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"Identification of therapeutic targets of B-ALL using Boolean logic"

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SCIENTIFIC ABSTRACT
B-cell acute lymphoblastic leukemia (B-ALL) is the most common childhood cancer. Almost all children can be cured of this disease using standard treatment options. Reducing toxicity, rate of infections, and behavioral changes are the main goals in developing next-generation targeted therapies. B-ALL arises from one of the blood cells from the B-cell differentiation path that also possess the ability to differentiate through a series of intermediate steps. The early steps of differentiation contain stem and progenitor cells which are considered the most aggressive cell types. We believe that targeting the stem and progenitor cells can cure the disease while reducing treatment-related toxicity. Molecular or epigenetic drivers that characterize the early steps of differentiation are poorly understood. We have developed mathematical tools to understand logical rules of gene expression patterns that provide information about the differentiation. The Boolean logical rules between pairs of genes are discovered from large collection of patient derived gene expression datasets. Published work using Boolean logic has successfully helped chart the changing landscape of gene expression signature during B cell differentiation, and during the initiation and progression of bladder and colon cancers. We will use these logical rules to build a computational model of differentiation that predicts molecular states of early stem and progenitor cells. This will help us to develop therapeutic targets for B-ALL.

LAY ABSTRACT
B-cell acute lymphoblastic leukemia (B-ALL) is the most common childhood cancer. Almost all children can be cured of this disease using standard treatment options. Reducing toxicity, rate of infections, and behavioral changes are the main goals in developing next-generation targeted therapies. B-ALL cells possess the ability to go through a series of intermediate steps towards a less aggressive state. The early steps along this path contain the most aggressive cell types that can be targeted to cure the disease. Molecular or epigenetic drivers that characterize the most aggressive state is poorly understood. We have developed mathematical tools to understand logical rules of gene expression patterns of these aggressive cell types. This will help us to develop targeted therapies for B-ALL.