Nanoscale Formulations of Tetrapyrroles for Imaging and Therapy

*Jonathan F. Lovell**

University at Buffalo
Buffalo, NY, USA
jflovell@buffalo.edu

Tetrapyrroles have been used in contrast detection methods dating to 1921 for fluorescence, 1951 for positron emission tomography (PET) and 1987 for magnetic resonance. We will discuss recent nanoscale approaches for formulating hydrophobic tetrapyrroles using 1) lipid conjugation and 2) surfactant stripping approaches.

Porphyrin-phospholipid (PoP) conjugates can be incorporated into conventional liposomes and behave like a conventional phospholipids in large part.[1] Unlike free porphyrins, PoP remains stably incorporated in the liposome bilayer in biological environment. Several additional functional properties are conferred to the resulting liposomes, including 1) Exposure to near infrared (NIR) light can trigger rapid permeabilization of the bilayer, depending on the liposome formulation.[2] This results in a single-agent "chemophototherapy" treatment for potent tumor ablation. 2) Insertion of cobalt into PoP enables seamless particleization of the liposomes with his-tagged peptides and proteins.[3] This approach enables PoP liposomes to serve as a unique vaccine adjuvant that result strong immune responses for a his-tagged malaria antigen.[4]

With high extinction coefficients in the near infrared, they are well-suited for photoacoustic imaging, when suitably formulated. Hydrophobic tetrapyrroles can also be formulated with a "surfactant stripping" approach. This enables intense near infrared absorption to get generated which in turn enables photoacoustic imaging in deep tissue (> 10 cm) and non-invasive imaging of mice[5] (**Fig 1**).

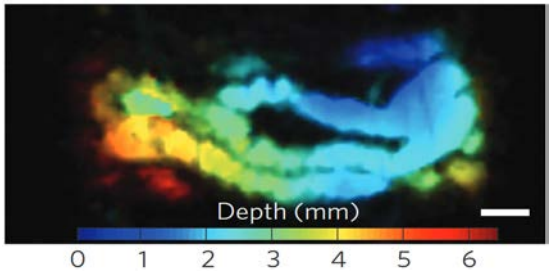

Figure 1: Non-invasive gut imaging of mice using surfactant-stripped tetrapyrrole micelles[5]

References

1. Lovell et al., Porphysome nanovesicles generated by porphyrin bilayers for use as multimodal biophotonic contrast agents, *Nature Materials*, 10 (2011) 324-332.
2. Carter et al., Porphyrin-phospholipid liposomes permeabilized by near-infrared light, *Nature Communications*, 5 (2014) 3546.
3. Shao et al., Functionalization of cobalt porphyrin-phospholipid bilayers with his-tagged ligands and antigens, *Nature Chemistry*, 7 (2015) 438-446.
4. Huang et al., A malaria vaccine adjuvant based on recombinant antigen binding to liposomes, *Nature Nanotechnology*, (2018) DOI:10.1038/s41565-018-0271-3.
5. Zhang et al., Non-invasive Multimodal Functional Imaging of the Intestine with Frozen Micellar Naphthalocyanines, *Nature Nanotechnology*, 9-631, 2014