Photodynamic Priming as a Means of Enhancing Nanomedicine Delivery and Overcoming Tumour Desmoplasia

Marta Overchuk¹,², Kara M. Harmatys¹, Shrey Sindhwani², Abdullah M. Syed², Maneesha A. Rajora¹,², Danielle M. Charron¹,², Juan Chen¹, Lili Ding¹, Martin G. Pomper⁴, Brian C. Wilson¹,⁵, Warren C.W. Chan², Gang Zheng¹,²,⁵

¹Princess Margaret Cancer Centre, University Health Network, Toronto, Ontario M5G 1L7, Canada; gang.zheng@uhnresearch.ca ²Institute of Biomaterials and Biomedical Engineering, University of Toronto, Toronto, Ontario M5G 1L7, Canada; ³Krembil Research Institute University Health Network, Toronto, Ontario M5G 1L7, Canada; ⁴Department of Radiology, Johns Hopkins School of Medicine, Baltimore MD 21205, USA ⁵Department of Medical Biophysics, University of Toronto, Toronto, Ontario M5G 1L7, Canada

Excessive extracellular matrix (ECM) deposition is one of the major barriers to nanoparticle extravasation and subsequent penetration in tumours. Tumour photodynamic priming (PDP), which activates photosensitizers with light to locally generate cytotoxic reactive oxygen species (ROS), was proposed as a means to enhance nanomedicine delivery by inciting vascular permeabilization or cancer cell death [1]. However, its effects in the context of tumour ECM remain elusive. Here, we investigate the use of a porphyrin-based photosensitizer and subtherapeutic light irradiation to enhance nanoparticle tumour accumulation and therapeutic efficacy against PSMA+ PC3 PIP subcutaneous mouse prostate cancer xenografts.

PDP-enabled Caelyx® tumour accumulation enhancement resulted in an improved therapeutic efficacy in the absence of off target toxicity, wherein 5 mg/kg was equally effective in delaying tumour growth as 15 mg/kg of Caelyx®. Furthermore, we are the first to demonstrate that subtherapeutic PDP resulted in a ~2-fold decrease in tumour collagen deposition and a significant reduction of ECM density in the subendothelial zone. Overall, this study demonstrated the potential of PDP to enhance tumour nanomedicine accumulation and alleviate tumour desmoplasia, highlighting the utility of PDP as a non-invasive priming strategy that can improve nanomedicine therapeutic outcomes in desmoplastic tumours.