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Therapeutic Microbubbles and Nested Nanobubbles for Drug Delivery

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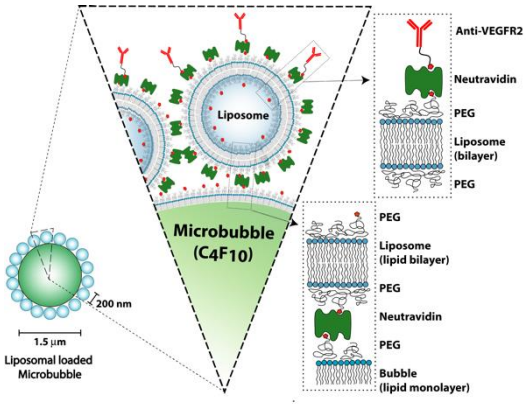
Abstract: The majority of cancer patients receive chemotherapy at some treatment stage which makes improving the efficacy of cytotoxic drugs an important goal. Despite large numbers of potent anti-cancer agents entering clinical development, a major obstacle to clinical translation remains the inability to deliver therapeutic doses to a tumour without toxicity in normal tissues causing intolerable side effects. Therefore, there has been intense interest in nanoformulations such as liposomes and nanoparticles to overcome these problems. So far however, few nanoformulated drugs have delivered consistent improvements in therapeutic index. This reflects inadequate tumour drug uptake and uncontrolled biodistribution, which prevent the use of more potent but toxic molecules 1,2. Herein, we describe the use of therapeutic microbubbles (thMBs), which combine VEGFR2 targeting and a localized ultrasound (US)-trigger for tumour-specific, enhanced cytotoxic drug delivery.



We show that thMBs improve tumour responses to low dose irinotecan or its active metabolite, SN38 in mouse tumour models. 89Zr PET radiotracing showed that the percentage injected dose (%ID) in tumours achieved with thMBs was twice that from VEGFR2-targeted SN38 liposomes alone. This demonstrates how US-triggered thMBs significantly increase drug delivery to tumours and provides a generic platform for effective targeted delivery of otherwise toxic therapeutics. The presentation will cover aspects of microbubble production, characterisation and application. We also indicate potential future direction utilizing nanobubbles to trigger liposomal release.