodynamic Treatment

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Due to rising antibiotic resistance, it is necessary to develop alternative ways to combat pathogenic bacteria. One alternative is photodynamic antibacterial chemotherapy (PACT). This work presents the conjugation of the photosensitizer Rose Bengal (RB) to lectins to improve its efficacy against Gram-positive and Gram-negative bacteria. Two lectins, concanavalin A (ConA) and wheat germ agglutinin (WGA), were covalently linked to RB. Spectroscopic and chromatographic data confirmed successful conjugation. Microscopic examination demonstrated that both lectins agglutinate cells of Gram-positive S. aureus, including clinical multidrug-resistant MRSA strains, and Gram-negative E. coli, P. aeruginosa, and S. paratyphi B, although ConA showed a more pronounced reaction. Photodynamic assays showed that ConA-RB achieved complete eradication of S. aureus at significantly lower concentrations and light doses than free RB or WGA-RB. ConA-RB also exhibited higher efficacy against Gram-negative bacteria compared to free RB at lower concentrations and shorter illumination periods. WGA-RB was less effective, showing preferential activity against S. aureus. Our findings suggest that lectin-RB conjugates offer a promising approach for selective antibacterial treatment under illumination.

Keywords: conjugation; photosensitizers; Rose Bengal; lectins; concanavalin A; photodynamic antibacterial activity

P53 is a critical tumour suppressor protein that plays a key role in regulating the cell cycle and preventing cancer development

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p53 is a critical tumour suppressor protein that plays a key role in regulating the cell cycle and preventing cancer development. p53 functions primarily as a tetramer transcription factor, activating the expression of genes involved in the response to various cellular stresses. Mutations in the TP53 gene, which encodes p53, are among the most common alterations observed in human cancers, leading to the loss of its tumour suppressive activities. Most of the TP53 mutations identified are dominant negative mutations, which suggests that mutated p53 (mut-p53) will interfere with wild type p53 (wt-p53) when they co-expressed in the cell. We hypothesize that delivery of wt-p53 mRNA by itself will not be effective as cancer treatment, due to the endogenous expression of the dominant negative p53. We suggest that repression of mut-p53 followed by exogenous expression of wt-p53, can transiently restore the native function of p53 in cancer cells, and will lead to apoptosis of the tumor cells. For this aim, we will generate lipid nanoparticles (LNPs) encapsulating both CRISPR inhibition (CRISPRi) mRNA targeting p53, and wt-p53 mRNA. While the CRISPRi-LNPs will repress the transcription of endogenous mut-p53, the exogenous wt-p53 will activate various genes that will lead to apoptosis of cancer cells. Our results show that sequential delivery of CRISPRi to repress endogenous mut-p53 and delivery of wt-p53 can lead to significant cell death of ovarian cancer cell lines. For the utilization of CRISPRi system, we screened for multiple p53 sgRNAs and found a promising candidate that led to ~80% repression of p53 mRNA levels. Next, we screened LNP formulations for efficient delivery to ovarian cancer cells. Our potential ability to restore the native function of p53 in cancer cells can be utilized as a strategy to target p53-bearing cancers independently from the p53 mutation type.

DIAGNOSTIC PROBE FOR SERUM RHEUMATIC HEART DISEASE BIOMARKERS DETECTION

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Rheumatic fever (RF) is a multisystem, immunologically mediated inflammatory disease that occurs as a delayed sequel to group A streptococcal (GAS) infection. Its subsequent complication, chronic rheumatic heart disease (RHD), remains a major public health problem in developing countries. It can damage at least one of the four valves, leading to heart failure and premature mortality.

In addition to antibiotic management, early diagnosis can resolve and prevent those outcomes. Previous studies have shown elevated serum levels of circulating adhesion molecules (CAMs), i.e., ICAM-1, VCAM-1, and E-selectin in patients with severe RHD. Thus, detection of these markers can be useful for RHD diagnosis.

We first designed polymeric probe based on a water-soluble N-((2-hydroxypropyl) methacrylamide) (HPMA) copolymer for serum E-selectin detection. The polymeric probe carries multiple copies of targeting E-selectin binding peptide (Esbp) for binding serum E-selectin, a near infrared fluorescence dye (IR783) to allow visualization, and a 6xHis-tag to allow surface immobilization. The polymer was characterized for the content of each co-monomer, and the optimal fluorescence properties were tested for its sensitivity to identify plasma levels of E-selectin.

The synthesized copolymer P-(6His)-(Esbp)-(IR783) with about 4 mol% of Esbp, 2.5 mol% of IR-783 and ~ 1 mol% of 6His-tag, demonstrated a limit of detection below the circulating biomarker levels (10 ng/mL), confirming its high sensitivity and strong potential for identifying RHD serum biomarkers. Ongoing experiments are evaluating the correlation between the polymeric probe signal and serum E-selectin concentration. In subsequent studies

we will apply this probe to detect E-selectin in mouse serum, followed by analogous investigations of serum ICAM and VCAM quantification.

