A CIRCULATING TUMOR CELL-BASED LIQUID BIOPSY TEST FOR HEPATOBLASTOMA

Woodfield, Sarah E[1], Roma H Patel[2], Andres F Espinoza[2], Richard S Whitlock[2], Andrew Badachhape[3], Aayushi P Shah[4], Saiabhiroop R Govindu[2], Sanjeev A Vasudevan[2], Sarah E Woodfield[2]

[1] Baylor College of Medicine, Department of Surgery, Pediatric General Surgery
[2] Baylor College of Medicine, Surgery, Pediatric General Surgery
[3] Texas Children's Hospital, Radiology, Pediatric Radiology
[4] Baylor College of Medicine, Surgery, Pediatric General Surgeryediatric Radiology

Keywords: hepatoblastoma, metastasis, circulating tumor cell

Background: Hepatoblastoma (HB) is the most common pediatric primary liver tumor and has the fastest rising incidence of all pediatric solid tumors. Patients with high-risk, treatment refractory, or relapse disease have a survival rate of less than 50%. Disease progression is currently monitored with MR imaging, CT scanning, and measurement of serum levels of Alpha fetoprotein (AFP). These assays involve exposing children to radiation and anesthesia and are not always accurate. The goal of this work is to develop and validate a liquid biopsy test for circulating tumor cells (CTCs) that would provide a less invasive and more accurate way of assessing prognosis and tumor response to therapy.

Materials/Methods: We developed a new method for quantifying CTC burden from primary patient whole blood samples using HB-specific markers indocyanine green (ICG), Glypican-3 (GPC3), and DAPI with microscopy and flow cytometry readouts. We further tested this assay with blood samples from our novel orthotopic patient-derived xenograft (PDX) mouse models of HB.

Results: We first showed that ICG accumulation is specific to HB cells, as compared to fibroblasts or other cancer cells, using fluorescence microscopy. We also showed that ICG accumulation can be used with microscopy and flow cytometry to identify HB cells in a mixed population of cells. With our mouse models, we showed the presence of triple ICG+/GPC3+/DAPI+ cells in the blood of animals harboring PDX tumors. Finally, with numerous primary patient blood samples, we used both standard and imaging flow cytometry to count and image triple ICG+/GPC3+/DAPI+ CTCs. These cell numbers were correlated with patient characteristics and outcomes.

Conclusions: This work shows the development and use of a liquid biopsy test for CTCs for HB, which has the real potential to improve the standard of care by offering a more accurate and less invasive means of monitoring disease before, during, and after therapy.

Images / Graph / Table: No image uploaded