

Combination therapies for drug-resistant cancers

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Some cancers can be effectively treated with drugs inhibiting proteins known as receptor tyrosine kinases, but not those cancers caused by mutations in the KRAS gene. A team of researchers led by Jeffrey Engelman, at Massachusetts General Hospital Cancer Center, Boston, has now identified a potential way to effectively use receptor tyrosine kinases inhibitors to treat individuals with KRAS mutant colorectal cancers — combine them with inhibitors of the MEK/ERK signaling pathway.

In cases in which tyrosine kinase inhibitors are effective they reduce signaling via both the PI3K/AKT and MEK/ERK signaling pathways. It is thought that KRAS mutant cancers are resistant to tyrosine kinase inhibitors because the mutant KRAS [protein](#) can directly activate ERK and PI3K signaling. However, Engelman and colleagues discovered that although mutant KRAS activates ERK signaling in human KRAS mutant [colorectal cancers](#), receptor tyrosine kinases control PI3K signaling.

Of potential clinical significance, treating mice xenografted to bear a human KRAS mutant colorectal cancer cell line with a combination of a receptor tyrosine kinase inhibitor and a MEK inhibitor induced tumor regression. These data suggest a way in which receptor tyrosine kinase inhibitors could be used to treat individuals with KRAS mutant colorectal cancers. However, the authors caution that heterogeneity among KRAS mutant cancers means that the approach would not work in all patients with such cancers.

More information: Receptor tyrosine kinases exert dominant control over PI3K signaling in human KRAS mutant colorectal cancers. View this article at: [www.jci.org/articles/view/5790 ... 7b5e1cfc10931ff45995](http://www.jci.org/articles/view/5790...7b5e1cfc10931ff45995)

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