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Biomimetic Microglia-Derived Nanoparticles for Reducing Traumatic Brain

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The Technion

Traumatic Brain Injury (TBI) occurs when an external force impacts the head, triggering a neuroinflammatory response primarily driven by microglial activation into the proinflammatory (M1) phenotype. Prolonged M1 activation leads to excessive neuroinflammation, causing brain tissue damage and increasing the risk of neurodegenerative diseases. In this study, we propose the use of biomimetic microgliaderived nanoparticles (MGsomes) to target inflamed brain regions post-TBI and reduce inflammation. MGsomes, coated with microglial membrane proteins, interact with activated microglia and absorb pro-inflammatory cytokines, acting as decoys to reduce inflammation.

This homotypic cell-to-cell interaction enables specific microglia targeting and promotes a shift toward the anti-inflammatory (M2) phenotype.

To evaluate this approach, we will fabricate and optimize MGsomes using a turbulent mixing nanoparticle fabrication method. We will assess their biocompatibility in neuron and microglia cultures, investigate their cytokine absorption capacity, and determine their impact on neuronal survival in vitro. Finally, we will examine MGsome biodistribution and therapeutic efficacy in a mouse TBI model, evaluating both molecular and behavioral outcomes. This study aims to establish MGsomes as a novel therapeutic strategy for reducing neuroinflammation and improving recovery following TBI.

Noninvasive Drug Delivery: Leveraging the Power of Epithelial Cells

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The biomimicry approach and bioengineering technologies have reached new heights in biomedicine and pharmacology. A prime example of the biomimetic approach is the novel class of drug delivery systems (DDS)—cell-based DDS. Various types of cells have been explored, such as mesenchymal stem cells, red blood cells, and platelet cells. However, none of these vessels are meant for noninvasive drug delivery. Herein, we focused on epithelial cells since they play a crucial role in barrier function and selective permeability, making them an attractive option. We aimed to harness the inherent bioadhesive properties of epithelial cells, allowing for prolonged retention at target sites and enhancing therapeutic efficacy. Epithelial-cell-based DDS may leverage inherent cellular uptake mechanisms, facilitating efficient internalization of therapeutic agents. In this project, we tested several epithelial cell lines (i.e., buccal TR146, intestinal Caco2, colon HCT 116, colorectal HT-29, and keratinocyte HaCAT) for proof of concept to serve as noninvasive DDS. The membrane-based vehicles (MBVs) hydrodynamic diameter ranged from 200 nm to 1200 nm, while the obtained polydispersity index range was 0.2–0.4. The surface charge (i.e., ζ potential) of MBVs ranged from -15±0.6 mV to -23±2.8 mV. Moreover, cryo-TEM imaging confirmed that our MBVs are spherical, mainly with a single wall. Our developed MBVs demonstrated impressive encapsulation efficiency of 40–60%. To assess their bioadhesion properties, a novel in vitro method was developed. We found significant superiority in self- and cross-bioadhesion for all the tested cell lines using this method. Additionally, it was determined that the bioadhesion force of TR146 MBVs was over 10 times stronger than that of common bioadhesive hydrogels (e.g., alginate and gelatin). Lastly, the cells' natural preference for self- or cross-cellular uptake was tested. Although no apparent tendency to a particular type of uptake was found, the effect of increasing MBVs concentration showed clear and enhanced uptake.

Stereoselective Interactions of Chiral Polyurea Nanocapsules with Albumins

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Exploiting the chirality of nanometric structures to modulate biological systems is an emerging and compelling area of research. In this study, we reveal that chiral polyurea nanocapsules exhibit significant stereoselective interactions with albumins from various sources despite their nearly neutral surface potential. Moreover, these interactions can be modulated by altering the nanocapsule surface composition, offering new opportunities to impact their distribution and, if used as a drug delivery system, the pharmacokinetics of the drug. Notably, these interactions promote preferential cellular internalization of only one chiral configuration. We synthesized chiral polyurea nanocapsules with reproducible sizes via interfacial polymerization between toluene 2,4-diisocyanate and d- or l-lysine enantiomers on a volatile oil-in-water emulsion interface, followed by solvent evaporation. Further synthesis optimization reduced the capsule size to a range compatible with in vivo administration, and capsules with alternating chiral patterns were also produced. The stereoselective interactions with albumins were assessed through capsule size changes, fluorescence quenching, and surface charge measurements. Biocompatibility, stability, and cellular internalization were evaluated. Additionally, scanning transmission electron and atomic force microscopy were carried out to assess the capsule shape, surface composition, and morphology. We discovered that d-nanocapsules exhibited 2.1–2.6 times greater albumin adsorption compared with their l-counterparts. This difference is attributed to the distinct morphology of d-nanocapsules, characterized by a more concave shape, central depression, and rougher surface. The extent of adsorption could be finely tuned by adjusting the d- and l-lysine monomer ratios during synthesis. Both chiral configurations demonstrated biocompatibility and stability with d-nanocapsules showing a 2.5-fold increase in cellular internalization.

