

Oncologists Wrestle with Drug Mechanisms

TESTS EMERGING AS CRITICAL FOR TARGETED THERAPIES

THEY CAME HOPING for news about “smart bombs,” “silver bullets,” and “rational” therapies that would help them improve some of cancer’s most pathetic cure rates. But if oncologists at this year’s American Society for Clinical Oncology (ASCO) meeting* learned anything, it was that the path to targeted cancer therapy is by no means clear.

Drugs thought to be highly targeted can still have multiple effects, and many work by means other than their intended mechanisms. One ASCO speaker presented evidence that Gleevec — Novartis’ wonder drug targeting the infamous Philadelphia chromosome mutation — also works as an inhibitor of tumor blood vessel growth.

Doug Hanahan, of the University of California at San Francisco, described animal studies combining Gleevec with another compound — Pfizer’s SU5416. The combination shrank tumors, and the group’s molecular studies suggest Gleevec can slow tumor blood vessel growth by picking off important cells called pericytes. Most important: “The treatment is not pulling the pericytes off the normal vessels,” Hanahan said.

Its not year clear why normal blood vessels are spared, but the combination works better by hitting different points in the blood vessel formation pathway. Hanahan suggested Gleevec should be tested with other angiogenesis inhibitors, and these studies should not be limited to tumors that express the drug’s traditional targets — cKIT, BCR-ABL, or PDGFR.

Show Me the Target

Gleevec is the result of about two decades of research, so it is both inspiring and un-nerving that the drug’s effects are still being worked out. And this is only one of several targeted therapies that has shown unanticipated effects.

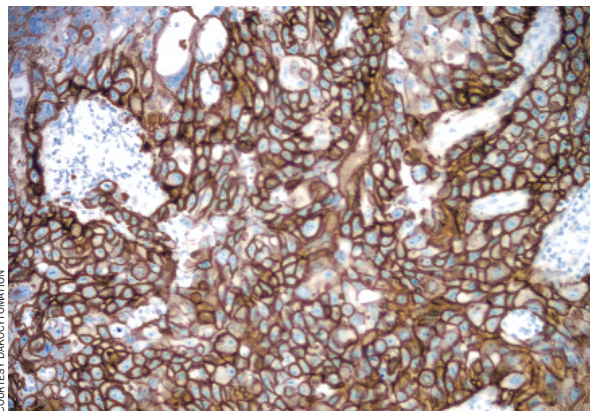
The key to understanding how these new drugs work and the best way to combine them in patients may lie in the hands of diagnostic test developers like DakoCytomation.

Dako makes the Her-2 test that was approved in tandem with Genentech/Roche’s

Herceptin; it has also recently released a test for EGFR. The Dako test was used in clinical trials of AstraZeneca’s Iressa and ImClone’s Erbitux, both of which target EGFR. Dako’s test is being used to guide prescribing of Erbitux, but not for Iressa because it did not help predict which patients respond to that drug.

“What’s starting to emerge is that the activation state of the receptor isn’t always the most important factor,” says Dennis Chenoweth, Dako’s corporate vice president of diagnostics. In some cases, he says, matching patients to drugs may require measuring “a combination of receptor expression on cell surface, signal transduction proteins, and various levels of activation.”

Dako already uses multiple reagent tests in some of its collaborations, and Chenoweth predicts further advances as “we get more



VERY EXPRESSIVE: DakoCytomation’s epidermal growth factor receptor (EGFR) pharmDx kit demonstrates high levels of expression of EGFR on the surface of cells in this specimen from a colorectal cancer patient.

sophisticated digital analysis capability.” As more features are studied per slide, computerized image analysis will become the norm.

But companies aren’t waiting for the fancier technology. “Everybody is doing this kind of testing in clinical trials [for targeted cancer drugs],” Chenoweth says. “Because at some point, the regulatory agency will say, ‘Show me the data.’” ●

BY MALORYE A. BRANCA

Real Estate Report Showcases Biotech Hubs

AT BIO 2004*, commercial real estate services firm Colliers International and its partner Spaulding & Slye Colliers announced the release of *Alchemy*, a global life science real estate report that includes in-depth information about nine major life science “clusters,” as well as emerging markets.

According to Nancy Kelley, senior vice president and managing director of life sciences for Spaulding & Slye and Colliers, the newness of the life science real estate industry means that little information has been available until now. The *Alchemy* report “is the first review and analysis of real estate trends,” she said.

The 80-page report discusses the drivers and challenges in the life science real estate industry, and explains the “geographic clustering” effect. It also details the features of life science real estate, including design criteria and building services, and how to redesign facilities for pharmaceutical manufacturing in order to reduce the cost of drug

discovery and development.

The Brookings Institution in 2002 identified nine economically strong and growing life science biotech centers in the United States. *Alchemy* features overall characteristics, supply and demand dynamics, and key trends for each of these major clusters. Each section lists major institutions and companies, the amount of available lab space, and rental prices for that particular geographic area.

Among the hubs, the Boston area topped the list for most money received from the NIH, and it tied for number one with San Francisco for number of biotechnology companies in the area. San Francisco also ranked first in amount of venture capital funding received by biotech companies in the area.

“The societal challenge [is] to speed drug development from the bench to the bedside, reduce the cost of healthcare delivery, and make it accessible to all,” Kelley said. “This challenge will require radical changes not only in science and in medicine, but also in the environments and buildings where these activities take place.” ●

BY SHABNAM SIGMAN

* ASCO, New Orleans, June 5-8.

proved in tandem with Genentech/Roche’s

* BIO 2004, San Francisco, June 6-9.