Project Title: “Ovarian Cancer PDT: Multi-intracellular targeting and Image-guided Dosimetry”

Project Overview:
We propose a comprehensive platform that integrates “Targeted Phototoxic Multi-Inhibitor Liposomes” (TPMILs) that selectively target tumor cells, and inhibit interconnected survival pathways associated with aggressive ovarian cancer (OvCa) with hyperspectral confocal fluorescence microendoscopy (hyperCFME). Specifically, the proposed therapeutic strategy comprises two key elements: (1) image-guided dosimetry for photodynamic therapy (PDT, a light-activated cytotoxic modality); and (2) simultaneous inhibition of intracellular EGFR, and associated crosstalk pathways, which have been correlated with poor prognosis in OvCa patients, and are implicated as acquired resistance mechanisms to inhibitors such as cetuximab (Cet)2, an FDA-approved monoclonal antibody (mAb). The proposal will be achieved in four specific aims and study impact will be 2-fold: First, it introduces image-guided dosimetry and treatment monitoring to provide real-time feedback of drug uptake, redistribution and tumor reduction not currently available. Second, it will guide new combination therapies by identifying optimal surface targeting and intracellular delivery strategies to improve the therapeutic index specifically for OvCa patients with Stage II-IV, resistant disease, and those receiving salvage therapies.