BONE MARROW CXCR4-TARGETED LIPOSOMES LOADED WITH BORTEZOMIB OVERCOME MULTIPLE MYELOMA RESISTANCE

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Introduction: Multiple myeloma (MM) poses a significant therapeutic challenge due to its persistent progression and low survival rate. Although the proteasome inhibitor, bortezomib, has revolutionized MM treatment, MM aggressiveness and drug resistance remain a critical concern. Furthermore, we have previously shown that the host in response to bortezomib generates pro-tumorigenic effects which can explain therapy resistance. Specifically, the MM microenvironment in the bone marrow compartment is enriched with pro-inflammatory macrophages which secrete IL-16 and IL-1β, contributing to MM expansion and regrowth.

Results: We developed AMD3100-targeted Bortezomib Liposomes (ATBL) designed for targeted delivery of bortezomib to MM cells in the bone. Uptake of ATBL into MM cells was dependent on CXCR4 and displayed increased concentration in cells expression CXCR4 compared to non-targeted liposomes, both in vitro and in vivo. Treating MM-bearing mice with ATBL achieved superior therapeutic efficacy compared to treatment with

free bortezomib or non-targeted bortezomib-loaded liposomes. Notably, therapeutic activity of ATBL was limited in mice inoculated with CXCR4-knockdown MM cells, highlighting CXCR4 as a potential biomarker for ATBL therapeutic response. Remarkably, ATBL was effective against an aggressive and bortezomib-resistant MM clone both in vitro and in vivo. Toxicity and biodistribution profiles demonstrated the safety, tolerability, and bone marrow-targeting ability of ATBL using in vivo, in vitro, and ex vivo models including lab-on-a-chip of bone marrow. Importantly, ATBL did not induce host-mediated pro-tumorigenic activities associated with MM aggressiveness, clearly differentiating it from bortezomib treatment. Additional results using a lipid nanoparticle strategy will be presented in the meeting.

Conclusions: This study highlights ATBL as a promising next-generation proteasome inhibitor-based therapy that incorporates bone marrow-targeting and MM ability and sensitizing elements to overcome drug resistance in MM.
to a particular type of uptake was found, the effect of increasing MBVs concentration showed clear and enhanced uptake.

Enhancing Therapeutic Efficacy and Immune Response with Bispecific Gold Nanoparticles in Cancer

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Introduction: Bispecific antibodies (bsAbs) emerge as a new promising cancer immunotherapy, redirecting immune cells to tumors and blocking survival pathways. However, their clinical use faces challenges, including complex design, poor pharmacokinetics, limited stability, and adverse effects in solid tumors' suppressive microenvironments [1]. This study presents a gold nanoparticle (GNP)-based nanoplatform leveraging GNPs' biocompatibility and tunable properties to enhance bsAb therapies [2].

Methods: GNPs were functionalized with trastuzumab and pertuzumab via a PEG linker. The resulting Bispecific-GNPs (BsGNPs) were assessed in breast cancer cell lines for cytotoxic ability (CyQuant analysis) and immune activation (via co-culture with human NK cells and flow cytometry). In a mouse model of breast cancer, BsGNPs were evaluated for tumor accumulation using computed tomography (CT) imaging, and for anti-tumor efficacy by tumor size measurements.

Results: The BsGNPs displayed uniform size distribution (~20 nm) and successful dual antibody conjugation. In vitro, it showed enhanced tumor cell targeting, immune cell engagement, and NK-cell activation compared to free Abs. In vivo, BsGNPs demonstrated targeted accumulation in tumor tissues and therapeutic efficacy in a mouse model of breast cancer.

Conclusion: This study demonstrates the successful development of BsGNPs, highlighting the potential of this approach for dual-antibody cancer therapy. Our results show enhanced in vitro and in vivo efficacy, along with precise tumor targeting. BsGNPs offer a significant advancement in nanoparticle-based treatment by combining the benefits of gold nanoparticle delivery with

synergistic, bispecific antibody targeting.

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Shear Responsive Red Blood Cell-Based Carriers for Targeted Delivery

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Introduction: Red blood cells (RBCs) possess unique mechanical properties that support their prolonged circulation and essential physiological functions, making them promising vehicles for drug delivery. Therapeutic agents can be loaded into RBCs using hypotonic pre-swelling or attached directly to the membrane. A key feature of RBCs is their remarkable deformability, which allows them to pass through even the narrowest capillaries. However, under elevated shear stress, pores may form in their membrane. Since many cardiovascular diseases are associated with high shear stress, this phenomenon can be leveraged for targeted, shear-responsive drug delivery, enabling localized therapeutic intervention.

