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» Biomerk Tumorgrafts™—An Alternative Approach to Xenografts By John McCleery

Overall, there has been great interest, but not much success, in both in vivo and in vitro methods to predict patient reaction to chemotherapy. However, the Biomerk Tumorgraft™ has been brought to our attention as an alternative approach to predictive tumor behavior. Here's what we have discovered thus far.

The discovery of biomarkers is advancing the notion of personalized medicine. In oncology, diagnostics development is at the heart of being able to find novel products that are effective and tolerable in patients. In their efforts to discover new ways to transform the drug development paradigm as well as the clinical management of cancer, the scientists at Champions Biotechnology Inc., a company founded by David Sidransky, MD, in May 2007, have developed their own diagnostics platform they call Biomerk Tumorgrafts™.



Doug Burkett, PhD,
President, Champions
Biotechnology Inc.

According to Champions President Doug Burkett, PhD, the traditional approach to tumor xenografts “has mostly been based upon models that originate from highly passaged, commercially available cell lines in which the cells are grown in cell cultures and then injected into mice. These models are known to have altered from the original patient tumor they were derived from and are not highly pre-

dictive of how drugs will perform in patients.” Biomerk Tumorgrafts differ in that they are directly implanted from human patients as whole tissue fragments into immune-deficient mice, passaged only a few times, always as whole tissue fragments, and never in tissue culture. “We do all our testing in these unique Tumorgrafts that are less than 10 passages—in mice only—away from the original human tumor,” said Burkett.

Champions believes that their platform may be its own bellwether as to how successful new compounds being developed are going to be in clinical cancer trials.

How the Biomerk Tumorgrafts Technology Works

Champions' scientists take tumors directly from patients and within one to two hours surgically implant the tumors into immune-deficient mice. “That quick transition helps ensure a successful implantation,” explains Burkett. Once the tumor grows to a certain size in the mice, it is extracted, fragmented, and then placed in additional mice. The tumors are then grown and are propagated in a manner that preserves the biological properties of the human tumor. By the third or fourth passage, “there are usually adequate mice to do a study by treating the mice with various drugs,” said Burkett.

To determine the optimal drug combination for an individual patient, the researchers test dozens of drug combinations—with either standard of care agents already on the market or some agents that are in clinical development or any combination thereof—against the personalized Tumorgrafts to find the most effective therapy combination. When they've

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found a combination that works, the information is provided to the patient’s physician and the patient is typically treated accordingly.

When asked if they’ve ever seen a drug combination that worked in the mice but not in the patient, Burkett responded, “So far, we’ve observed a 100 percent correlation. If we’ve found a treatment that works in the Tumorgraft mice, it has worked as predicted in the patient. And, every time we’ve tested Tumorgrafts against agents that a patient was resistant to, the Tumorgrafts were also resistant.”

In the personalized oncology business, this new technology means that a sample of a patient’s tumor can go through the implantation/propagation process in the mice and be tested simultaneously against a variety of anti-cancer agents to try and discern what works best for the patient by using the mice.

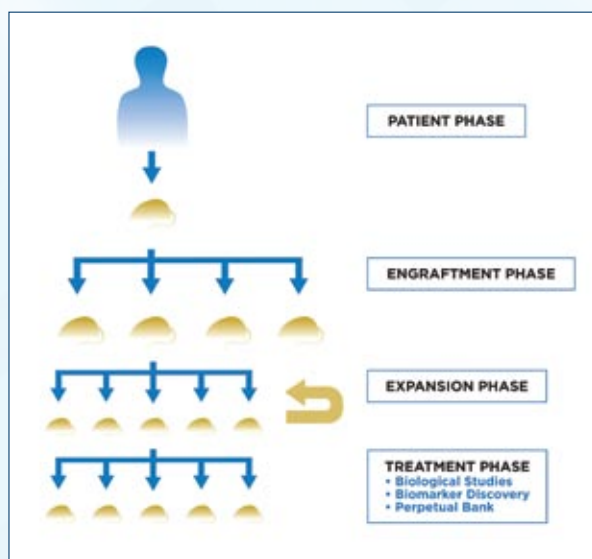


Figure 1. Phases to Treatment. Source: Champions Biotechnology Inc.

