Acute Changes in Leukocyte Populations After Focal Irradiation of the Intestine

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Radiation is an important therapeutic modality for abdominal and pelvic cancers, but gastrointestinal injury limits the dose. The intestine is the largest compartment of the immune system in the body. Interactions between the immune system and gastrointestinal mucosa may mediate the response to irradiation (IR). To assess changes in leukocyte populations after focal irradiation, we used an animal model, previously validated by our lab, which allows us to cause highly focal radiation damage. This model involves a minimally invasive surgical implantation of a radiopaque marker on the surface of the mouse jejunum. Mice were imaged with a cone-beam CT to locate the marker. They were then administered 18 Gy IR (with 5x5 mm collimation) on the marker site using the Small Animal Radiation Research Platform (SARRP). Focal damage was characterized by radiation injury scoring on H&E stained tissues as well as through cell proliferation (EdU incorporation) and apoptosis (TUNEL) assays. Immunohistofluorescence was used to study neutrophil, B and T lymphocyte, and macrophage populations in the lamina propria from 1, 3.5, 7, and 14 days post-IR. A 12-plex cytokine magnetic bead assay was used to assess CD4+ T-cell associated cytokines. Complete blood counts with differentials were conducted to assess hematologic changes at the same time points post-IR. Irradiated mice exhibited a significant reduction in cell proliferation 1 day post-IR as indicated by EdU incorporation assay. Neutrophils were significantly increased in the lamina propria at the marker site 3.5 days post-IR. Additionally, neutrophils were found to be elevated in the peripheral blood 14 days post-IR. Other leukocyte populations remained unchanged in the peripheral blood. Finally, an increase in circulating reticulocytes was noted 14 days post-irradiation, suggesting a regenerative response. This ongoing study indicates that there are major changes within the intestinal immune compartment following focal irradiation of the small intestine. Further, there may be an associated systemic effect despite the very limited area exposed to IR possibly related to dose and irradiated volume.

Brett Bell is currently a biochemistry major at UPenn. Brett spent his 10 weeks in the lab of Dr. Costas Koumenis while in the SUPERS program.