The childhood blood cancer B-cell precursor acute lymphoblastic leukemia (B-ALL) responds to treatment with dexamethasone in ~90% of patients, but there are few therapeutic options in children resistant to dexamethasone. The mechanism by which dexamethasone kills B-ALL cancer cells, and the determinants of response to therapy are unclear. In a collaboration lead by Dr. Miles Pufall (University of Iowa), we used our functional genomics platform to uncover genes controlling the response of the childhood cancer to the anti-cancer drug dexamethasone. Integrating the results from this genetic screen with transcriptomic data revealed that dexamethasone was effective against B-ALL by suppressing B cell development genes. It also uncovered a regulatory feedback loop involving Phosphoinositide 3-kinase delta (PI3Kδ). A combination therapy of dexamethasone with the PI3Kδ inhibitor idelalisib killed even highly resistant B-ALL cells and showed synergistic anti-cancer effects in a mouse model of B-ALL.

The results from our study are in press at *Blood*:


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