

# Drug has ability to cure type of leukemia

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In people with chronic myeloid leukemia (CML), the drug Imatinib has been shown to drive cancer into remission, but the disease often returns when treatment is stopped. New research by UC Irvine scientists indicates that Imatinib could cure CML under certain circumstances if it is taken over a long enough period of time.

Mathematician Natalia Komarova and biologist Dominik Wodarz also developed a tool that eventually could help doctors determine which combination of drugs would be most beneficial to a CML patient, and they determined why, in some cases, Imatinib does not block cancer growth. The results of their study will appear Oct. 3 in the journal PLoS ONE.

CML is a quick-progressing cancer that starts in the bone marrow and moves into the blood. The disease proceeds in three stages, the last one characterized by patient survival of only a few months. In 2007, an estimated 4,570 people in the United States will develop CML, and 490 people will die from it, according to the National Cancer Institute, a division of the U.S. National Institutes of Health.

The drug Imatinib is a promising cancer treatment because it has few side effects, and it specifically targets cancer cells. In their study, the UCI scientists focused on Imatinib and the behavior of cancerous stem cells. Just as normal stem cells maintain organs and a functioning body, cancer stem cells are thought to maintain cancer growth and are tough to kill with treatment.

Many scientists believe that Imatinib can kill regular cancer cells but not stem cells. When treatment ends, the remaining stem cells can produce more cancer cells, thus exacerbating the disease. According to this view, there is no hope to cure CML.

The UCI scientists, however, believe Imatinib can kill cancerous stem cells but not when the stem cells temporarily stop dividing, a state known as quiescence. All cancerous stem cells have the ability to enter the quiescent state. Evidence indicates that when such sleeping stem cells wake up, Imatinib can kill them.

In their paper, the scientists present a mathematical formula that can calculate how long it would take to kill all of the stem cells and cure the cancer. This length of time – which could be different for each patient – is based on how often the cancerous stem cells fall asleep and how quickly they wake up. Once the scientists can test their theory with patients, they will be able to determine how long the cure might take.

“There is evidence that a complete cure is possible. Several patients have been reported to have no symptoms after two months without therapy, which is thought to suggest a complete cure,” Komarova said. “This evidence supports our theory. Basically, one has to be on therapy long enough for all of the stem cells to wake up and be killed by the drug.”

In addition to sleeping stem cells, another barrier to eradication by Imatinib is that cancer cells can mutate to become unresponsive to certain drugs. Conventional thought is that if sleeping stem cells prolong a cure, other cancer cells will have ample time to mutate and become drug resistant.

The UCI scientists, however, have proved this theory wrong. Their calculations show that mutant cells develop early on, in many cases before the patients know they are sick, and do not develop during the

treatment process. Using mathematics, they developed a way to calculate the probability that certain mutations exist in a patient. Based on this, one can determine what course of treatment should be used to overcome the resistance.

“The model requires the number of cancer cells that exist, how fast the cells divide and die, and how fast they go to sleep and wake up,” Wodarz said. “Once you have those numbers, you can determine how many drugs to use in combination to make sure drug resistant mutants do not become problems.”

Source: Public Library of Science

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