Possible new approach to treating deadly leukemia in babies

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A Loyola University Health System study points to a promising new approach to treating an aggressive and usually fatal leukemia in babies.

The study involved a type of leukemia called mixed lineage leukemia, or MLL. Only 25 to 50 percent of babies diagnosed with MLL leukemia survive the disease.

The study demonstrated how it may be possible to kill cancerous MLL cells by targeting a protein called DOT1. Researchers showed that, without the DOT1 protein, cancerous MLL cells died, said Charles Hemenway, MD, PhD, senior author of the study.

"We are focusing on the unique biology of MLL leukemia," Hemenway said.

The study was presented at the 2011 meeting of the American Association for Cancer Research.

Between 5 and 10 percent of all leukemias are MLL positive. In children older than 1 who have MLL leukemia, the survival rate is about 75 percent. By comparison, the survival rate for most other childhood leukemias is about 90 percent. Adults who have MLL leukemia also have lower survival rates than adults with other types of leukemia.

MLL is a subtype of leukemia caused by a mutation in a gene called MLL. The mutated gene codes for an abnormal MLL protein, which

turns a blood cell into a cancer cell. For reasons researchers don't understand, MLL leukemia is more resistant to chemotherapy than other forms of leukemia.

In previous studies, Loyola researchers developed a small molecule, called PFWT, that binds to the MLL protein. This binding effectively disables the MLL protein, leading to the death of the cancer cell. Later this year, Hemenway plans to begin testing PFWT molecules on mice that have MLL leukemia.

The new study points to a second possible way to attack MLL cells, by targeting the DOT1 protein. DOT1 works in conjunction with the MLL protein. The study demonstrated that DOT1 is critical for keeping cancer MLL cancer cells alive.

Researchers cultured MLL cells from mice. From these cells, researchers removed the gene that codes for the DOT1 protein. Without the gene, the cell no longer produced the DOT1 protein, and without the DOT1 protein, the cancerous cells died.

Loyola researchers are collaborating with researchers from Nemours/Alfred I. duPont Hospital for Children to identify molecules that could disable DOT1.

Hemenway said a double-barrel approach -- targeting both the DOT1 and MLL proteins --potentially could be a more effective treatment than current chemotherapy, with fewer side effects. But it will take years of additional research and testing before such a treatment would be available for patients.

Hemenway said several other Loyola researchers are studying MLL leukemia. "There are a lot of opportunities for collaboration," he said.

Provided by Loyola University Health System