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Chemical penetration enhancers (CPEs) as a novel method for non-invasive detection of amniotic fluid

Our group proposed the use of CPEs, as a mean to enhance chorioamnion (CA) membrane transport.

A novel method for applying CPEs was developed using nano-PLGA particles as carriers. The proposed mechanism suggests that nano-PLGA penetrate the CA membrane and most likely get trapped between the two membranes which compose the CA. Then, the CPE is continuously released and high "local" concentration is achieved. This effect is probably reversible. The enhancement degree varies for different nano-PLGA encapsulating CPEs and can reach up to five times fold vs. free CPEs.

A novel approach for detection of low-concentration biomarkers: The efficacy of cancer treatment depends on the pathological state of the disease; the earlier the detection and diagnosis, the more efficient is the treatment. One of the most promising approaches for earlier detection is based on cells excreted bio-molecules that are specific to the tumor type and age. The objective of the research is to develop a novel platform for *in-vivo* biomarker tracing to detect early stage cancer. This research is done in collaboration with Dr. Giora Enden from Biomedical Engineering Department.

Development of modified starch based complexes and ultrasound application for targeted siRNA delivery: RNA interference (RNAi) is a natural process of sequence-specific post transcriptional gene silencing, by which gene expression is inhibited. The mechanism pathway utilizes small interfering RNAs (siRNA) molecules to degrade mRNA transcripts before translation into peptide sequences. Although siRNA is being tested in a variety of clinical trials, the remaining challenge before widespread clinical use is developing an efficient and safe non-viral delivery mechanism. In this research, we are establishing and characterizing siRNA delivery systems based on modified starch complexes as an siRNA carrier, due to its natural properties and the ability to minimally provoke the immune system upon administration.

Ultrasound triggered polymer degradation, an approach for inferior vena cava filter resorption: Venous Thrombosis is a pathological condition when micro- thrombi formed in the normal fibrinolytic system in the blood stream, grow and form blood clots within a vein, usually in the deep veins of the thighs (DVT). When a blood clot detaches from the vessel's wall and travels in the blood stream (Embolism), it risks blocking the blood stream in small blood vessels. The major and life-threatening complication of a Venous Thrombo-embolism is a Pulmonary Embolism (PE) that occurs when the blood clot blocks an arterial blood vessel in the lungs. Existing medical treatments include anticoagulation medication, tissue plasminogen activator, and Inferior Vena Cava filter. This filter is a medical metal device inserted by catheter to the Inferior vena cava, physically preventing the passage of large life-threatening blood clots from the lower part of the body to the heart. In most cases, the need of the filter is temporary therefore we propose a new approach to determinate the filter functionality in a non- invasive manner. We propose an improved filter in which metal wires will be connected by a degradable polymer joint, replacing the existing metal one. The polymer properties enable enhanced degradation on demand after exposure to Focused Ultrasound radiation. Upon degradation, the metal wires polymer joint will open, enabling free flow of the blood stream, while the metal wires retract and stay attached to the blood vessel's wall.

Prolonged administration of surfactants to the lungs of prematures based on PLGA based nano particles: In this research, we are developing nano particles based on poly(lactic-glycolic) copolymers for the sustained delivery of surfactants and surfactant

proteins in the lung, as a tool for more effective surfactant replacement therapy. The development of nano particles based on PLGA provides a vehicle to deliver surfactant constituents into the peripheral airways, the spreading of which into distal areas of the lung can be enhanced by the presence of surfactant, per se, which helps to distribute pharmaceuticals throughout the lung. Since repeated intubation or instillation into the airway is challenging in small infants, the development of sustained release vehicle, that could provide medication for long periods of time in the lungs in preterm infants, would be a potential important therapy for a disease for which there are presently no effective treatments.

Bio-inspired nano-carriers for sub-cellular targeted therapeutics (FTA program): Developing bio-inspired nano-carries (NCs) aimed at sub-cellular targeting of therapeutics. Uniquely, this program presents a comprehensive drug delivery approach that includes aspects such as: design of new nano-carriers, synthesis and characterization, intracellular trafficking, sub-cellular recognition, and localized cargo discharge, up to the level of in-vivo proof of efficacy

Development of pectin based nano-system for gene therapy: The main objective of this research is to develop a safe and stable platform approach for non-viral cancer gene delivery system based on pectin derivatives, combining the use of non-invasive HIFU as a mean for effective gene transfection. Modified pectin is a galactoside residues rich polymer that has an affinity for certain types of cancer cells. By binding to galectin-receptors on cancer cells, modified pectin cannot just prevent metastasis, but also might have a preferred incorporation pathway into cells as a DNA carrier. Our approach advantages are mainly the ligand targeting to tumor cells induced by modified pectin-galectin interactions, and non-invasive HIFU for more efficient transfection followed by tumor ablation if needed.

Ultrasound induced increased skin permeability of modified starch-miRNA complexes for psoriasis treatment: Psoriasis is a disease that is characterized by abnormally increased keratinocyte proliferation, abnormal differentiation of the epidermis and systemic and local inflammation, which result in the formation of chronic erythematous and scaly lesions. MicroRNAs (miRNAs) are 22 nucleotides that can suppress the expression of protein-coding genes by targeting cognate messenger's RNAs for translational repression or degradation. One of the main challenges for psoriasis treatment is efficiently delivering these miRNA oligos to the basal cells. Since skin is permeable to molecules smaller than 500Da, delivery of miRNA (14kDa) requires methods that enhance transdermal delivery. Sonophoresis is a non-invasive method where ultrasound is used to increase the permeability of skin. The project goal is to develop an efficient delivery system for the specific miRNAs sequences to the Keratinocytes based on modified starch as a miRNA carrier and enhance skin permeability by applying ultrasound.