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EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR) TARGETED MULTIFUNCTIONAL PHOTOSENSITIZERS FOR BLADDER CANCER IMAGING (FLUORESCENCE/PET) AND THERAPY

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Recurrence reduction and complete tumor eradication are critical for survival of bladder cancer patients. We have developed novel multifunctional agents for image-guided (PET/fluorescence) photodynamic therapy (PDT) for treating bladder cancer with low and high expression of epidermal growth factor receptor (EGFR). A photosensitizer (PS)-erlotinib conjugate recently developed in our laboratory showed high selectivity to EGFR positive bladder cancer tumor cells (UMUC-3), with enhanced PDT efficacy than the related non-targeted analog. We have used both active and passive approaches for improved tumor-specificity. These results provide an opportunity to select the PS (combination with radioactive and non-radioactive analog) for imaging bladder cancer and subsequent treatment by fluorescence-guided surgery, a see and treat approach in combination with PDT and/or chemotherapy (U S Patent application: submitted). Depending on the stage of cancer, we propose to follow use of PDT with intra-vesical therapy for non-muscle invasive bladder cancer (NMIBC), or as a part of multimodality bladder preservation therapy for muscle-invasive bladder cancer (MIBC). In a parallel study, we have shown that 3D culture system derived from lung and head/neck cancer patients helps to determine tumor-specificity of the PS and the photo-induced STAT3 dimerization can be used as a biomarker in optimizing the PDT-treatment of bladder cancer. We expect that translating these key findings into clinical practice will create a paradigm shift in treatment for loco-regional control of disease. Recent results from our laboratories will be presented.

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