Preclinical detection of colorectal cancer for evaluation of chemotherapeutics and radiopharmaceuticals

Benjamin Y. Durkee

Colorectal cancer (CRC) is the second leading cause of cancer-related death in the U.S. Micro-imaging technologies, including microCT, microPET, and microOC have made it possible to non invasively study cancer progression with results that are substantially translatable to the clinic. With the availability of small animal models of spontaneous colon cancer progression, development of new methods for detection and treatment of CRC in the preclinical setting may be more expedient than clinical trials.

This thesis establishes microCT as a non invasive mode for detection of colonic polyps; detection is possible by 2D and 3D methods. Tumor volume measurements are highly reproducible, regardless of reader experience. Volume measurements allow tumors to be monitored non-invasively in a longitudinal study. The longitudinal study design provides up to four times greater statistical power than the traditional cross-sectional design, and may be used for evaluation of agents of chemoprevention and chemotherapy.

Statistical power may be further improved by treating Min mice with dextran sodium sulfate (DSS) and piroxicam to affect tumor distribution, mimicking that seen in human disease. Polyp progression is dynamic as polyps may grow, remain static or spontaneously regress.

Differentiating between benign and malignant tumors is a major challenge faced by clinicians, especially when managing polyposis. NM404 is a PET imaging radiopharmaceutical that has shown selective retention in 43 types of cancer. We present evidence that NM404 may not be significantly retained in any type of colonic tumor in Min mice and may be selectively retained by more advanced tumors in the PIRC rat model. Imaging by NM404 PET/CT dual modality virtual colonoscopy may allow clinicians to non-invasively detect, localize and characterize (benign v. malignant) colonic tumors.