MedicalXpress

Gene mutation improves leukemia drug's effect

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Gene mutations that make cells cancerous can sometimes also make them more sensitive to chemotherapy. A new study led by cancer researchers at Ohio State University shows that a mutation present in some cases of acute leukemia makes the disease more susceptible to high doses of a particular anticancer drug.

The findings, from a Cancer and Leukemia Group B clinical cooperative group study led by Dr. Clara D. Bloomfield, an internationally known AML specialist at the Ohio State University Comprehensive Cancer Center, could change how doctors manage these patients.

The research is published online in the June 16 issue of the *Journal of Clinical Oncology* with an accompanying editorial.

The retrospective study shows that people with acute myeloid leukemia (AML) whose leukemic cells have mutations in the RAS gene are more likely to be cured when treated after remission with high doses of the drug cytarabine.

It also suggests that testing for RAS mutations might help doctors identify which AML patients should receive high-dose cytarabine as their post-remission therapy.

"This appears to be the first example in AML of a mutation in an oncogene that favorably modifies a patient's response to the dose of a routinely used chemotherapeutic drug," Bloomfield says.

"If confirmed, AML patients in the future will likely be screened for RAS mutations, and those who have one may get high-dose cytarabine for post-remission therapy rather than a stem-cell transplant."

Typically, people with newly diagnosed AML are treated first with drugs intended to drive the disease into complete remission, Bloomfield says. When that is achieved, patients are given additional chemotherapy, such as high-dose cytarabine, or more aggressive therapy, such as a stem cell transplant, to prevent relapse and to cure the malignancy.

But high-dose cytarabine is the better therapy for some patients, and the findings of this study may enable doctors to identify those individuals.

The research analyzed the outcome of 185 AML patients age 60 or less who had achieved complete remission following initial therapy. Thirty-four of the patients (18 percent) had mutations in the RAS gene, and of these, 22 received high-dose cytarabine and 12 received the drug at low dose.

The high-dose patients with RAS mutations had the lowest relapse rate – 45 percent experienced disease recurrence after an average 10-year follow-up compared with 68 percent for those with normal RAS genes.

"That means fifty-five percent of patients with RAS mutations were cured compared with 32 percent of high-dose patients with normal RAS," Bloomfield says.

Of patients who received low doses of the drug, all those with the mutations relapsed, as did 80 percent of those with normal RAS genes.

"These data strongly suggest that mutations in RAS influence the response of AML patients to high-dose cytarabine, and they support the use of these mutations as biomarkers for this therapy," says Bloomfield,

who is also a Distinguished University Professor, the William G. Pace III Professor in Cancer Research and an OSU Cancer Scholar.

Source: Ohio State University Medical Center