Developmental Timing Effect on Tumor Recurrence in Mouse Medulloblastoma Models

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Objective

Does developmental timing play a role in radiation resistance and tumor recurrence in medulloblastoma mouse models?

Why Does it Matter?

Medulloblastoma is the most common pediatric brain cancer, typically affecting individuals from birth to age five. Medulloblastoma occurs in the cerebellum (refer to Figure 1) which is the structure in the lower posterior part of the brain responsible for motor control, balance, and coordination. Current treatments for medulloblastoma include tumor resection, chemotherapy, and radiation. Approximately 80% of pediatric patients with medulloblastoma are able to respond to radiation treatment. The remaining 20% of patients, however, are unable to respond to radiation treatment and die from the disease. We have induced a medulloblastoma-producing oncogene at two different points during brain development, in order to study how the developmental timing affects the clinical behavior of the tumor. By understanding the difference between the two models and their responses to radiation treatment, we aim to develop more targeted treatments for the patients resistant to radiation.

Figure 1. Human Patient. Seven year old patient with tumor.
Results

Without radiation treatment, the mice with medulloblastoma die by the time they are 20 days old, as seen in Figure 2. However, preliminary results collected from tumor mice that have been radiated show that the G-Smo mice are more resistant to radiation treatment and die early even with treatment. On the other hand, the M-Smo mice respond well to treatment and go on to live into adulthood, which can be seen in Figure 3.

The M-Smo mice are more similar to the 80% of patients with medulloblastoma that respond well to radiation treatment while the G-Smo mice are more similar to the 20% of patients resistant to radiation and die with the disease. These results allow us to gain insight as to whether or not cell of origin plays a role in radiation resistance and tumor recurrence to facilitate developing targeted treatments for the patients resistant to treatment.

Figure 2. Medulloblastoma in G-Smo Mouse. Medulloblastoma in G-Smo mouse at postnatal day 12 that received no radiation treatment.

Figure 3. G-Smo versus M-Smo Survival Curve. G-Smo mice (Blue) live to an average of 20 days after treatment. M-Smo mice (Green) live to an average of 100 days after treatment.