Fighting against cancer: a novel matrix-metalloproteinase-2 triggered liposomal drug release approach

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Abstract – Cancer is the leading cause of death worldwide and each year more than 10 million people are diagnosed with this severe disease [1]. Although remarkable approaches have been achieved in cancer treatment, conventional chemotherapy and radiation lack of specificity and have a high systemic toxicity. Despite killing only tumor cells the therapeutic agents affect also “normal” cells and cause toxicity to the patient [2]. Hence, since decades cancer research aims the targeted release of drugs at the tumor site. For this reason liposomes are considered as one of the effective drug delivery system (DDS), which surface can be modified with biomolecules in order to target cancer cells. Furthermore, liposomes, which structure is extremely close to biological membranes; they possess an excellent biocompatibility and biodegradability. They can entrap hydrophobic as well as hydrophilic agents and keep their stability while circulating in the body until they reach their target. More than ten types of liposomal drugs have been approved and are nowadays available on the market [3]. Nevertheless, most of these approved drugs designed for cancer are reaching the tumor by the enhanced permeability and retention (EPR) effect, and are not equipped with controlled-release function (only by degradation of liposome), and the slow release hinder the bioavailability of encapsulated drug and require higher liposome dose.
This research is dealing with the development of functionalized liposomes, which release mechanism is controlled at the cancer-related enzyme. As matrix metalloproteinases (MMPs), especially MMP-2, also known as gelatinase, plays an important role in many cancer types, the goal is to use this enzyme as a DDS marker. MMP-2 is known to be overexpressed in invasive tumors due to the increased need of extracellular matrix (ECM) degradation; therefore it can be used as an excellent trigger for drug release [4]. At the current stage a novel liposomal-cargo-release mechanism is under development, which can be triggered by an environmental responsive linker (see Fig. 1). Preliminary results of in-vitro experiments show a promising controlled release of the drug doxorubicin induced by an external light irradiation trigger (see Fig. 2).

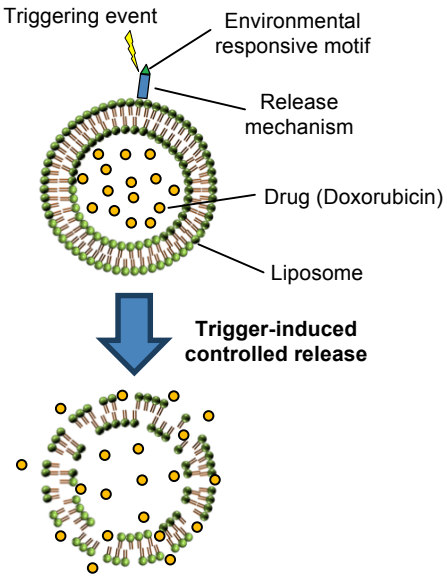

Fig.1: Schematic of controlled liposomal liposomes.

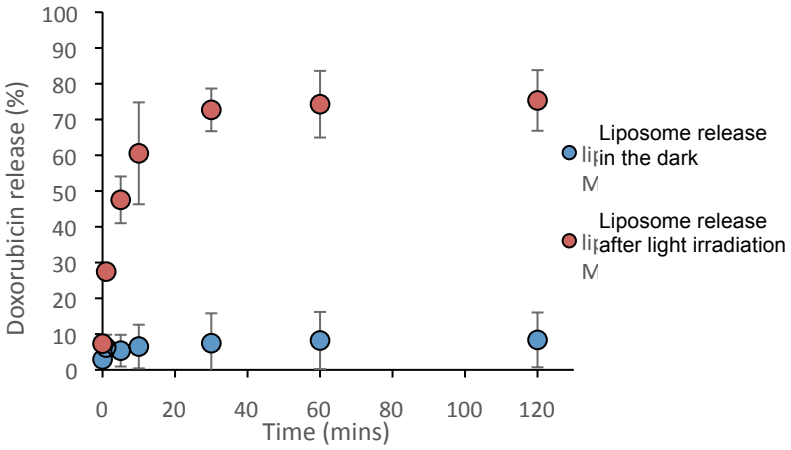

Fig.2: Preliminary result of light-triggered drug release and non-triggered drug release.

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