Methods: Human RBCs were collected and loaded with FITC-Dextran via hypotonic dialysis. The loaded RBCs were then perfused through life-sized vessel models representing healthy and stenotic arteries with varying degrees of narrowing (0%, 25%, 75%, and 90% stenosis). Computational fluid dynamics (CFD) simulations were conducted for all models using Ansys Fluent®, with meshing performed using Fluent Meshing. Flow cytometry was used to analyze RBCs before and after perfusion. To assess structural integrity and function, RBCs were also perfused through pulmonary capillary microfluidic devices. CD47, a membrane glycoprotein involved in immune self-recognition, was labeled to evaluate membrane preservation.

Results: Flow cytometry results revealed significant FITC-Dextran release from RBCs in the 75% and 90% stenosis models, correlating with CFD results of regions of high shear stress and velocity. CD47 expression remained consistent, indicating preserved membrane integrity. Microfluidic

experiments confirmed RBC deformability was maintained and no notable FITC release occurred, suggesting the release in stenotic models was shear-induced.

Conclusion: Shear-responsive RBCs offer a promising biomechanically activated platform for targeted, localized drug delivery to flow-restricted and stenotic arteries. This approach may also be adapted for other vascular diseases characterized by abnormal hemodynamics.

From Micro-Crystals To Nano-crystals for Enhanced Delivery and Biological Applications

Roy Goldraich, Maya Amnony, Edwar Odeh, Elissar Ibrahim, Shady Farah

Nanocrystals have emerged as a promising strategy to overcome the limitations of poorly water-soluble drugs, a challenge that affects nearly 40% of marketed drugs and 70% of molecules in development. This project focuses on the size reduction of drug crystals from the microscale to the nanoscale, targeting a mean particle size of approximately 50 nm. The transformation into nanocrystals enhances critical drug properties, including saturation solubility, dissolution rate, bioavailability, and tissue permeability. These attributes make nanocrystals especially attractive for improving systemic delivery, injectability, and passage through physiological barriers such as the blood-brain barrier (BBB).

Mechanical top-down methods were used to reduce particle size, with initial dynamic light scattering (DLS) measurements indicating a mean size of 268 nm and a polydispersity index (PDI) of 0.2258. Optimization aims to achieve a narrower size distribution (PDI < 0.2) and reduced particle size, key to ensuring enhanced pharmacokinetics and minimizing phenomena like Ostwald ripening.

Characterization by optical and scanning electron microscopy confirmed successful downsizing and morphological changes, consistent with nanocrystal formation. Future work will involve solid-state characterization using DSC, TGA, and XRD to assess thermal stability and crystallinity. Additives will be employed to mitigate aggregation and enhance formulation stability.
Guided by recent literature, the project also anticipates potential downstream applications, such as nanocrystal-based drug carriers for oral, intravenous, or targeted therapies. These formulations can be adapted with surface coatings or ligands for site-specific delivery, including tumor or brain targeting. This ongoing work aims to contribute to the growing field of nanocrystal-enabled drug delivery, bridging the gap between formulation challenges and clinical efficacy.

Engineering and Formulating Long-Releasing Hollow-like or Condensed Progesterone Hormone Microcrystals with Controlled Polymorphism and Delivery Properties

Edwar Odeh, Merna Shaheen-Mualim, Noor Wishahi, Neta Kutner, Muhammad Hijazi,and Shady Farah

Progesterone is an endogenous steroid hormone that has important roles in the reproductive system in the female body of humans and other species. Its major roles are in the menstrual cycle, pregnancy, and embryogenesis. Progesterone crystals have been obtained from several crystallization techniques, including the solvent:anti-solvent method. In this study, two crystal shapes of progesterone (hollow-like and condensed microcrystals) are produced using this method, with high yields, controlled polymorphism, crystal habits and release profiles.

Hollow microcrystals and condensed microcrystals were developed in an isopropyl alcohol (IPA) and double-deionized water (DDW) system, and an acetonitrile (AcN) and DDW system, respectively. The microcrystals were characterized using a brightfield microscope and scanning electron microscopy (SEM), differential scanning calorimetry (DSC), powder X-ray diffraction (PXRD), and single X-ray diffraction (SXRD).

Microscopic analysis revealed that microcrystals from the IPA:DDW system are hollow with diverse crystal habits, while those from the AcN:DDW system are more condensed. Size distribution measurements show that both microcrystals have a broad size distribution of one stable polymorph, making them suitable for tunable release. These microcrystals were examined for release capabilities and found to exhibit prolonged and controlled release over 14 days under accelerated release conditions, highlighting their potential for long-term and localized delivery systems.