As a result, the company states on their Web site that because their Tumorgrafts more closely reflect human cancer biology, they can “more accurately predict the effectiveness of chemotherapeutic drugs in patients.”

Reporting the Information from the Tumorgrafts

It typically takes 3 to 5 months to implant the human tumor, propagate it, test it against numerous drugs, and then generate a final report that recommends a drug or drug combination. “This typically occurs while a patient is being treated with the standard first-line oncology drug. Our intent is to have results ready before the patient requires their next therapeutic treatment,” explains Burkett.

The comprehensive analysis entails exactly how each drug or drug combination affected the tumor and details which drugs are most effective, partially effective or least effective with inhibiting growth or causing the tumor to regress in size.

Cost and Reimbursement

The cost of doing the test is much higher than that of traditional animal models. “It’s a very expensive and time-consuming undertaking,” said Burkett, “one that includes anesthesia and performing surgery on mice.” Although there is no insurance reimbursement for patient testing, Champions is working on initiatives to bring the cost down. Eventually, they hope their database will be large enough that they can take a patient’s tumor, characterize it, and then match it up against another tumor they’ve already tested and provide information that way. For cancer patients,

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“the business is currently limited only to those who can afford this expensive process,” said Burkett.

Drug Development Using the BiomerK Tumorgrafts

The BiomerK Tumorgraft technology is also being applied to drug development by testing drug candidates against Tumorgrafts derived from many different patients. The platform also enables biomarker discovery. “Let’s say, for example, we test a drug on 15 Tumorgrafts derived from 15 patients and see that the drug is only effective on 5 of the Tumorgrafts. We can analyze what those 5 Tumorgrafts have in common that the other 10 don’t,” said Burkett. This information, of course, can lead to the discovery of biomarkers and the development of a companion diagnostic. This enables a targeted clinical development program because you can enrich clinical trials toward patients most likely to benefit from the drug,” he explained.

Keeping an Eye on the Future

It is Champions’ intent to build a low attrition pipeline of cancer drugs that they own, co-own, or to which they have royalty rights, to predict which of the novel drug candidates will most likely succeed in clinical trials. Their \$2.5 million funding to date has come from non-domestic investors who invested at a price substantially above market with no warrant coverage. Additionally, the company has two synergistic businesses that generate revenue to keep the burn rate low.

Ultimately, they are looking only to develop compounds that perform well in their Tumorgrafts. “With all the data we’ve been

able to accumulate, it is apparent that drugs that don’t succeed in our Tumorgrafts are not going to succeed in clinical trials. But the ones that are effective in the Tumorgrafts are going to have a high probability of succeeding in clinical trials; those are the ones in which we want to invest,” said Burkett.

The young company is still in the process of forming their managing and marketing teams, but has recently appointed three key executives to business and operational positions. Increasingly, as word gets out “business is coming in and revenue is growing,” said Burkett. Most recently, the company has established collaboration with Gradalis Inc. and the Mary Crowley Cancer Research Center (MCCRC). Together, the partners will seek an Investigational New Drug permission from the U.S. Food and Drug Administration to utilize the Tumorgraft technology to develop personalized vaccines for cancer patients.

Additionally, the company has also entered into a royalty agreement with Concordia Pharmaceuticals for the use of Salirasib, an RAS antagonist, in combination with another targeted drug. Under the terms of the agreement, Champions will use its platform to evaluate a combination therapy indication for Salirasib. Johnson & Johnson subsidiary Centocor is also utilizing Champions’ BiomerK Tumorgrafts to evaluate promising antibodies and an agreement is also in place with Eli Lilly subsidiary, ImClone Systems Inc. **JM**

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