A potential new way to make a good anti-leukemia drug even better

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A recently identified cancer-causing protein makes the anti-leukemia drug imatinib, less effective. By blocking the protein, an international team of researchers was able to slow the spread of leukemia cells in culture. The study, which will appear online on October 20 in the *Journal of Experimental Medicine,* suggests that the most effective treatment for leukemia may rely on a combination of targeted drugs, rather than a single miracle drug.

Imatinib is currently the most popular therapy for chronic myeloid leukemia (CML). CML is a type of blood cancer that is most common among middle-aged adults and accounts for 15-20% of all cases of adult leukemia in the western world. Accumulation of cancer cells in the patient's blood causes infections, anemia, and other potentially life-threatening complications.

CML is associated with the abnormal fusion of a portion of chromosome 21 with a cell growth-promoting enzyme called ABL, which makes the enzyme perpetually active. Imatinib slows down the spread of cancer by blocking the enzyme's activity. But the drug doesn't work in everyone and resistance often develops, most likely because the drug only targets mature cells, leaving self-renewing cancer stem cells behind.

Now, Xiaoyan Jiang and a team of researchers from the British Columbia Cancer Agency in Vancouver and other institutions may have discovered what protects the stem cells from imatinib. The team found that a protein called AHI-1, which has been found in leukemia cells in

the past, is highly expressed in CML stem cells. When Zhou and colleagues blocked AHI-1 in cancer cells from imatinib-resistant CML patients, they restored the ability of the drug to kill the cells. The next step, says Jiang is finding a drug that blocks AHI-1, which could potentially be given in combination with imatinib in the future.

Source: Rockefeller University