

Oakland University-Beaumont Team Develops a New Method for Using Radiation to Treat Cancer

Biological and Biomedical Sciences graduate student Jonathan Kane recently published an article about the **Effect of Irradiation on Tumor**

Microenvironment and Bone Marrow Cell Migration in a Preclinical Tumor

Model (International Journal of Radiation Oncology Biology Physics, Volume 96, Pages 170-178, 2016). This research was a collaboration between faculty at Oakland University, including Thomas Raffel and CBR member Gerard Madlambayan of the Department of Biological Sciences, and Brian Marples and George Wilson of the Beaumont Health System Department of Radiation Oncology. The coauthors include Beaumont Research Assistants Sarah Krueger and Alaa Hanna.

The OU-Beaumont collaboration between Marples and Madlambayan was initiated by an OU-Beaumont Multidisciplinary Research Award. This partnership highlights what can be achieved when OU graduate students work in translational research laboratories at Beaumont. The goal of the research is to test a new radiation therapy protocol for treating cancer.

Traditionally, radiation is given in fractions of 2 grays per day (a gray, or Gy, is a unit of radiation dose, equal to one joule of energy deposited in one kilogram of tissue). Kane and his collaborator's modification is to give ten 0.2-gray pulses of radiation separated by 3 minutes each



Kane (back) and an OU undergraduate studying cancer

Kane graduated with his PhD in April 2016, after defending his dissertation about the Characterization of the Tumor Microenvironment and Bone Marrow Derived-Cell Migration in Response to Changes in Radiation Delivery. He was mentored jointly by Madlambayan and Marples. Kane now works for the company Xstrahl, a leading designer and manufacturer of x-ray therapy systems for use in cancer, where he is building relationships with their current and future clients to drive the field of cancer research forward.



Gerard Madlambayan

Below are excerpts from the introduction of the article (references removed).

Recent studies have recognized that changes in the pattern of radiation delivery exert significant effects on the tumor microenvironment. This microenvironment consists of a heterogeneous population of cells that can influence growth through paracrine interactions, cell-to-cell contact, and differentiation/proliferation of primitive cells.

Standard radiation therapy (SRT) is typically given as a series of 1.8- to 2-Gy/d fractions over a period of 6 to 7 weeks to exploit tumor radiobiology and allow for reoxygenation. In preclinical studies using human xenografts, we recently demonstrated that altering the pattern of daily radiation delivery by protracting overall treatment time using a series of 0.2-Gy dose pulses affected the underlying tumor radiobiology. Pulsed radiation therapy (PRT), consisting of 10 0.2-Gy fractions with each individual 0.2-Gy dose separated by 3 minutes, was shown to be more tumoricidal than the same total dose given continuously as SRT. The enhanced efficacy of PRT reflected the maintenance of tumor oxygenation during the protracted course of treatment....

Given the positive effects of PRT on maintaining tumor vasculature, we hypothesized that by allowing tumor microenvironments to remain more oxygenated, PRT would result in better overall tumor killing compared with SRT. We further postulated that this effect would be mediated by decreased tumor hypoxia, leading to lower VEGF [vascular endothelial growth factor] and SDF-1a [stromal-derived factor-1a] production and subsequently lower recruitment of BMDCs [Bone marrow derived cells] in PRT-treated tumors when compared with SRT-treated tumors. Using a rapidly proliferating Lewis lung carcinoma (LLC) allograft model [a mouse model commonly used in cancer research], we found evidence for improved tumor killing with PRT relative to SRT and strong support for our hypothesized mechanism.