FAK inhibitor effectively blocked colon cancer cell growth and viability

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Researchers are one step closer to providing a new therapy for colon cancer, after findings revealed that a small molecule focal adhesion kinase (FAK) inhibitor known as Y15 effectively blocked cell viability, promoted detachment and apoptosis, and decreased tumor growth in mice. These findings were presented at the American Association for Cancer Research special conference on Colorectal Cancer: Biology to Therapy, held Oct. 27-30, 2010.

"We believe that these types of novel small molecule inhibitors may be the future direction for cancer therapy," said Melissa Heffler, M.D., a research associate at Roswell Park Cancer Institute in Buffalo, N.Y. "We are excited that Y15 showed efficacy in decreasing colon cancer cell growth. This is just the first step in pushing these molecules closer to clinical use."

Because more than 80 percent of colon cancers overexpress FAK, Heffler and colleagues investigated whether inhibiting FAK action would affect the growth of colon cancer cells in the laboratory. They first evaluated whether Y15 would decrease the growth of SW620, a highly aggressive colon cancer cell line, in vitro. They then administered the drug to mice to evaluate whether it would decrease tumor growth in vivo. According to Heffler, Y15 is unique because it blocks the site of Y397, which is not specifically targeted by other drugs.

In vitro results showed that Y15 decreased FAK expression and activation in a dose- and time-dependent manner. Compared with

control, a 1 μM dose of Y15 inhibited cell viability. Cell detachment also decreased as dosage increased, with nearly 100 percent of cells detached at 50 μM of Y15.

In mice treated with Y15 after being injected with SW620 cells, tumor volume was significantly less after 19 days of treatment than that of mice treated with Y15A derivative or a negative control.

"Although we have shown the efficacy of this inhibitor in treating other types of cancers, like neuroblastoma and breast and pancreatic cancers, metastatic colon cancer can be especially difficult to treat," Heffler said. "Our inhibitor has worked on these cells, and early data have suggested that it might even work better than the standard colon cancer chemotherapy, 5-fluorouracil."

The researchers plan to further study Y15 in comparison to and in combination with 5-fluorouracil and plan to investigate its effect on the inhibition of metastases in vivo using a mouse model. They recently submitted untreated and treated cells to a microarray facility for gene analysis and hope to use those data to identify the detailed mechanism by which Y15 influences tumor growth.

"Our preclinical results are promising and will, hopefully, lead to further investigation of this FAK inhibitor in a clinical setting," Heffler said. "Ideally, we ultimately hope to provide novel therapies for clinicians to employ for the benefit of their patients fighting cancer."

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