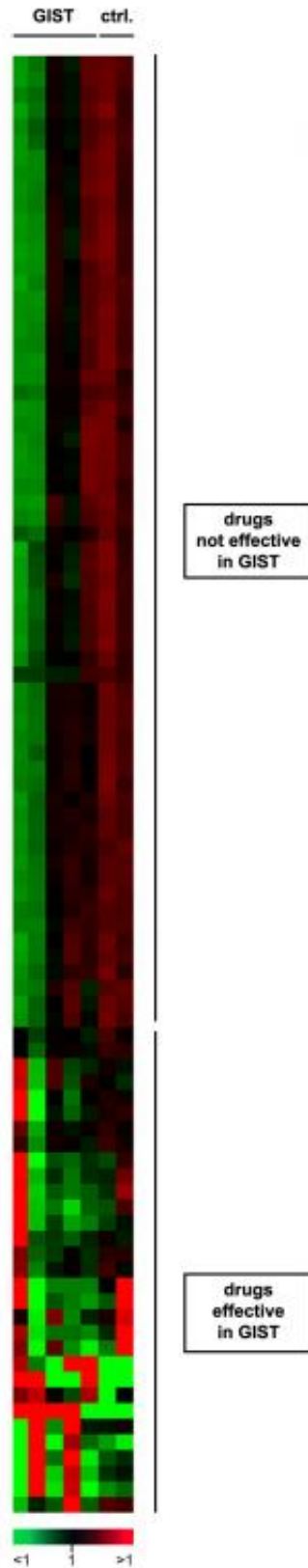


# **Laboratory detective work points to potential therapy for rare, drug-resistant cancer**

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University of Pittsburgh Cancer Institute researchers screened 89 FDA-approved cancer drugs to see if any of them would be effective against a rare type of

tumor. Surprisingly, 37 of the drugs, or 41.5 percent, exhibited promising activity against the tumor in laboratory tests, with two identified as candidates for future clinical trials. The brighter colors indicate anti-cancer activity. Credit: UPCI

University of Pittsburgh Cancer Institute (UPCI) scientists have shown that old drugs might be able to do new tricks.

By screening a library of FDA-approved [anticancer drugs](#) that previously wouldn't have been considered as a treatment for a rare type of cancer, UPCI scientists were surprised when they found several potential possibilities to try if the [cancer](#) becomes resistant to standard [drug treatment](#).

The discovery, which will be published in the February 15th issue of *Cancer Research*, demonstrates that high-throughput screening of already FDA-approved drugs can identify new therapies that could be rapidly moved to the clinic.

"This is known as '[drug](#) repurposing,' and it is an increasingly promising way to speed up the development of treatments for cancers that do not respond well to standard therapies," said senior author Anette Duensing, M.D., assistant professor of pathology at UPCI. "Drug repurposing builds upon previous research and development efforts, and detailed information about the drug formulation and safety is usually available, meaning that it can be ready for [clinical trials](#) much faster than a brand-new drug."

Dr. Duensing and her team ran the screening on 89 drugs previously approved by the FDA in an attempt to find more treatment options for patients with [gastrointestinal stromal tumors](#) (GISTs), which are

uncommon tumors that begin in the walls of the gastrointestinal tract. According to the American Cancer Society, about 5,000 cases of GISTs occur each year in the United States with an estimated five-year survival rate of 45 percent in patients with advanced disease.

GISTs are caused by a single gene mutation and can be successfully treated with the targeted therapy drug imatinib, known by the trade name Gleevec. However, about half of the patients treated with Gleevec become resistant to the drug within the first two years of treatment.

After studying how samples of GIST responded to various concentrations of the 89 drugs in the laboratory, Dr. Duensing and her colleagues identified 37 compounds that showed some anticancer activity in at least one of the concentrations tested. Importantly, they noted that the most promising candidates all belonged to only two major drug classes: inhibitors of gene transcription and so-called topoisomerase II inhibitors. Based on these findings, the research team selected the two most promising compounds for further testing – gene transcription inhibitor mithramycin A, which is in clinical trials to treat Ewing sarcoma, and topoisomerase II inhibitor mitoxantrone, which is used in [metastatic breast cancer](#) and leukemia.

Both drugs were highly effective in fighting GIST in laboratory tests. Moreover, the mechanism of action of each drug was linked to the specific underlying biology of these tumors.

"These are very encouraging results," said Dr. Duensing. "The next step will be moving our findings to clinical exploration to see if the results we found in the lab hold up in patients."

Provided by University of Pittsburgh Schools of the Health Sciences

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