Liposome Imaging in Optically Cleared Tissues

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Three-dimensional (3D) optical microscopy is a useful tool for studying nanoparticle delivery in biological tissues. Unfortunately, most of the methods required to render tissues transparent for 3D microscopy destroy or degrade clinically relevant nanoparticles. As a result, it is not possible to study the distribution of nanoparticles such as liposomes using 3D microscopy. Here, we have developed a nanoparticle tag termed REMANT, which is capable of surviving tissue clearing and enables the liposome distribution in optically clear tissues to obtained. We also show that using REMNANT, the release rate of liposome encapsulated therapeutic agents can be determined. Using this method, we found that liposomes release their cargo >100 fold faster in tissues in vivo when compared to in vitro assays. This allowed us to design liposome formulations with optimized drug release rates resulting in an enhanced ability to kill tumour associated macrophages. Our tag opens up new avenues for studying the chemical properties and pharmacodynamics of administered organic materials in an intact biological environment. Our approach provides insight into the in vivo behaviour of degradable nanomaterials which can used to improve future generations of therapeutic agents.

Reference: