

# Cancer Researchers Identify New Mutant Genes

June 3 2009

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(PhysOrg.com) -- University of New Mexico Cancer Center researchers have identified a genetic mutation underlying one of the most common childhood cancers, acute lymphoblastic leukemia (ALL). The discovery could lead to more effective treatments for a subset of ALL patients who experience minimal benefit with current therapies by using drugs that are already in clinical trials for similar blood diseases in adults.

The research team from the UNM Cancer Center worked in collaboration with St. Jude Children's Research Hospital, the National Cancer Institute (NCI) and the Children's Oncology Group/CureSearch to publish the find, which appears online in the early edition of the *Proceedings of the National Academy of Sciences*.

[Acute lymphoblastic leukemia](#) occurs when [white blood cells](#), which normally help fight off [viruses](#) and [bacteria](#), don't mature properly. As more of these underdeveloped cells build up, healthy, infection-fighting cells are crowded out. The disease accounts for about three out of four childhood leukemia cases, and affects about 1 in 29,000 children nationwide every year; New Mexico has an average of 37 ALL cases diagnosed annually.

With the most advanced treatment options available today, cure rates are now upwards of 85 percent. The challenge lies in treating the remaining high-risk cases, which have proven especially difficult to overcome because they arise from different, unidentified [genetic mutations](#). Scientists haven't been able to accurately identify those high-risk cases,

and effective treatment for those patients remains elusive.

“Our studies of these leukemia subtypes indicate that leukemia is not necessarily a single-cause disease,” says Cheryl Willman, director and CEO of the UNM Cancer Center and senior co-author of the study. “A patient may have multiple different genetic lesions that target different cellular pathways to induce leukemia. Therefore, it is very important to develop new therapies that target these specific mutations.”

UNM Cancer Center researchers joined collaborators to look at different patients’ gene-expression patterns and their outcomes to identify a panel of genes to sequence. They found that some high-risk ALL cases are caused by mutations in genes that produce kinases, which are enzymes that function as biological on-off switches in cells. The mutations keep the kinases continually “on”, triggering the characteristic uncontrolled production of abnormal white blood cells in leukemia.

By analyzing the genetic sequences of kinases known to have a role in white blood cell proliferation in 187 patients with high-risk ALL, the researchers found mutations in about 10 percent of the cases in a type of kinase known as JAK. JAK is known to have mutations in other types of leukemia and other similar diseases.

“What’s really exciting about this particular study is that we found that drugs that blocked the activity of the mutant JAK kinases prevented uncontrolled cell proliferation,” Willman explains. “Our discovery of JAK as a target now allows us to develop [clinical trials](#) with JAK inhibitors for children and adults with this form of disease.”

“These mutations and this signature identify a subset of the high-risk ALL patients who might be candidates for a targeted therapy, similar to what the highly effective drug Gleevac has done for chronic myelogenous [leukemia](#) (CML) patients,” adds Richard Harvey, scientific

director of the UNM-CMCD and co-author of the study.

“Pathways associated with these mutant genes are currently being targeted by several pharmaceutical companies, and our hope is that these drugs will quickly find their way into clinical trials. Children across the country with ALL will benefit from these findings, but there have been indications that certain ethnicities, in particular Hispanics, are more frequently found with these high-risk cases. If this holds true, this research will certainly benefit children in New Mexico.”

The research team will continue to explore other kinase gene [mutations](#) and other enzymes that are common to high-risk ALL cases. The group is applying the same research techniques to adult leukemias in hope of finding similar patterns, which could lead to more effective treatments for other cancers.

Provided by University of New Mexico ([news](#) : [web](#))

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