Discovery suggests potential new treatment for deadly blood cancer

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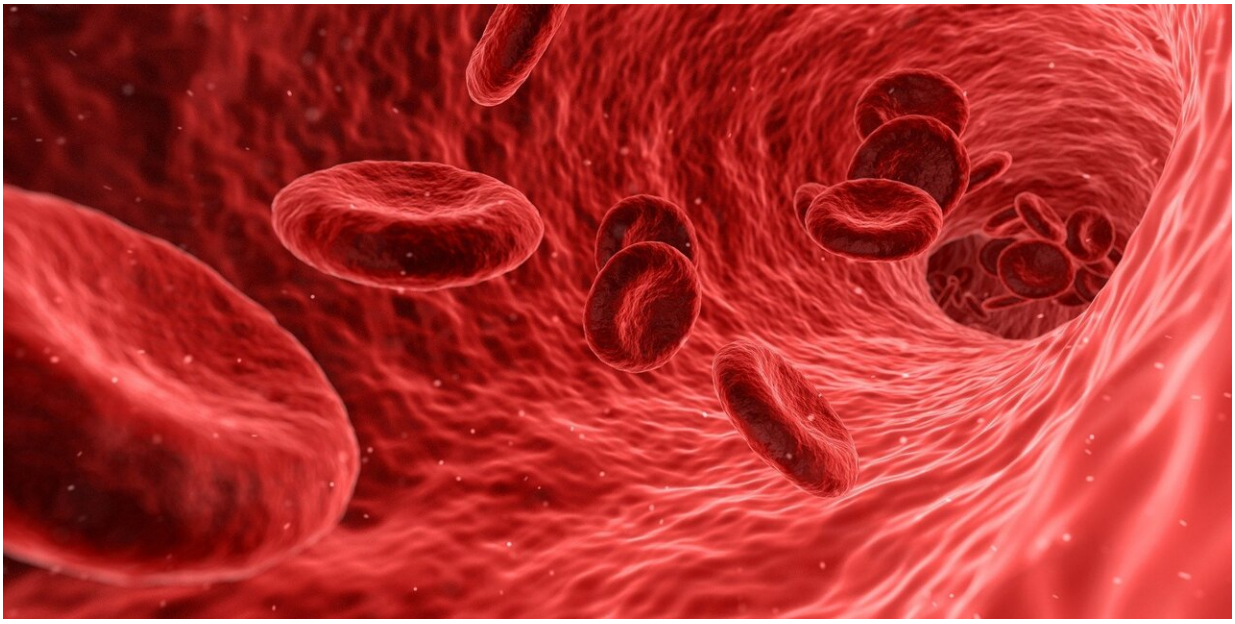

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A drug used to treat certain advanced breast cancers may offer a new treatment option for a deadly blood cancer known as myelofibrosis, new research from UVA Cancer Center suggests.

The drug, palbociclib, may be able to prevent the scarring of bone marrow that existing treatments for myelofibrosis cannot. This scarring disrupts the marrow's production of blood cells and causes severe anemia

that leaves patients weak and fatigued. The scarring also reduces the number of platelets in the blood, making clotting difficult, and often causes an enlarged spleen.

"Current therapies only provide symptomatic relief without offering significant improvement of bone marrow fibrosis. So, there is a critical need to develop more effective therapy for myelofibrosis," said senior researcher Golam Mohi of the University of Virginia School of Medicine's Department of Biochemistry and Molecular Genetics. "We have identified CDK6, a regulator of cell cycle, as a new therapeutic target in myelofibrosis. We demonstrate that CDK4/6 inhibitor palbociclib, in combination with ruxolitinib, markedly inhibits myelofibrosis, suggesting this drug combination could be an effective therapeutic strategy against this devastating blood disorder."

Myelofibrosis: A dangerous cancer

Myelofibrosis is a form of leukemia. It occurs in approximately 1 to 1.5 of every 100,000 people, primarily those who are middle-aged or older. Patients with intermediate or high-risk cases typically survive only 16 to 35 months.

Existing treatments for myelofibrosis do not address the bone marrow scarring that is a hallmark of the disease. The drug ruxolitinib is used to relieve patients' symptoms, but Mohi's new research suggests that pairing the drug with palbociclib may make a far superior treatment.

Palbociclib, by itself, reduced bone marrow scarring in two different mouse models of myelofibrosis. It also decreased the abnormally high levels of white blood cells seen in myelofibrosis and shrank the mice's enlarged spleens.

Combining the drug with ruxolitinib offered even more benefits,

restoring the bone marrow and white blood cell counts to normal and dramatically reducing the size of the mice's enlarged spleens.

Additional research is needed to determine if the findings will hold true in human patients, but Mohi and his team are hopeful. They note that palbociclib is known to quiet the activity of bone marrow in patients with metastatic breast cancer (cancer that has spread to other parts of the body), and they hope there will be beneficial effects in patients with myelofibrosis.

"A combinatorial therapeutic approach involving palbociclib and ruxolitinib will enable lowering the doses of each of the inhibitors and thus reducing toxicities while enhancing the therapeutic efficacy," they write in a new scientific paper outlining their findings.

New treatments for myelofibrosis are particularly needed because ruxolitinib treatment does not offer significant reduction in bone marrow fibrosis and often loses its effectiveness with prolonged use, the researchers note.

"The findings from this study are very exciting, and they support the clinical investigation of palbociclib and ruxolitinib combination in patients with myelofibrosis," Mohi said.

Mohi and his team have published their findings in the journal *Cancer Research*.

More information: Avik Dutta et al, CDK6 is a therapeutic target in myelofibrosis, *Cancer Research* (2021). DOI: 10.1158/0008-5472.CAN-21-0590

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