Development of Water-Soluble Functionalized Oligomers with Controlled Bleach Releasing Properties for Long-Term Antiviral Applications

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Recently COVID-19 pandemic has spread globally and claimed millions of lives. Surface contamination is considered one primary route that spreads viruses, especially in public areas/surfaces. The leading measure includes disinfecting surfaces using bleach e.g., several times a day. Therefore, there is a need for new, efficient, and stable disinfectants with controlled release properties to protect surfaces from viral contamination and transmission. Reported research efforts focus on small-molecule-based surface decontamination, including solutions such as bleach and ethanol. In this work, we are focusing on utilizing functional polymers by synthesizing a new class of antiviral oligomers modified with n-halamine and quaternary ammonium functionalities as long-lasting disinfecting materials with controlled and long-term bleach releasing. The most active oligomers demonstrated better antiviral activity compared to household bleach, with over 99.8% effectiveness against SARS-CoV-2 as well as other viruses at far lower concentrations by 60 times. Furthermore, these materials demonstrated viral deactivation and sustained efficacy against viruses on various surfaces for the long term, while causing no harm to human cells. Thus, these polymers are promising alternatives for future pandemics, as well as long-lasting with controlled release features for routine use.

Development of a High-Throughput Assay for Screening Platelet-Rich Clot Dissolution Using Automated

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Introduction/Background: Platelet-rich thrombi are major contributors to heart attacks and strokes, yet they are poorly responsive to current thrombolytic agents such as tissue plasminogen activator (tPA) [1]. N-acetylcysteine (NAC), a thiol-containing compound, has recently shown potential in dissolving these clots [2], [3]. However, traditional methods for assessing thrombolytic efficacy, such as platelet aggregometry, are low-throughput and resource-intensive, limiting large-scale screening of potential agents.

Methods/Materials: We developed a 96-well high-throughput assay for quantitative evaluation of platelet-rich clot dissolution. Platelet-rich plasma (PRP) was prepared from human whole blood and induced to clot with collagen. Clot formation occurred under orbital shaking in the presence of various test compounds. The assay employed an automated LionHeart FX microscope to image and quantify clot formation based on clot area in each well. NAC and BOC-Cysteine, a structurally similar thiol compound, were used as test agents in the initial assay validation.

Results: Automated image analysis revealed a significant reduction in clot area in wells treated with both NAC and BOC-Cysteine compared to untreated controls. The effect was concentration-dependent and not observed in vehicle-only (DMEM) conditions, confirming that clot dissolution resulted from drug activity rather than mechanical effects or medium interference. These results validate the assay's ability to detect pharmacologically relevant thrombolytic activity.

Conclusions: We have established a rapid, reproducible, and scalable method for assessing clot dissolution in a high-throughput format. This system supports screening of FDA-approved drugs and novel NAC-based

formulations. Future work will focus on expanding the chemical library, validating hits using aggregometry and microfluidic platforms, and exploring mechanistic pathways underlying thiol–mediated clot degradation.

Protein Crystallization for Drug Delivery Application

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Over the past 2 decades, biopharmaceuticals have grown exponentially in treating multiple conditions such as cancer, cardiovascular diseases, and viral infections. However, their application faces many challenges, including poor stability and limited delivery options. Protein crystals offer a promising solution for these limitations, providing stable, high-concentration, low-viscosity formulations with controlled and prolonged drug release.

In this study, we investigate the crystallization of lysozyme, an antimicrobial enzyme and part of the innate immune system. Beyond its antimicrobial activity, lysozyme is reported to have anticancer, antioxidant, and antiviral properties, highlighting its potential as a multifunctional therapeutic agent. The developed crystals were investigated for physical and chemical properties. By studying these bioactive crystals, we aim to develop a carrier-free lysozyme crystal-based system for drug delivery applications.

Precision 4D Printing of Multifunctional Olive Oil-Based Acrylate Photoresin for Biomedical and drug delivery application

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Since the development of 3D printing technology, significant efforts have been made to develop new 3D printable materials for biomedical and drug delivery applications. Despite recent advancements, the limited availability of photoactive resins has driven ongoing research into novel photoresins with multifunctional capabilities. In this context, we report a biobased photoresin derived from modified olive oil, designed for high-resolution, solvent-free 4D printing with multifunctional capabilities. The physicochemical properties of the printed polymers were fine-tuned using acrylic acid as a diluent and comonomer. The mechanical properties of the printed polymers closely resemble various soft tissues, such as ligaments, articular cartilage, and soft collagenous bone, highlighting their potential for soft tissue engineering applications. Furthermore, the printed polymers exhibit excellent shape memory 4D attributes and exceptional antimicrobial properties against both gram-negative and gram-positive bacteria, underscoring their multifunctional nature. Additionally, the polymers demonstrate outstanding hemocompatibility and good cytocompatibility towards mouse fibroblast cells, further suggesting their suitability for soft tissue engineering. These developed materials were also studied for their ability to incorporate hydrophobic drugs. In summary, our newly developed biobased resin offers an environmentally friendly alternative to traditional fossil-based photoresins, meeting the growing demand for advanced photoresins with superior high-resolution printing and smart properties for potential tissue engineering and potentially as a carrier platform for localized and long-term drug delivery applications.

