

CHILDREN AND CANCER

GENETIC LINCHPIN

Leukemia Deadlier for Native, Hispanic Kids

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Physicians have long known that leukemia is especially deadly for Hispanic and Native American kids, but couldn't answer the question why.

A new study co-authored by a New Mexico researcher points to genetic factors — not socioeconomic factors — that make the cancer deadlier for children with Native American ancestry.

The study, published this month in the online edition of Nature Genetics, is the first to show a genetic explanation for the lower survival rates of Hispanic and Native American children with acute lymphoblastic leukemia, or ALL, said Dr. Cheryl Willman, director and CEO of the University of New Mexico Cancer Center and a co-author of the study.

Researchers who analyzed the genomes of 2,500 kids with leukemia found that children with Native American ancestry have a higher risk of relapse and don't respond as well to standard treatments for leukemia, the study said.

It also found that 41 percent of self-reported Hispanic kids with leukemia had enough Native American genetic ancestry to put them at higher risk of relapse.

The study, led by St. Jude Children's Research Hospital in Memphis, Tenn., also found that leukemia patients with Native American ancestry benefited more than other children from more chemotherapy.

But Willman said intensive chemotherapy can result in horrendous side effects such as brain damage and sterility. A better alternative are drugs that target the effects of specific mutations found in children most at risk of relapse, she said.

The study alerts doctors making life-and-death decisions about cancer therapies to use genetic tools to determine ancestry rather than relying on self-reporting by patients and their families, Willman said.

New drugs, including those under development at UNM Cancer Center, offer promising treatments for children at greatest risk but require doctors to use precise methods to understand genetic ancestry, she said.

"We can't just rely on self-reported race because, in today's modern genome science, it's too imprecise," Willman said.

ALL is diagnosed in about 5,000 U.S. children each year, including about 45 New Mexico children.

“We’ve known for some time that the survival rate in Hispanic and Native American children (with ALL) has been worse,” she said. “The question is, why?”

Many cancer experts have offered socioeconomic explanations, speculating that Hispanic and Native American families fail to seek care or don’t finish their therapy, Willman said. But the study argues against those explanations, she said, because the children studied were treated with uniform protocols and completed their therapies.

The study “is one of the strongest proofs that your race and ethnicity, determined by genetic ancestry, really predicts your response to cancer therapy,” she said.

The findings generated controversy during its peer review process because it contradicts long-held explanations for the poor outcomes of Hispanic and Native American children, she said. “People are shocked by the findings.”

Researchers have identified a pair of harmful gene mutations prevalent among Hispanic and Native American children with leukemia who have low survival rates, Willman said. Those mutations are associated with five-year survival rates lower than 40 percent, she said. One of those mutations, called the Janus kinase, or JAK mutation, was identified in 2009 by UNM researchers.

UNM now is leading a nationwide trial to test a drug that inhibits the harmful effects of the JAK mutation, Willman said. Researchers hope to complete the drug trial this year.

UNM researchers also have identified 13 drugs that target the second mutation, called CRLF2, and now are performing mouse studies to identify promising candidates for drug trials, she said.



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Dr. Cheryl Willman, director and CEO of the University of New Mexico Cancer Center, and Richard Harvey, scientific director of the UNM Center for Molecular and Cellular Diagnostics, discuss research indicating that genetic factors explain why Native American and Hispanic children often have lower survival rates than other children with leukemia.

Survival rates

Five-year survival rates for U.S. children 18 and younger with acute lymphoblastic leukemia, or ALL.

ALL CHILDREN:
84.8 percent

HISPANIC:
80.2 percent

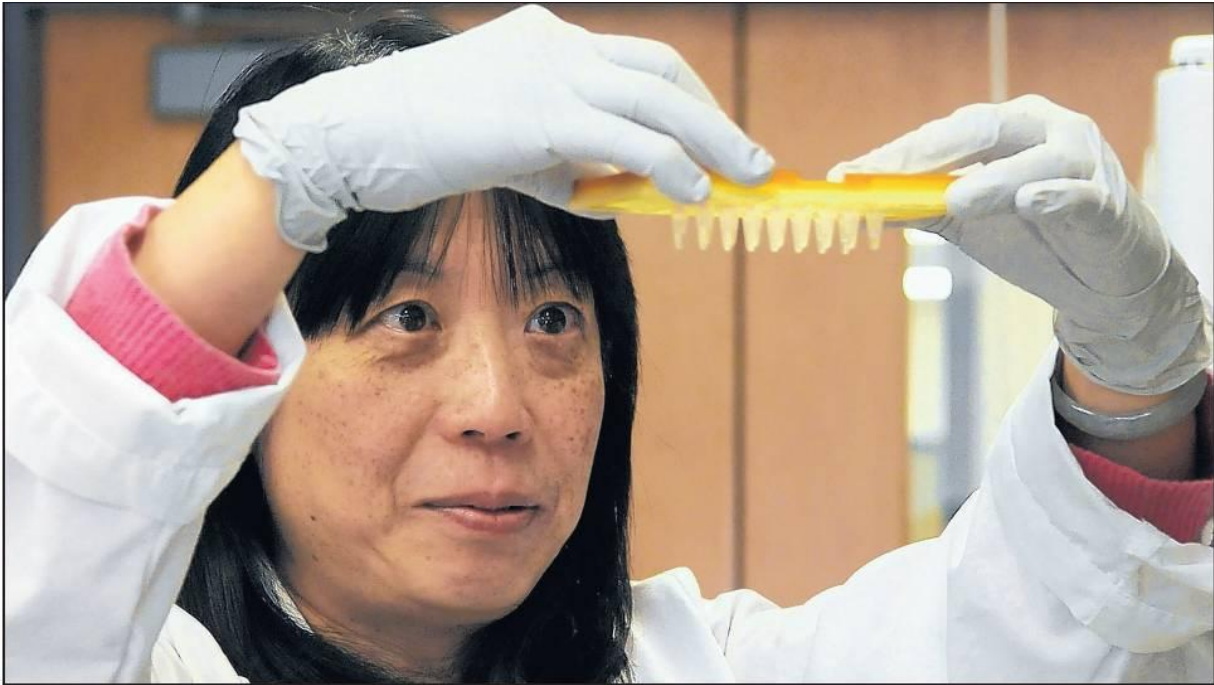
ANGLO:
86.7 percent

NATIVE AMERICAN:
77.5 percent

Source: New Mexico Tumor Registry



Enzymes are added to genetic samples from patients to make the results more visible in computerized scanning techniques.



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I-Ming Chen, a University of New Mexico professor of pathology, prepares genetic material from the blood or bone marrow of a leukemia patient at the UNM Cancer Center. The work helped identify genetic mutations associated with severe cases of childhood leukemia.