Viral Photodynamic Therapy in Tumor Microenvironment

Zi-Xian Liao\textsuperscript{a}, Pan-Chyr Yang\textsuperscript{b}, Ivan M. Kempson\textsuperscript{c}\textsuperscript{*}

\textsuperscript{a}Institute of Medical Science and Technology, National Sun Yat-sen University, Kaohsiung 80424, Taiwan
\textsuperscript{b}Department of Internal Medicine National Taiwan University College of Medicine, Taipei 10051, Taiwan
\textsuperscript{c}Future Industries Institute, University of South Australia, Mawson Lakes, S.A. 5095, Australia

Presenting and Corresponding Author E-mail Address: ivan.kempson@unisa.edu.au

Photodynamic therapy (PDT) is a clinically approved, minimally invasive therapeutic procedure that can exert a selective cytotoxic activity toward malignant cells.\textsuperscript{1} The procedure involves administration of a photosensitizing agent followed by irradiation at a wavelength corresponding to an absorbance band of the sensitizer. In the presence of oxygen, a series of events lead to direct tumor cell death and damage. Moreover, clinical studies revealed that PDT can be curative particularly in early-stage tumors. However, the major challenge of PDT has a lack of selectivity and efficacy of photosensitizers. The genetically-encoded red fluorescent protein (KillerRed) leads to irreversible DNA damage and cell killing via an apoptotic pathway upon irradiation with a narrow light bandwidth of 520–590 nm due to formation of highly-cytotoxic levels of ROS.\textsuperscript{2} Additionally, the US Food and Drug Administration (FDA) has approved virotherapy for use in cancer treatment.\textsuperscript{3} We present an improved technique that switches to promote cellular uptake and delivery of recombinant adeno-associated virus serotype 2 (AAV2) encoded the photosensitive protein of KillerRed triggered by lactate in tumour microenvironment \textit{in vivo}.\textsuperscript{4} Also, we show that AAV2 chemically conjugated with iron oxide nanoparticles (~5 nm) have remarkable ability to be remotely guided under magnetic field.\textsuperscript{5} Transduction is achieved with micro-scale precision. Furthermore, the KillerRed was enabled localized PDT; or light-triggered virotherapy. Otherwise, our approach has achieved a chemo drug (doxorubicin, DOX) resistant human breast adenocarcinoma MCF-7 (CDR-MCF-7) cell line for PDT.\textsuperscript{6} These proof-of-principles demonstrate guided and highly localized micro-scale, light-triggered virotherapy.