Synthesis of Multifunctional Biodegradable Polyesters for Drug delivery and Biomedical Applications

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Many polyesters are considered excellent degradable polymeric candidates for drug delivery thanks to the reversibility of the ester bonds in their backbone in different PH environments. This property, in addition to the possibility of synthesizing them from naturally extracted monomers, makes them a unique category of biodegradable materials. While this is one of the major requirements, among others, to be applicable for biomedical applications. We synthesized a library of polyesters, including IU, using two major synthesis protocols with various conditions. Here we present one method that was used in the synthesis process of Citric acid-PolyEthyleneGlycol 400-Imidazolidinyl Urea co-polymer (CA-PEG400-IU), based on a two-step reaction. The first step is the pre-polymer CA-PEG400 preparation, while the second one is the reaction of this pre-polymer with IU, resulting in the production of this co-polymer, among others. This polymer showed very promising results in various aspects along with degradability and high anti-microbial activity, making it a promising candidate in drug delivery.

Enhancing Drug Permeability Into Solid Tumors Via Optoelectronic Silicon Nanowires-Mediated Electrop

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Objective: Many solid tumors are harder to treat due to physical barriers that often limit therapeutic agent distribution and efficacy. Several external stimuli methods, such as ultrasound, ionizing radiation, and photothermal stimulation, are being tested to improve drug delivery into solid tumors.

Electroporation (EP) uses electric pulses to permeabilize cell membranes to insert macromolecules such as oligonucleotides and proteins in in-vitro cell cultures.

Currently, EP is applied invasively, requiring electrodes to be placed in direct contact with the cells to deliver the electrical pulses.

In this study, we evaluate optoelectronic silicon nanowires (SiNWs) which are semiconducting nanomaterials capable of light-triggered electrical stimulation, as a tool to remotely induce membrane poration as a minimal-invasive strategy to enhance permeability in 2D and 3D cancer models.

Methods: 2D and 3D in vitro models of Head and Neck Squamous Cell Carcinoma cultures (Cal33) were used to test SiNWs photoelectrical effects. Uptake of SiNWs was visualized via bright-field, light-sheet fluorescence, and confocal microscopy, followed by 3D reconstruction in Imaris.
Samples were optically stimulated using LED pulses by using Incucyte microscope and a tailor-made LED system. Viability was assessed with the CellTiter-Glo assay, and membrane permeability was tested by propidium iodide penetration assays.

Results: Confocal and light sheet microscopy confirmed SiNW internalization in both 2D cells and 3D spheroids. Post-stimulation cell viability showed high safety profile and optically stimulated spheroids exhibited an increase in

non-permeable propidium iodide uptake compared to unstimulated controls.

Conclusion: Preliminary results show that optoelectronic stimulation using SiNW enhances spheroids' permeability. In future work, we plan to optimize the method to achieve better poration results and to enhance the permeability of different macromolecules, drugs, and nanoparticles for cancer treatment.

Mucoadhesive Chitosan-Polydopamine Hydrogels for Oral Delivery of Liposomes Targeting the Brain

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Most current strategies for delivering therapeutics to the brain rely on IVs, which are invasive and reduce patient compliance. Oral drug administration offers a non-invasive alternative, but it faces challenges including drug degradation in the gastrointestinal tract and limited absorption across the blood-brain barrier (BBB). To address these challenges, we aim to develop a chitosan-based hydrogel coated with polydopamine (PDA) for the oral delivery of liposomes functionalized with targeting ligands. This system serves as a targeting ligand to facilitate BBB transport and may provide neuroprotection for gut-to-brain delivery.

The hydrogel is formed by crosslinking chitosan with genipin, creating a biocompatible, mucoadhesive matrix with tuneable swelling properties suitable for gastrointestinal residence. A PDA coating is applied to enhance hydrogel stability in the gut and improve mucoadhesion while providing chemical handles for further modification. Critically, the hydrogel serves a dual protective role: it shields the liposomes from the harsh gastrointestinal environment while simultaneously protecting the intestinal lining from potential irritation caused by the therapeutic agents carried within the liposomes.

Swelling experiments demonstrated that the concentration of PDA within the coating influences both the swelling behaviour of the hydrogel and the release kinetics from the gel, as assessed using metronidazole as a small model molecule to simulate drug release profiles. This tunability allows optimization of the system for controlled release aligned with therapeutic needs.

In summary, chitosan hydrogel-PDA system loaded with targeted liposomes offers a promising non-invasive strategy for the oral delivery of neurotherapeutics, aiming to improve absorption in the gut and targeted

delivery to the brain for neurodegenerative disease treatment. Future work will focus on in vivo evaluation of pharmacokinetics, biodistribution, and therapeutic efficacy to advance this system toward clinical application.

