

Researchers develop more effective way to discover and test potential cancer drugs

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Researchers have created a new phenotypic screening platform that better predicts success of drugs developed to prevent blood vessel tumor growth when moving out of the lab and onto actual tumors.

"This platform allows us to predict what's going to happen in preclinical models," said Enrique Zudaire, Ph.D., staff scientist in the radiation oncology branch of the [National Cancer Institute](#), who presented the findings at the AACR-NCI-EORTC International Conference:

Molecular Targets and [Cancer Therapeutics](#), held Nov. 12-16, 2011.

"This not only shortens the amount of time that you would need to do screenings and drug discovery but also enhances dramatically the success you're going to have in the next phases."

Zudaire and colleagues developed a phenotypic, high-content, cell-specific fluorescence platform that examines the effectiveness of angiogenesis inhibitors, which shut down or impede [tumor growth](#) by hampering [blood vessel formation](#) and thus starve the tumor.

Past research has mainly focused on identifying single molecular targets for angiogenesis inhibitors. The new phenotypic platform evaluates how angiogenic inhibitors affect simultaneously entire cells and several steps of the angiogenesis process.

"If you do a screening for activity of a particular enzyme, that's all you're going to get: a drug that targets that specific [enzyme activity](#). That tells you little about how the enzyme works in a complex organization," said

Zudaire. As a result, he explained, when many of these drugs advance to phase 2 clinical trials, they are either ineffective or result in side effects that are toxic to the patient.

Researchers validated the platform by screening the 1,970 small molecules that are part of the National Cancer Institute Developmental Therapeutics Program Diversity Set. Through the phenotypic platform, they identified more than 100 lead compounds that were then tested in preclinical models. All tested compounds showed antitumor activity, and some blocked tumor growth more effectively than current, FDA-approved antiangiogenic drugs.

This screening platform also ensures that researchers do not precondition the system to a known target. "We sometimes assume we know a lot about how these tumor systems work and what we should target," said Zudaire.

The researchers proposed that most of the therapeutically relevant information in pathological systems rests on the complex interactions between the different components of the system rather than on the components themselves. Interrogating these systems in an unbiased manner will reveal not only single [molecular targets](#) but unknown interactions between them, which are relevant for the disease.

Ultimately, using this type of phenotypic platform can make drug development more efficient and cost-effective.

"If we improve the initial phases of [drug discovery](#), we can decide where to invest time and money on drugs that are a lot more likely to work," Zudaire said. "This study is proof of principle that the platform works. From here, we can design assays that are more complex and better able to describe what the in-vivo situation will be."

Provided by American Association for Cancer Research

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