Tyrosinase-loaded Multicompartment Microreactor toward Melanoma Depletion

Melanoma is a malignant skin cancer occurring with increasing prevalence with no effective treatment. A unique feature of melanoma cells is that they require higher concentrations of L-tyrosine (L-tyr) for expansion than normal cells. As such, it has been demonstrated that dietary L-tyr restriction lowers systemic L-tyr and suppresses melanoma advancement in mice. Unfortunately, this diet is not well tolerated by humans. An alternative approach to impede melanoma progression will be to administer the enzyme tyrosinase (TYR) which converts L-tyr into melanin. Herein, a multicompartment carrier consisting of a polymer shell entrapping thousands of liposomes is employed to act as a microreactor depleting L-tyr in the presence of melanoma cells. It is shown that the TYR enzyme can be incorporated within the liposomal subunits with preserved catalytic activity. Aiming to mimic the dynamic environment at the tumor site, L-tyr conversion is conducted by co-culturing melanoma cells and microreactors in a microfluidic set-up with applied intra-tumor shear stress. It is demonstrated that the microreactors are concurrently depleting L-tyr, which translates into inhibited melanoma cell growth. Thus, the first microreactor where the depletion of a substrate translates into anti-tumor properties in vitro is reported.
This white paper considers the future of plasma science and technology related to the manufacturing and modifications of plastics and textiles, summarizing existing efforts and the current state-of-art for major topics related to plasma processing techniques. It draws on the frontier of plasma technologies in order to see beyond and identify the grand challenges which we face in the following 5–10 years. To progress and move the frontier forward, the paper highlights the major enabling technologies and topics related to the design of surfaces, coatings and materials with non-equilibrium plasmas. The aim is to progress the field of plastics and textile production using advanced plasma processing as the key enabling technology which is environmentally friendly, cost-efficient, and offers high-speed processing.
**Artificial Organelles: Intracellular Sub-compartmentalized Microreactors to Conduct Enzymatic Cascade Reactions**

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Intracellular Microreactors as Artificial Organelles to Conduct Multiple Enzymatic Reactions Simultaneously

The creation of artificial organelles is a new paradigm in medical therapy that aims to substitute for missing cellular function by replenishing a specific cellular task. Artificial organelles tackle the challenge of mimicking metabolism, which is the set of chemical reactions that occur within a cell, mainly catalyzed by enzymes. So far, the few reported carriers able to conduct enzymatic reactions intracellularly are based on single-compartment carriers. However, cell organelles outperform by conducting multiple reactions simultaneously within confined sub-compartments. Here, the field of artificial organelles is advanced by reporting the assembly of a microreactor consisting of polymer capsules entrapping gold nanoclusters (AuNCs) and liposomes as sub-compartments. The fluorescence properties of AuNCs are employed to monitor the microreactors uptake by macrophages. Encapsulation is demonstrated and functionality of microreactors with trypsin (TRP) and horseradish peroxidase (HRP)-loaded liposomes is preserved. Multiple enzymatic reactions taking place simultaneously is demonstrated by exposing macrophages with the internalized microreactors to bis-(benzyloxy carbonyl)-Ile-Pro-Arg)-Rho-110 and Amplex Red substrates, which are specific for TRP and HRP, respectively. Conversion of the substrates into the respective fluorescent products is observed. This report on the first microreactor conducting multiple enzymatic reactions simultaneously inside a cell is a considerable step in the field of artificial organelles.

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Multicompartment Artificial Organelles Conducting Enzymatic Cascade Reactions inside Cells

Cell organelles are subcellular structures entrapping a set of enzymes to achieve a specific functionality. The incorporation of artificial organelles into cells is a novel medical paradigm which might contribute to the treatment of various cell disorders by replacing malfunctioning organelles. In particular, artificial organelles are expected to be a powerful solution in the context of enzyme replacement therapy since enzymatic malfunction is the primary cause of organelle dysfunction. Although several attempts have been made to encapsulate enzymes within a carrier vehicle, only few intracellularly active artificial organelles have been reported to date and they all consist of single-compartment carriers. However, it is noted that biological organelles consist of multicompartment architectures where enzymatic reactions are executed within distinct subcompartments. Compartmentalization allows for multiple processes to take place in close vicinity and in a parallel manner without the risk of interference or degradation. Here, we report on a subcompartmentalized and intracellularly active carrier, a crucial step for advancing artificial organelles. In particular, we develop and characterize a novel capsosome system, which consists of multiple liposomes and fluorescent gold nanoclusters embedded within a polymer carrier capsule. We subsequently demonstrate that encapsulated enzymes preserve their activity intracellularly, allowing for controlled enzymatic cascade reaction within a host cell.

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Multicompartment microreactors with preserved intracellular activity: A step towards the creation of artificial organelles

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Recent advances in compartmentalized synthetic architectures as drug carriers, cell mimics and artificial organelles

Compartmentalization is a key feature of biological cells which conduct their metabolic activity in individual steps isolated in distinct, separated compartments. The creation of architectures containing multiple compartments with a structure that resembles that of a biological cell has generated significant research attention and these assemblies are proposed as candidate materials for a range of biomedical applications. In this Review article, the recent successes of multicompartiment architectures as carriers for the delivery of therapeutic cargo or the creation of micro- and nanoreactors that mimic metabolic activities, thus acting as artificial cells or organelles, are discussed. The developed technologies to assemble such complex architectures are outlined, the multicompartiment carriers’ properties which contribute to their performance in diverse applications are discussed, and their successful applications are highlighted. Finally, future directions and developments in the field are suggested.