

## Study finds therapeutic targets for rare cancer in children

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The first study of Ewing's sarcoma that screened hundreds of genes based on how they affect cell growth has identified two potential anti-cancer drug targets, according to a scientific paper by the Translational Genomics Research Institute (TGen) published this month in the journal *Molecular Cancer*.

Ewing's sarcomas are rare, but [aggressive cancer](#) lesions that occur most frequently in the bones of teenagers. They represent nearly 3 percent of all childhood cancers. Patients are treated with a combination of surgery, radiation and chemotherapy. This cancer can reoccur after surgical removal, and often spreads to the lungs, other bones and bone marrow. Once it spreads, or metastasizes, only 1 in 5 patients survive more than 5 years.

These lesions harbor unique [chromosomal abnormalities](#) that give rise to fusion genes that act as cancer-inducing proteins, or oncoproteins.

TGen researchers used RNAi-based phenotypic, or loss-of-function screening, a method of silencing hundreds of individual genes in a high-throughput format, to analyze 572 kinases that are expressed in human cells. Kinases are enzymes that modify other proteins. Using this technique, the authors discovered two protein kinases with important roles in the growth and survival of Ewing's [sarcoma](#) cells. [Cancer cells](#) died when investigators stopped the normal function of the two protein kinases called STK10 and TNK2.

"RNAi-based phenotypic profiling proved to be a powerful gene target discovery strategy, leading to successful identification and validation of STK10 and TNK2 as two novel potential therapeutic targets for Ewing's sarcoma," said Dr. David Azorsa, a TGen Senior Investigator and the paper's senior author.

This was the first study demonstrating the use of this kind of phenotypic profiling to identify unique kinase targets for Ewing's sarcoma, according to the paper.

By identifying kinases that regulate the growth of Ewing's sarcoma cells, TGen investigators anticipate a rapid translation of their discoveries into clinical drug trials and specific remedies for individual patients, advancing the prospects of personalized medicine.

"We undertook this study with the goal of identifying specific kinases that can be targeted to modulate Ewing's sarcoma cell growth and survival," said Dr. Shilpi Arora, a TGen Staff Scientist and the paper's lead author. "In addition to the identification of specific kinase targets, we were able to obtain a better understanding of contextual vulnerabilities in Ewing's sarcoma."

Provided by The Translational Genomics Research Institute

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