Study to Improve Hepatoblastoma Treatment Uses Patient Derived Xenograft Models

Hepatoblastoma (HB) is the most common malignant cancer of childhood. Current treatments are complex and include chemotherapy, surgical resection, and sometimes liver transplantation. Curative therapy greatly impacts long-term quality of life and still, for some the cancer can return. Therefore, a significant need to develop new treatment options exists, especially for more aggressive and relapsed tumors.

One limitation in the study of HB is the lack of available animal models which represent the human disease. We propose to identify and characterize how HB develops using experimental models known as patient derived xenografts (PDX). In this system, we surgically implant a portion of human HB into a mouse to grow and expand the tumor for further examination (figure 1.A). Our HB PDX models mirror the human disease both genetically and in microscopic appearance (figure 1.B and 1.C).

We are examining the molecular biology of HB formation by studying gene overexpression with particular focus on Glypican 3 (GPC3). Earlier experiments revealed that the GPC3 gene was significantly overexpressed in a number of human tumors. We are working to determine how different forms of GPC3 may contribute to tumor growth and, more importantly, how they may be used to stop HB growth.

Using the generous Markham funds, our laboratory has been able to expand the number of working PDX models available as well as begin preliminary experiments on these tumors using both accepted and novel chemotherapeutic treatments.
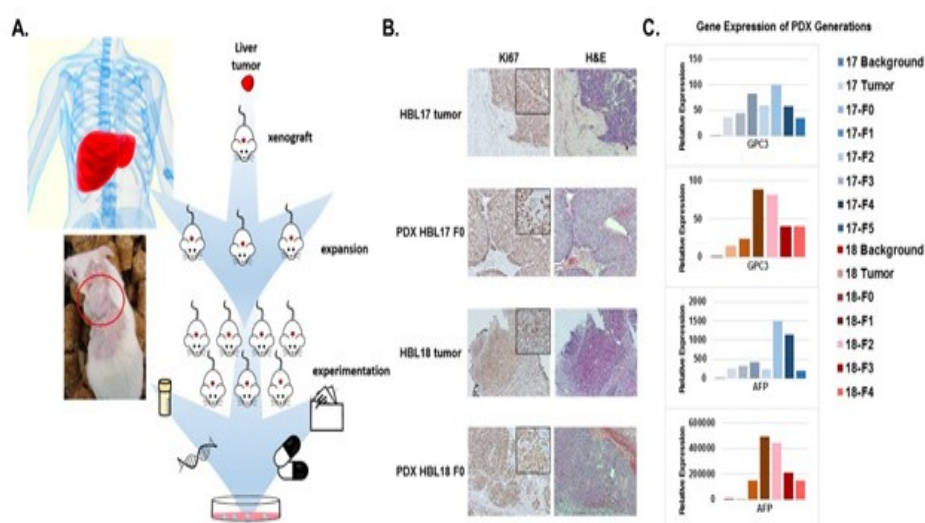

Figure 1. A. Schematic of PDX model showing process of implantation of tumor, growth and experimentation, including cryopreservation, molecular analysis, generation of cell lines, drug testing and database of effective treatments. B. Histology of patient source tumor and first generation PDX tumor (F0) of HB- 17 and HB-18 showing proliferation by H&E and Ki67 (4x with zoomed in 10x inlay, magnified 3x in Ki67 panel). C. Real time PCR of Patient source tumor, background liver and PDX generations demonstrating passaged PDX HB tumor maintains tumor phenotype (generation of PDX tumor indicated by F0, F1, F2, F3, F4, F5).