Predicting patient response to gleevec in gastrointestinal stromal tumors

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Researchers at Fox Chase Cancer Center uncovered a genetic pattern that may help predict how gastrointestinal stromal tumor (GIST) patients respond to the targeted therapy imatinib mesylate (Gleevec). Moreover, their findings point to genes that could be suppressed in order to make these tumors respond more readily to imatinib.

Lori Rink, Ph.D., a postdoctoral fellow in the laboratory of Andrew K. Godwin, Ph.D. at Fox Chase, presents their findings today, at the 100th Annual Meeting of the American Association for Cancer Research. The study uses tumor specimens collected as part of a Phase II trial on the use of the drug before surgical resection for GIST, which is led by the Radiation Therapy Oncology Group, a national clinical cooperative group funded by the National Cancer Institute.

"Imatinib has been the first drug that has really made a dent in GIST progression - up to 80 percent response - yet some GIST patients have little or no response to the drug," says Rink "We are looking to see how we can help clinicians make better decisions in applying imatinib or additional therapies to their GIST patients."

Rink and her colleagues followed 63 GIST patients in the RTOG trial, who were given imatinib before surgery for primary or recurrent tumors. Using tumor samples collected before and after the patients were given the drug, the researchers studied which genes were active in the tumors and then compared these profiles of gene expression to how well the tumors responded to short-term imatinib treatment.

According to Rink, they found a selection of 38 genes that were expressed higher in tumors that did not respond well to imatinib. Of these, they identified 20 KRAB-zinc finger genes that encode for proteins that typically act as transcriptional repressors of other genes. Ten of these genes, Rink says, are located to a single section of Chromosome 19.

"Our data indicate that if we can alter the activity of some of these KRAB-zinc finger proteins, we may be able to enhance the effectiveness of imatinib therapy," Rink says.

Source: Fox Chase Cancer Center (news : web)