Exploring Nanoporphyrin-mediated Photodynamic Therapy as a Treatment for Oral Cancer in a Murine Model

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Abstract

Oral squamous cell carcinoma (OSCC) accounts for 2.1% of all cancers and is a form of head and neck squamous cell carcinoma, the 6th most common cancer world-wide. It is a very aggressive cancer, with high recurrence rates. It is estimated that up to 13,190 patients in the United States alone died from this cancer in 2016, including deaths from associated comorbidities.¹

The Lam lab previously developed a novel cholic acid and porphyrin-based nanoparticle termed nanoporphyrins (NPs) that can allow simultaneous delivery of chemotherapeutic drugs and photodynamic/photothermal therapy (PDT/PTT) to synergize treatment for tumors that are accessible to light irradiation. See Figure 1.

This study sought to explore the use of NPs for oral cancer in the murine model. Human OSCC was xenografted in the oral mucosa of nude athymic mice. NPs were administered to mice in order to assess in vivo pharmacokinetics, tumor targeting, and cutaneous toxicity after phototherapy. These initial results indicate that while the NPs demonstrate minimal skin toxicity, tumor targeting could be improved for enhanced targeted photodynamic therapy.

Nanoporphyrin Schematic

Results

Future directions

Future experiments will be aimed at improving tumor targeting of the NP as well as assessing efficacy of the NP with and without chemotherapeutic agents. Covalytically ligating a tumor-specific peptide to the NP is hypothesized to improve tumor targeting. Encapsulating drugs within the micelle is also hypothesized to reduce the intensity of light required for tumoricidal activity to spare healthy tissue. In addition, synthesizing disulfide bond cross-linked NPs may prevent early dissociation of the micelles.

Discussion and Conclusions

- Formulated NPs form micelles of appropriate and narrow size distribution with a mean diameter of ~30 nm.
- NPs localized to the tumor site within 24 hours, although not specifically.
- A larger sample size would yield a more conclusive result. In addition, certain tumors can be partially or extensively necrotic or have occulted or compressed vessels that can hinder NP accumulation.² Impurities or degradation of the nanof ormulation could also account for a weaker accumulation in tumor tissue.
- After 48 hours, NPs accumulated in most organs, particularly the liver and lung.
- This finding could be explained by the liver’s rich blood supply and numerous fenestrated endothelia causing pooling of opsonized NPs and premature micellar dissociation. Resident macrophages of the liver and lung also readily take up nanoparticles.
- Negligible cutaneous toxicity was observed when mice were irradiated with 660nm light 24 hours after NP administration.
- This is clinically important because the spectrum of solar radiation includes wavelengths that can excite photosensitizers and cause adverse side effects such as burning, blisters, and crusting.

References


Acknowledgments

Sincere thanks to Dr. Lam for allowing me to work in his laboratory for the past year, as well as Dr. Lin for her mentorship throughout the ongoing project. Funding for this project was provided by the Daniel T. O’Connor, MD Memorial Research Grant.

Nanoporphyrins, nanoparticles, liposomes and other macromolecular drugs sized between 10-100 nm in diameter or 40-800 kDa in molecular weight tend to selectively accumulate in tumor tissue due to the hyper-permeability of disorganized tumor vasculature and poor functional lymphatic drainage, compared to normal tissue. This is referred to as the enhanced permeability and retention (EPR) effect and is the rationale behind using nanoparticles for cancer therapy.²

PDT is a treatment strategy for many diseases including acne, psoriasis, wet age-related macular degeneration, and cancer by photodissociating the photosensitizer, light, and oxygen that can allow simultaneous delivery of chemotherapeutic drugs and photothermal therapy (PDT/PTT) to synergize treatment for tumors that are accessible to light irradiation. See Figure 1.

The photosensitizer we use in our NPs is porphyrin, an analogue of pyropheophorbide-a (Por), a porphyrin with a mean diameter of ~30 nm.

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