Researchers identify new approach to help control drug resistance in leukemia

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Researchers then took this success a step further. Using a method developed in their laboratory to rapidly and accurately forecast drug-resistant Bcr-Abl mutations, Deininger and colleagues established a resistance 'profile' for SGX393. Though SGX393 showed a handful of mutation weak spots, the T315I mutation was absent among thousands of samples surveyed in the laboratory. In contrast, T315I was frequently recovered when running the screen with any of the other drugs.

"Because the resistance profile of SGX393 nicely complemented those of the other drugs and none of the drugs individually controlled all of the mutations, we extended our study to look at using a combination of the drugs. Remarkably, we found that the combination of SGX393 with either Sprycel or Tasigna completely suppressed resistance," said Christopher Eide, research technician. He is a co-author with fellow OHSU Cancer Institute researchers Thomas O'Hare, Ph.D., Jeffrey Tyner, Ph.D., Amie Corbin, and Matthew Wong.

"Our pre-clinical study suggests that rationally combining two Bcr-Abl inhibitors with different resistance profiles could provide a dragnet to protect against resistance," O'Hare said. "The idea is that each drug is especially adept at handling certain Bcr-Abl mutants and that the drugs can team up to eliminate cells carrying mutants that neither drug could eliminate on its own."

"The effectiveness and safety of Gleevec for most patients remains remarkable," said Deininger. "However, it is important for patients to

know that, with the addition of a drug such as SGX393 to the set of current approved CML drugs, we may have the therapeutic tools to achieve and maintain even more effective and longer control of their cancer. This is not equivalent to a cure, but it could potentially represent an important advance in the management of CML."

Source: Oregon Health & Science University