Purpose: The objectives are to: 1) longitudinally monitor and evaluate the physiology and oxygenation status of pancreatic tumor after treatment by anti-angiogenic drug (DC101, anti-VEGFR2 monoclonal antibody); and 2) to generate oxygen within tumor using a novel device, Implantable Micro-Oxygen Generator, IMOG. Functional and molecular imaging modalities, Dynamic Contrast-Enhanced CT (DCE-CT) and Photoacoustic Computed Tomography Spectroscopy (PCT-S) will be used to longitudinally monitor tumor responses to DC101 or IMOG, develop a suitable time window for further combined radiotherapy, and identify prognostic factors to help develop individualized treatment plan in pancreatic cancer.

Methods: A cohort of athymic mice bearing human BxPC-3 pancreatic tumors was divided into six groups: control (n=9), DC101 therapeutic group (n=9), radio-therapeutic group (RT, a single fraction of 5 Gy x-ray, n=9), DC101 plus RT (n=9), IMOG control group (n=14), and IMOG plus RT (n=19). For the control and DC101 groups, DCE-CT and PCT-S scans were acquired at baseline, 2 days, 1 week, and 2 weeks post treatment. Based on the imaging results, radiotherapy was applied at 1 week post DC101. IMOG produced oxygen was in vivo measured by NeoFox Oxygen Measurement System and 3-D monitored by PCT-S. Radiotherapy will be applied immediately after IMOG stimulation.

Results: The preliminary DCE-CT and PCT-S results showed that at one week post DC101 treatment, the tumor vasculature was temporarily normalized with better oxygenation. The combination of DC101 and radiotherapy significantly reduced tumor growth compared to single treatment. IMOG significantly produced oxygen within tumor upon ultrasonic stimulation, and IMOG generated oxygen sensitized the tumors to combined radiotherapy.

Conclusions: DCE-CT and PCT-S provide uniquely monitoring over tumor physiology and oxygenation changes in response to DC101 or IMOG. We believe that applying radiotherapy in the 'normalization window' after DC101 or immediately after IMOG initiation period will greatly augment treatment outcomes for pancreatic tumor.