Panel predicts whether rare leukemia will respond to treatment

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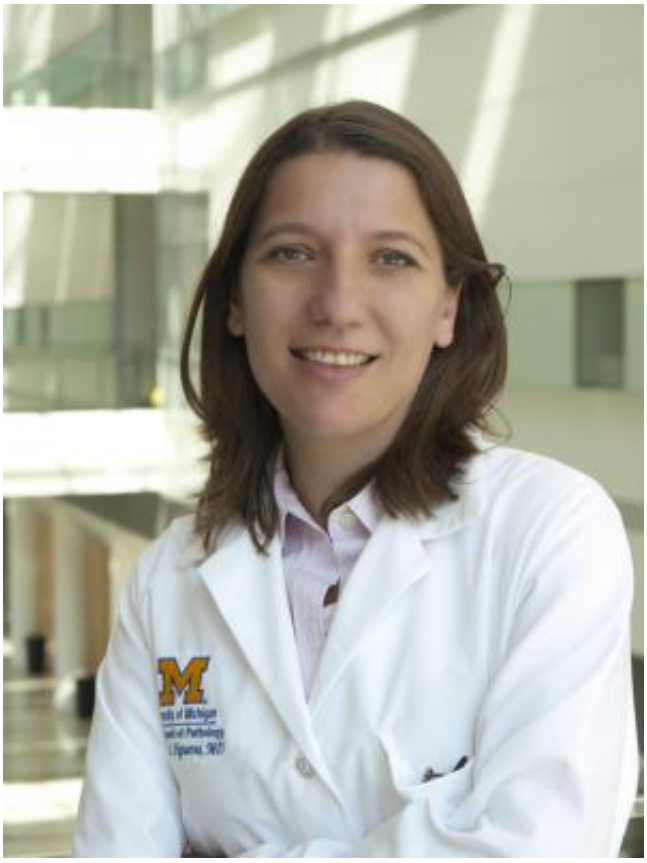

Maria E. Figueroa, M.D.. Credit: University of Michigan Health System

Patients with chronic myelomonocytic leukemia have limited treatment options, and those that exist are effective only in fewer than half of patients. Now, a new study identifies a panel of genetic markers that predicted which tumor samples would likely respond to treatment.

The finding could lead to a test to help doctors know which patients could be spared from a lengthy course of treatment that's unlikely to work.

Finding an effective biomarker is particularly crucial for this disease because the current treatment is slow-acting, which means patients must undergo as much as six months of treatment before there are signs of response.

"The slow kinetics is what gets us. It's not just one week or one dose to see signs of response. A good biomarker test could potentially prevent patients who are unlikely to respond from receiving prolonged, unwarranted treatments," says study author Maria E. Figueroa, M.D., assistant professor of pathology at the University of Michigan Medical School.

Chronic myelomonocytic leukemia, or CMML, is a cancer that begins in the blood-forming cells of bone marrow. It primarily affects older adults. Previous research has tried to identify genetic differences but with little success.

In the current study, published in the *Journal of Clinical Investigation*, researchers from the University of Michigan Comprehensive Cancer Center and the University of Florence in Italy used next generation gene sequencing techniques to dive deep into the DNA of CMML tissue samples treated with the drug Decitabine.

By harnessing this advanced technology to look beyond the usual regions of a gene, the researchers were able to find a number of differences between the samples that responded to treatment and those that did not.

The team combined a series of markers into a panel, which they then tested against 28 additional CMML samples from a research team at the

Gustave Roussy Cancer Center in France. They found the panel was 87 percent accurate in predicting response to Decitabine.

In addition, the researchers looked at the non-responders to try to understand why they were resistant to Decitabine. They found two proteins, CXCL4 and CXCL7, were overexpressed. When cells exposed to high levels of these chemokines were treated with Decitabine, the drug's effect was blocked.

"We are pursuing this to understand why these proteins block the effect of the drug and whether we can develop a new compound that could be used along with Decitabine to turn non-responders into responders," Figueroa says.

In addition, the team is working to refine and translate its panel to a viable biomarker test that could be used in the clinic. More research is needed before a test would be available.

More information: Specific molecular signatures predict decitabine response in chronic myelomonocytic leukemi, *Journal of Clinical Investigation*, published March 30, 2015. doi:10.1172/JCI78752

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