

# New gene findings will help guide treatment in infant leukemia

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Pediatric oncologists have identified specific genes, dubbed partner genes, that fuse with another gene to drive an often-fatal form of leukemia in infants. By more accurately defining specific partner genes, researchers expect to better predict which infants may benefit from particular treatments.

Oncologists also aim to use this latest knowledge to develop new and more effective therapies for this difficult-to-treat type of [blood cancer](#), called acute lymphoblastic [leukemia](#) (ALL). Their goal is to target treatments to specific genes and other associated factors that become abnormal because of the gene fusions.

Blaine W. Robinson, Ph.D., a research scientist at The Children's Hospital of Philadelphia, will present research findings in infant ALL at the annual meeting of the American Society of [Hematology](#) on Dec. 8. His group collaborated with the Children's Oncology Group (COG), a cooperative, multicenter research organization, on this research, sponsored by the Leukemia & Lymphoma Society.

ALL is the commonest of all the pediatric cancers. While the survival rate for children older than one year of age with ALL has increased over time with advances in chemotherapy, the outlook for infants (patients less than one year old) with the disease generally has been grim. Infants with ALL have a poor prognosis and a much higher mortality rate compared to other children, and curative treatments for them are far behind the therapy for childhood ALL.

For the majority of these high-risk infants, the problem is within the structure of a specific chromosome. In an abnormality called the MLL translocation, the MLL gene on chromosome 11 breaks and joins with any one of many different "partner" genes from other chromosomes. The rearranged genetic region, called a translocation, leads to the production of a fusion gene and an abnormal protein and, ultimately, to leukemia.

The current study covered 221 infants with ALL in a COG clinical trial. Researchers detected MLL translocations in the ALL cells of 74 percent of the patients. The two most common partner genes that fused with the MLL gene were AF4 on chromosome 4 and ENL on chromosome 19. Both of these translocations were associated with a very poor prognosis; event-free survival (EFS) rates were 34 percent with AF4 and 29 percent with ENL, compared to the overall EFS rate of 46 percent among all infants in the study—still far inferior to survival rates that are seen in children above age one.

The EFS rates with these two partner genes were even lower when the infants were less than 90 days old at diagnosis. Conversely, the survival rates were better when these partner genes fused to MLL in the leukemia cells of older infants. Though age was already known to be a classic prognostic factor in infant ALL, the differences in survival in younger versus older babies when these specific partner genes are involved had not been so clear.

In contrast, outcomes were better for infants with ALL when the third most common partner gene, AF9, fused to MLL, or when the MLL gene was unaffected. In these patients, the respective EFS rates were 68 and 66 percent. The researchers also analyzed white blood cell counts (WBC)—another classic prognostic factor in leukemia. They found that when MLL was fused to AF4, the infants were far more likely to have higher WBC, while the WBC was lower when MLL fused to AF9.

More refined knowledge of how the different partner genes of MLL in infant ALL are connected to the underlying molecular biology of the disease may guide the researchers to more appropriate treatment decisions. "Our ability to classify ALL based on specific partner [genes](#) of MLL may provide a new way to categorize which infants might benefit from specific types of treatment," said senior author Carolyn A. Felix, M.D., a pediatric oncologist and expert in infant leukemia at Children's Hospital, and a professor of Pediatrics at the University of Pennsylvania School of Medicine. "We also hope these findings will contribute to the development of new, molecularly targeted therapies for infants with this grim form of cancer that we seek to conquer."

Gregory Reaman, M.D., chair of the Children's Oncology Group, added, "As [infants](#) with ALL represent the group of children with the highest risk of treatment failure, despite successive attempts to intensify conventional therapy, these clues to potentially tailoring molecularly targeted treatment approaches are very exciting."

Source: Children's Hospital of Philadelphia ([news](#) : [web](#))

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