The right combination: Overcoming drug resistance in cancer

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Overactive epidermal growth factor receptor (EGFR) signaling has been linked to the development of cancer. Several drug therapies have been developed to treat these EGFR-associated cancers; however, many patients have developed resistance to these drugs and are therefore no longer responsive to drug treatment.

In a recent research article published in the Journal of Clinical Investigation, Goutham Narla and colleagues at Case Western Reserve University sought to better understand the molecular players in the EGFR signaling pathway in hopes of finding new drug targets for EGFR-associated cancers. Using cancerous human lung tissue and a mouse model of EGFR-associated lung cancer, The Narla team discovered that two tumor suppressor genes, KLF6 and FOXO1, function to disrupt overactive EGFR signaling.

After treating the cancerous lung tissue and cancer-prone mice with an FDA-approved drug called trifluoperazine hydrochloride (TFP), which increases the activity of FOXO1, they restored the effectiveness of the anti-EGFR drug erlotinib and reduced tumor growth.

Their work identified new drug targets for EGFR-associated cancers and suggests that combinatorial drug therapy regimens may improve treatment outcome.

More information: Targeting the FOXO1/KLF6 axis regulates EGFR signaling and treatment response, *Journal of Clinical Investigation*, 2012.