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Study finds why some cancer drugs may be ineffective

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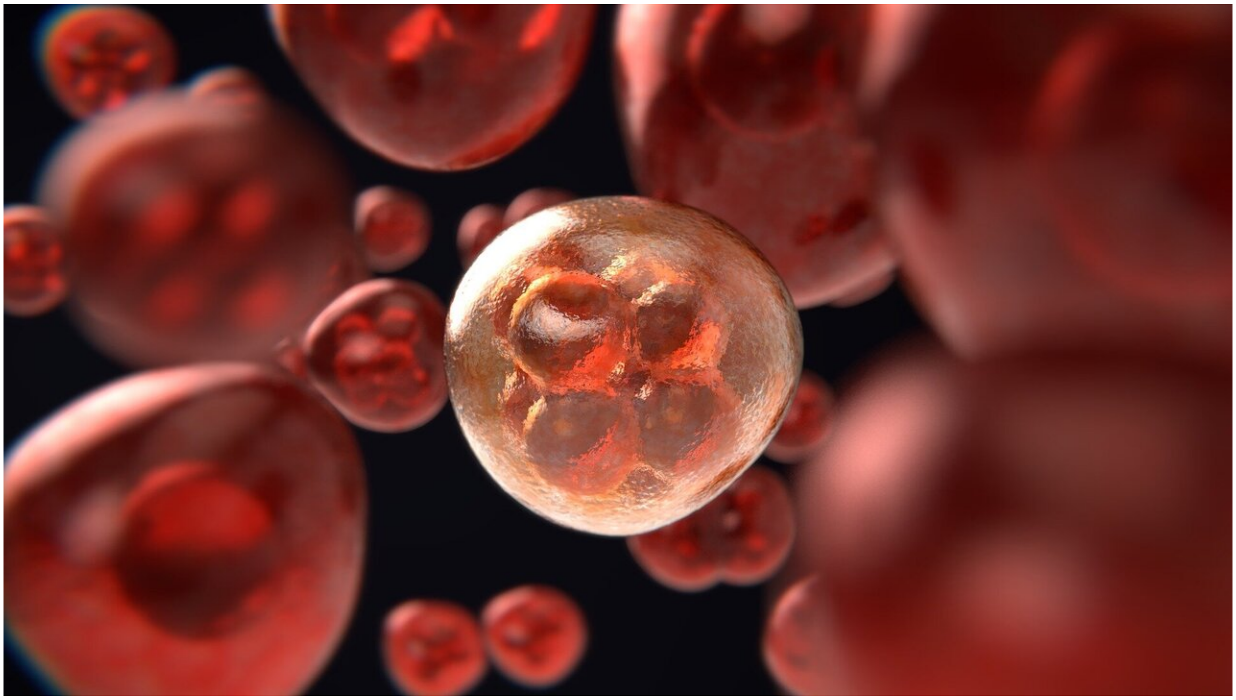

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A possible explanation for why many cancer drugs that kill tumor cells in mouse models won't work in human trials has been found by researchers with The University of Texas Health Science Center at Houston (UTHealth) School of Biomedical Informatics and McGovern Medical School.

The research was published today in *Nature Communications.*

In the study, investigators reported the extensive presence of mouse viruses in patient-derived xenografts (PDX). PDX models are developed by implanting human tumor tissues in immune-deficient mice, and are commonly used to help test and develop cancer drugs.

"What we found is that when you put a human tumor in a mouse, that tumor is not the same as the tumor that was in the cancer patient," said W. Jim Zheng, Ph.D., professor at the School of Biomedical Informatics and senior author on the study. "The majority of tumors we tested were compromised by mouse viruses."

Using a data-driven approach, researchers analyzed 184 data sets generated from sequencing PDX samples. Of the 184 samples, 170 showed the presence of mouse viruses.

The infection is associated with significant changes in tumors, and Zheng says that could affect PDX as a drug testing model for humans.

"When scientists are looking for a way to kill a tumor using the PDX model, they assume the tumor in the mouse is the same as cancer patients, but they are not. It makes the results of a cancer drug look promising when you think the medication kills the tumor—but in reality, it will not work in human trial, as the medication kills the virus-compromised tumor in mouse," Zheng said.

He hopes his findings will change researchers' approach to find a way to kill tumor cells.

"We all share the common goal of hoping to find a cure for cancer. There are 210 ongoing NIH-funded projects relevant to PDX models, with a combined annual fiscal year budget of over $116 million. We need to tighten up quality control and use models that are not compromised so that the treatments we give to future patients are effective," Zheng said.

This work is a collaboration between the Texas Therapeutics Institute, Institute of Molecular Medicine (IMM) at McGovern Medical School, and the Data Science and Informatics Core for Cancer Research at the School of Biomedical Informatics.

"As a team, we synergized the strengths of McGovern Medical School's virology research and School of Biomedical Informatics' data analysis expertise, and it has led to the success of this project," said Zhiqiang An, Ph.D., co-senior author of the study, professor and Robert A. Welch Distinguished University Chair in Chemistry at McGovern Medical School.

More information: Zihao Yuan et al. Presence of complete murine viral genome sequences in patient-derived xenografts, *Nature Communications* (2021). DOI: 10.1038/s41467-021-22200-5

Provided by University of Texas Health Science Center at Houston

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