3D Printing of Personalized Catheters with Smart pH-Responsive Coating for Improved Functionality for Long-Term Therapy Delivery

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Hydrocephalus is a common brain disorder. The existing gold standard treatment method for hydrocephalus depends on surgical cerebrospinal fluid shunting using "one-size-fits-all" catheters, which are subjected to various complications, such as flow resistance, blockage, mechanical malfunctions, host-immune response, and microbial infection. Herein, we proposed implementing three-dimensional (3D) printing technology to develop the next generation of catheters with improved functionality and controlled liquid flowability, which can also be used as part of drug delivery systems. Our suggested technology is based on imaging data on the final destination in a personalized manner. In this work, we report for the first time, digital light processing (DLP) 3D printing of helical-shaped, flexible catheters using commercially available KeySplint soft resin. These catheters are fully customizable, where different parameters can be manipulated, such as diameter, the number and placement of drainage holes tailored to individual patient needs. The stability study of the 3D-printed KeySplint samples proved

the structural stability under physiological conditions for at least 3,240 hrs (135 days). Moreover, to further enhance the catheter's functionality, a pH-responsive smart surface chemistry was introduced on the catheter surface using two strategies (via plasma coating and by simply mixing with 3D printing resin). The coating can respond dynamically to tackle two critical challenges related to catheters: blockage of the catheters and infection/biofilm prevention via chemical intramolecular rearrangement. Both CB-OH coated and 5% CB-OH mixed 3D-printed catheters significantly inhibited bacterial biofilm formation compared to the catheter control. Additionally, the CB-OH coated 3D-printed helical catheters showed a 37-folds reduction in particle deposition per unit volume relative to conventional 3D-printed linear catheters. Thus, the proposed surface-functionalized 3D-printed personalized catheters could provide a promising solution for many medical implants and treatments, as well as a methodology for long-term therapies and delivery of drugs.

Targeted cell-derived NanoGhost as a platform for metastasis high resolution diagnostics

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Research Objectives: Metastasis, the spread of cancer cells to distant organs, remains the primary cause of cancer-related mortality. Although cancer research advanced significantly in the last decade, currently there are no curative treatments for metastatic disease. Consequently, early detection is critical for improving clinical outcomes. Current imaging modalities lack the resolution and sensitivity needed to identify metastases at early stages. The objective of this study is, therefore, to develop a high-resolution diagnostic platform for metastatic cancer using our proprietary Nano-Ghosts (NGs) technology—nanovesicles derived from mesenchymal stem cell membranes that preserve their native orientation and targeting functionality. We aim to engineer diagnostic Nano-Ghosts (dNGs) by the incorporation of contrast agents within these vesicles, allowing early-stage detection due to the NGs targeting abilities and specificity.

Methods and results: To evaluate the NGs targeting potential towards metastases we performed a series of in vitro and in vivo experiments. In vitro uptake studies were conducted using metastatic cancer cell lines, which demonstrated the specificity of the NGs targeting. The specific targeting to metastatic tumor was further confirmed in vivo, following NGs systemic administration to mouse metastasis model. To generate the diagnostic tool dNGs, two types of contrast agents were incorporated into the NGs; gold and iron oxide nanoparticles to use for CT and MRI imagin, respectively . Contrast agent incorporation was verified both through Cryo-TEM imaging and ICP for quantification and entrapment efficiency.

Conclusions: This study demonstrate the potential of the dNGs as a high-resolution diagnostics tool for metastasis. The combination of the natural homing abilities of the NGs with their physical properties enable the incorporation of contrast agent, constitutes the dNGs as a perfect candidate

for metastasis delivery. The dNGs will be further examine in-vitro and in vivo to study their targeting abilities and the detection limit sensitivity in MRI.

Ginger-derived biofilm antagonistic 3D-printable photoresins for complex implant designs for multifunctional biomedical and potential delivery applications

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3D printing has created a paradigm in the last decade, while revolutionizing personalized drug delivery and implants by enabling intricate, customizable designs that also enable the customization of drug delivery systems or patient-specific implants. However, several issues are still a major concern when discussing implants, such as their design complexity, host-immune response, the development of biofilm on the implant surface, and recurrent infections brought on by these colonized implants. Ongoing discoveries henceforth direct the biodegradable nature-based implants, which have the least implant rejection probability and are a major focus in the biomedical area. This work offers, first-ever, unique ginger-based 3D-printable resins. Here, the Zingerol (Zing-OH, a ginger-based component) has been modified into photo-printable compositions that can print high-resolution complex designs, introducing a photo-initiator. Briefly, the Zing-OH has been amended via different functional group backbones, resulting in Zing-OH-based compositions (ether, ester, and urethane) and their respective prints. Moreover, the Zing-OH prints' thermal, mechanical, and biodegradation properties can be fine-tuned by simply customizing the backbone. Furthermore, the shape memory efficacy and the human bone (nasal cartilage, vestibular, cortical, femur, etc.) mimicking mechanical properties (exhibiting 24-142 MPa compressive strength) makes them more enticing. In tandem,

the prints are also hemocompatible as well as cyto-friendly against human skin (HaCaT) and lung (BEAS-2B) cells, and mouse fibroblast (NIH-3T3) cells. Simultaneously, the outstanding anti-biofilm and anti-oxidant efficacy of the Zing-OH prints make them more appealing due to their potential to prevent implant rejection, thus making them promising tools for bone-tissue engineering and drug-delivery applications.

