



PLATFORM DEVELOPMENT FOR TARGET IDENTIFICATION IN HIGH RISK PEDIATRIC LEUKEMIAS

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Dr. Ferrando and Dr. Mullighan's final report due date has been postponed to December of 2020 due to COVID-19.

PROJECT UPDATE

Despite much progress in understanding the genetic basis of childhood leukemias, there are a limited number of targeted therapies available for the treatment of high risk patients. New high screening technologies for the identification of candidate drugs and druggable gene targets offer much opportunity by leveraging genome-wide analysis of genetic dependencies and large scale drug libraries of bioactive compounds. However, realizing these advances is limited by the paucity of immortalized leukemia cell lines representative of high risk leukemia patients. To overcome this obstacle, we have systematically addressed the generation of new cell lines from relapsed leukemia samples. These efforts have resulted in the generation of two new leukemia cell lines (CUTLL3 and CUTLL4) from relapsed and refractory leukemias. Proof of principle of

the soundness of these efforts are provided by high throughput drug screens using our newly generated CUTLL3 line, which

"The support of the Brian Morden Foundation and Alex's Lemonade Stand Foundation has been instrumental in advancing our drug discovery efforts for the treatment of high risk leukemia patients. We have used the funding to support the development of innovative approaches to establish new models of high risk leukemia, and to test the activity of new classes of compounds to kill leukemia cells. We are honored and grateful for their recognition of the fundamental importance of high-risk high-pay transformative research with potentially deep clinical impact."

have identified inhibition of cholesterol metabolism as a new therapeutic target against this disease. Ongoing work aims to further expand the repertoire of high risk leukemia cell models for drug discovery using advanced cell line immortalization protocols and leukemia bone marrow organoids.

