# Phenotypic Profiling Identifies Novel Anticancer Drugs

A profiling platform built on 3-dimensional (3D) scaffolding and fluorescent reporter endothelial cells has pinpointed angiogenesis inhibitor candidates with properties that correlate well with results in animal testing.

The system is a "surrogate assay that mimics the *in vivo* tumor microenvironment," says Enrique Zudaire, PhD, staff scientist in the National Cancer Institute's (NCI) Radiation Oncology Branch. The endothelial cells, which make up the vasculature around tumors that is targeted by antiangiogenic drugs, "rearrange over time to form capillary-like structures," says Zudaire, who presented the platform at last week's Molecular Targets and Cancer Therapeutics conference in San Francisco.

High-speed imaging of VEGF receptor 2–nonexpressing fluorescent reporter cells and a custom software program that automatically analyzes more than 30 parameters of tube formation allow rapid evaluation of how small molecules affect entire cells and multiple steps in angiogenesis, Zudaire says.

While validating the profiling platform by screening the 1,970 small molecules in the NCI Developmental Therapeutics Program Diversity Set, Zudaire and colleagues found over 100 small molecules that inhibited tube formation and growth of endothelial cells. When 7 of these agents were tested in a leiomyosarcoma xenograft mouse model of angiogenesis, the results correlated very closely with platform data. One agent was slightly better at blocking tumor growth, compared with bevacizumanab (Avastin; Genentech), the gold standard for angiogenesis inhibitors, notes Zudaire.

The platform collects large amounts of data in a single assay and can identify likely targets more quickly and efficiently than traditional high-throughput screening of small molecules, Zudaire suggests.

"Even more important, the drugs that come out of these assays have a better probability of working in preclinical models," he says, given their close correlation with results in animal models.

This approach can be extended to model other events, for example by incorporating tumor cells from patients, Zudaire adds.

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