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Novel drug combination offers therapeutic promise for hard-to-treat cancers

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Researchers at Brigham and Women's Hospital (BWH) have identified a new combination of targeted therapies that, together, may treat two aggressive tumor types that until now have not had effective treatments. These findings are published in *Cancer Cell* on September 13, 2011.

While numerous anti-cancer drugs are being developed, many tumors do not respond to currently available single therapies. As such, there is a major push to identify new drug combinations that can work together to treat these resistant cancers . The drug combination identified by BWH researchers was shown to successfully treat two models of aggressive cancers: a nervous system tumor associated with neurofibromatosis type 1, and KRAS-mutant lung cancer, a form of lung cancer that accounts for about 25 percent of all lung cancers. "Without a targeted treatment that works, these two cancers are currently being treated with chemotherapy with variable success," said Dr. Karen Cichowski, Associate Professor in Genetics at BWH and lead author of the paper. "By identifying a more effective targeted treatment, the outcome and survival rate for these cancers may see a drastic improvement, and patients may avoid the typical side-effects of chemotherapy."

Researchers took the approach of combining two targeted agents, one the mTOR inhibitor rapamycin, which suppressed tumor growth, along with the HSP90 inhibitor IPI-504 from Infinity Pharmaceuticals, which triggers a specific kind of stress in cancer cells. Together, but not alone, these drugs promoted dramatic tumor regression in these two distinct cancers in mice. "It's like hitting the tumor cell from two different

angles," explains Dr. Cichowski. "Using one drug to put on the brakes and another to apply stress to an already stressed cancer cell, which ultimately triggers its self-destruction".

These studies have inspired the testing of a drug combination that is now in a Phase I clinical trial, specifically in KRAS-mutant lung cancer. "The identification of this promising therapeutic combination sets the stage for developing other combinations and may also prove effective in other cancers through further research," said Dr. Cichowski.

Provided by Brigham and Women's Hospital