NOVEL PATIENT-DERIVED XENOGRAFT MOUSE MODELS OF HEPATOBLASTOMA REPLICATE UNIQUE TUMOR SUBCLONES

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Background: Hepatoblastoma (HB) is a rare childhood tumor of the liver that affects 2 in 1 million children a year. Most treatment options for this tumor are broad and limited. Patient-derived xenograft (PDX) models provide new avenues to treat hepatoblastoma by testing targeted agents with individual, well studied models. While models of multiple risk levels were tested, this paper focuses on two specific relapse models, HB28(+) and HB28(-), that were developed from the same patient but show contrasting characteristics.

Materials/Methods: Immunocompromised mouse livers were implanted with primary tumor samples and tumor growth was measured with MRI and ELISA. ELISA was used to evaluate amounts of human Alpha-FetoProtein (AFP) in the blood of these mice. Bulk and single cell RNA sequencing, mutation testing, Immunohistochemistry (IHC) for Hematoxylin and Eosin (H&E), Beta-Catenin, and Glypican-3 (GPC3), IHC slide analysis, and drug testing with Cisplatin were used to validate the tumors and show how the two models differed from each other.

Results: One relapse patient generated two differed PDX models that showed varying responses to the tests done above. HB28(-) seems to have no human AFP secretion in the blood and shows no expression of the gene. On the other hand, HB28(+) does show secretion of human AFP in the blood and expression of the gene. Both models retain all mutations found in the patient. IHC slide analysis indicated tumor growth in both models, with different histology patterns between the two models, and lung metastasis in both models. Drug testing of the models showed more resistance to Cisplatin with the HB28(+) model.

Conclusions: The two HB28 models showed unique and contrasting characteristics, and each model replicated sub-clones of the patient primary tumor, facilitating further drug testing. Future studies on the practicality of PDX models will guide treatment testing beforehand with real-time application to patients.

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