Engineering fully quaternized (Dimethylamino)ethyl methacrylate-based photoresins for 3D printing of biodegradable antimicrobial releasing polymers

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Medical devices are widely used in the medical field to treat different illnesses and diseases. However, bacterial infections are one of the significant problems associated with medical devices and are recognized as a concern in healthcare worldwide. Addressing this problem has driven the exploration of new materials that exhibit antibacterial properties. In this regard, Quaternary ammonium compounds (QACs), which are organic salts with an alkane chain and a charged part of quaternary ammonium groups, can be an excellent candidate. Dimethylamino ethyl methacrylate (DMAEM) derived quaternary ammonium monomer and crosslinker to prepare photoresins for DLP (Digital light processing) 3D printing. The structure of the synthesized monomer and crosslinker was confirmed via FTIR (Fourrier Transform Infrared) and 1HNMR (Hydrogen Nuclear Magnetic Resonance), while the physicochemical properties of the 3D printed polymer were investigated using TGA (Thermogravimetric Analysis), DSC (Differential Scanning Calorimeter) and UTM (Universal testing machine). After optimizing the printing conditions and monomer:crosslinker ratio, high-resolution 3D printed objects were printed. Additionally, in vitro biodegradation, cytocompatibility, and hemocompatibility tests revealed that the printed polymers are biodegradable, cytocompatible, and hemocompatible in nature. More importantly, the printed polymers exhibited strong antibacterial activity against both gram-negative and gram-positive bacteria, suggesting their potential utility in personalized antibacterial medical devices.

Formulating Multifunctional Bioactive Polymeric Hydrogels with Drug-Releasing Capabilities for Potential Wound Healing Management

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An integral skin barrier is essential for retaining body fluid, thermal insulation, and protection from exogenous pathogens. Upon injury, a four-stage orchestrated healing process starts: hemostasis, inflammation, cell proliferation, and remodeling to restore the skin's protective function 1. Scar formation, followed by wound healing, will reduce the strength and the elasticity of the skin and cause a lack of its functional components, such as hair follicles and sweat glands. These features make our skin prone to secondary injury that may lead to complicated conditions.

Thus, in this study, we're aiming to improve the wound healing outcomes via reducing or completely preventing scar tissue formation, by developing a bioactive wound dressing hydrogel with drug-releasing capabilities that can modulate the different aspects of the wound healing process. In this work, hydrogels with various controlled-release formulations were prepared and characterized.

Crystalline Formulations of Multiple Combined Drugs for Parallel Release Features

Noor Wishahi, Edwar Odeh, Neta Kutner, Elissar Ibraheem, Merna Shaheen-Mualim, Shady FarahNoor Wishahi, Edwar Odeh, Neta Kutner, Elissar Ibraheem, Merna Shaheen-Mualim, Shady Farah

Crystalline drug formulations have been shown to improve the pharmacokinetic, pharmacodynamic, and targeting properties of low-solubility drugs, making them an excellent method of introducing medicine into the body. Crystalline-based medicines contain crystals made of only pure drug and no other ingredients, resulting in a carrier-free drug delivery system (DDS) with a low risk of inducing an immune response. Another advantage of crystalline-based DDS is that the drug concentration is independent of the carrier's loading capacity, allowing complete control of the medicine dose (100% loading capacity). And finally, when it comes to the need to prevent foreign body responses (FBR) in long-term implantations, crystalline drug formulations provide a prolonged release profile, which is a highly desirable feature.

There are several crystallization methods reported in the literature; the solvent-antisolvent crystallization method is one of the most famous among them. By using this technique, crystalline formulations of multiple combined drugs can be obtained. These combinations offer simultaneous targeting of several targets, thus introducing innovative solutions for complex, challenging medical issues.

In this work, multiple releasing drug formulations are developed to address the problem of FBR using the solvent-antisolvent method. The resultant crystals are characterized using a brightfield microscope and scanning electron microscopy (SEM), differential scanning calorimetry (DSC), thermogravimetric analysis (TGA), nuclear magnetic resonance (NMR), and powder X-ray diffraction (PXRD). The crystals' release profile was also examined under accelerated conditions, and they were found to exhibit prolonged release, highlighting their potential as a long-term DDS.

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