In recent years, Phase I/II clinical trials of photodynamic therapy performed at our institute have assessed the safety and potential efficacy of PDT for several indications. Furthermore, these trials have provided a wealth of data on the biology of PDT in clinical application. Clinical findings have confirmed some expectations that stem from preclinical data, but they have also raised new questions based on observations not previously made in animal models. We describe the iterative process used to develop new preclinical models and systems for the purpose of substantiating and then researching novel observations rising from clinical application of PDT.

For example, in a clinical trial of PDT for early stage/premalignant head and neck cancer we found clinical data to corroborate preclinical findings that associate tumor oxygenation and PDT outcome. However, these clinical data also identify the potential for physiologically informed light delivery to provide individualized optimization of PDT. Toward this goal, a blood flow-informed light delivery system has been developed and is being tested in murine studies. In a second example, clinical trials of PDT for malignant pleural mesothelioma have demonstrated that a stronger inflammatory response to surgical debulking (prior to PDT) associates with shorter overall survival. This observation suggests that mitigation of surgery-induced inflammation may increase the efficacy of intraoperative PDT. Animal models have been developed to study the effect of acute inflammation on PDT, and in ongoing studies the mechanisms of these interactions are being elucidated.