

Study pinpoints malignant mesothelioma patients likely to benefit from drug pemetrexed

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Previous studies have hypothesized that low levels of the enzyme thymidylate synthase (TS) likely mark patients who will benefit from the drug pemetrexed – but results have been inconclusive at best and at times contradictory. A University of Colorado Cancer Center study recently published in the *Journal of Thoracic Oncology* provides an explanation why: only in combination with high levels of a second enzyme, FPGS, does low TS predict response to pemetrexed in patients with malignant pleural mesothelioma.

"The hope is that oncologists could test a patient for TS and FPGS levels and so discover if the patient should be treated with [pemetrexed](#) or if another therapy might be more appropriate," says the paper's first author, Daniel C. Christoph, MD, PhD, medical oncologist at the West German Cancer Center, working as an international [postdoctoral researcher](#) in the lab of CU Cancer Center investigator, Fred Hirsch, MD, PhD.

Pemetrexed works by inhibiting the enzyme TS, which cancer cells need in order to replicate their DNA. So it stands to reason that tumors already low in TS would be most affected by the drug – blocking the remaining TS would effectively stop the ability of [cancer cells](#) to synthesize new DNA. However, Christoph and colleagues tested 84 samples of mesothelioma in which patients had been treated with pemetrexed and found that low levels of TS only in combination with

concurrently high levels of FPGS predicted patients' response to the drug.

The study also explained the mechanism by which FPGS increases the clinical effectiveness of pemetrexed:

"High levels of FPGS allow pemetrexed to stay longer inside cells, giving the drug longer to work against TS," Christoph says. Of the samples tested, patients with low TS and high FPGS had more response to pemetrexed and longer durations of survival.

According to Christoph, the current study provides the preclinical work needed to justify exploring the predictive power of TS and FPGS in mesothelioma patients. A prospective observational study of these biomarkers could lead to their wide use in predicting patients' response to pemetrexed.

Provided by University of Colorado Denver

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