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New lab test could identify imatinib resistance

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Scientists in Japan may have developed a way to accurately predict those patients who will resist treatment with imatinib, which is the standard of care for chronic myeloid leukemia (CML).

Results are published in *Clinical Cancer Research*, a journal of the American Association for Cancer Research.

Imatinib, currently sold as Gleevec by Novartis, revolutionized the treatment of leukemia when it was approved in 2001. Yet imatinib comes with its own set of problems, chiefly resistance. Although resistance is relatively rare, occurring among 2 percent and 10 percent depending on the definition, it can cause unwanted problems both biologically and psychologically.

New drugs under development for the treatment of CML often tout their ability to overcome imatinib resistance, but determining who will develop resistance remains a challenge.

At the Hokkaido University Graduate School of Medicine, Yusuke Ohba, M.D., Ph.D., an associate professor, and colleagues tested the feasibility of a fluorescence resonance energy transfer biosensor in measuring the activity of leukemia cells.

"Using this test, we are now able to identify and predict the most suitable treatment option for individual chronic myeloid leukemia patients," said Ohba. "This technique is both sensitive and practical to use; it is

especially useful for patients who are in relapse, a case in which the clinician's important decision regarding the next step in treatment must be made quickly and accurately."

Working with laboratory cells, the researchers developed a series of assays that measured protein levels and known activity markers within CML lines. Using these measurements, they were able to identify not only the drug-resistant cells within the cultures, but also accurately determine the next therapeutic option, including dose escalation, combination therapy or second generation inhibitors.

"The most critical issue in dealing with imatinib resistance is what to switch over to," said Ohba. "If the patient is switched to another drug to which they are also resistant, then the treatment will just be a waste of time and detrimental to the patient's condition."

In an accompanying editorial also published in Clinical Cancer Research, Yingxiao Wang, Ph.D., an assistant professor in the bioengineering department at the University of Illinois Urbana-Champaign, said this study is a "pioneer work."

"The entire cancer community is talking about personalized medicine, and key to that is knowing when an individual person will have a unique response," said Wang. "This project is an important step forward."

Provided by American Association for Cancer Research