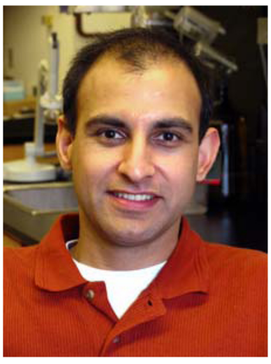


Congratulations to

Imran Rizvi, Daina Burnes, Jonathan Celli and **Conor Evans**

Who won a prize for their poster "Imaging Drug Penetration and Metabolic Activity in 3D Ovarian Cancer Models" at this year's Dana-Farber/Harvard Cancer Center Ovarian Cancer Researchers' Symposium.

Imaging Drug Penetration and Metabolic Activity in 3D Ovarian Cancer Models
Imran Rizvi, Jonathan Celli, Conor L. Evans, Daina Burnes and Tayyaba Hasan

Poor survival rates associated with advanced ovarian carcinoma emphasize the need to develop better research tools to predict the clinical efficacy of novel therapeutic regimens. Increasing evidence suggests that monolayer cultures and animal models typically overestimate the potency of a therapeutic agent and are highly limited in their ability to evaluate drug efficacy for humans. Overestimation of cell killing in monolayer cultures is due in large part to the isolation of cells from their host microenvironment, which diminishes their ability to cope with stress. Animal models restore some architectural and microenvironmental cues, but they inherently lack the ability to recapitulate the traits of a human host. Along with pharmaceutical companies and academic laboratories, the National Institutes of Health, Environmental Protection Agency and the National Toxicology Program have acknowledged the critical need to develop more sophisticated research models to complement, or replace, current systems.

Our lab has published promising pre-clinical results using photodynamic therapy (PDT), an emerging light-based modality, in combination with Erbitux, an antibody targeted against the epidermal growth factor, to synergistically treat advanced ovarian carcinomatosis. As this therapeutic strategy moves into clinical trials, we are investigating the mechanisms underlying the observed synergism to optimize the combination regimen. Based on breast cancer models described by Drs. Mina Bissell and Joan Brugge, we have developed 3D cultures for ovarian carcinoma as our in vitro research platform to conduct these mechanistic studies. Ovarian cancer cells seeded on Growth Factor Reduced (GFR) Matrigel™ beds spontaneously form 3D acinar structures that more closely resemble *in vivo* tumor nodules than cells in monolayer. As with other treatments, preliminary experiments suggest that the 3D acini are less sensitive to PDT than cells in monolayer. This differential response more closely mimics in vivo doses than monolayer cultures and could be attributed to heterogeneity in drug penetration as well differences in signaling and architectural cues between the two systems. Using multi-photon and confocal microscopy, we have shown that benzoporphrin derivative (BPD) and Erbitux® are unevenly distributed in 3D acinar structures, which could have implications for treatment efficacy. Furthermore, we are using multiphoton microscopy of intrinsic fluorophores to nonpurtubatively investigate the patterns of metabolic activity in the acinar structures.

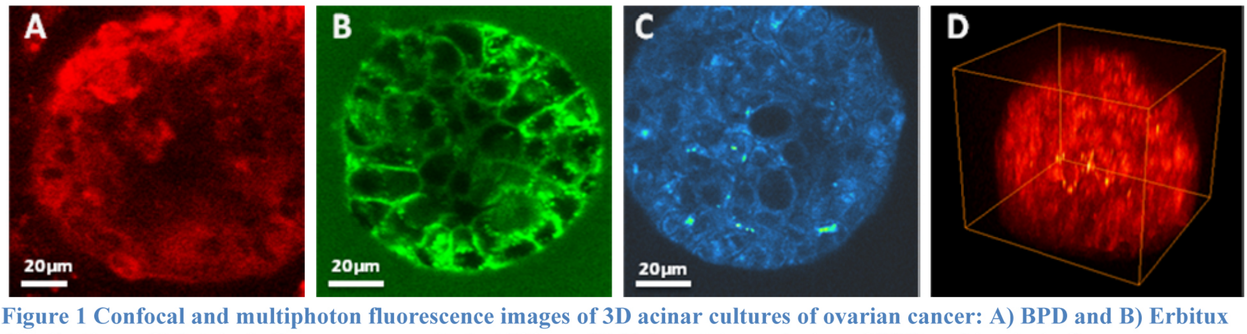

Figure 1 Confocal and multiphoton fluorescence images of 3D acinar cultures of ovarian cancer: A) BPD and B) Erbitux distributions; C) Intrinsic fluorescence excited at 720nm; D) Volumetric rendering of BPD and intrinsic fluorescence. Figures C and D are presented in false-color intensity scale. The scan volume for Figure D is 110µm x 105µm x 100µm.