

Targeting low-oxygen patches inside lung cancer tumors could help prevent drug resistance

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With the right treatment schedule, medications known as hypoxia-activated prodrugs (HAPs) could help prevent drug resistance in a subtype of lung cancer, according to a study published in *PLOS Computational Biology*.

HAPs work by killing cancer cells in low-oxygen patches of a tumor that are difficult for standard drugs to penetrate. However, HAPs have not yet shown significant benefits for patients in clinical trials. Danika Lindsay and Jasmine Foo of the University of Minnesota and their colleagues at the University of Southern California set out to investigate how to make HAPs more effective.

They built a mathematical model to monitor the development of [drug resistance](#) in a non-small cell [lung cancer](#) (NSCLC) tumor with a mutation in a gene called EGFR; most people with this subtype develop resistance 12 to 18 months after starting standard treatment with the drug erlotinib.

The team used the model to explore different possible combinations of erlotinib and a HAP known as evofosfamide. They tested a spectrum of dosages and treatment schedules to see which most successfully prevented erlotinib resistance in the virtual tumor cells.

Of all the combinations, the most effective were those that alternated

between erlotinib and evofosfamide while minimizing the time between each evofosfamide dose and the next erlotinib dose. These combinations were better at preventing virtual erlotinib [resistance](#) than was either drug on its own.

"Use of hypoxia-activated prodrugs, if carefully timed in combination with current standard therapies, may be useful for eradicating tumors in NSCLC patients," says study senior author Jasmine Foo.

Although their findings suggest an optimal [treatment](#) schedule for erlotinib and evofosfamide in EGFR-driven NSCLC, the authors say, this strategy must be validated by preclinical experiments before it can be tested in patients.

Provided by Public Library of Science

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