BEYOND GENOMICS:
FUNCTIONAL TESTING BRINGS GREATER PRECISION TO PERSONALIZED MEDICINE

What's Next? Be Armed with Therapeutic Options.

YOURPDX™ – AN ADVANCED FUNCTIONAL APPROACH TO PRECISION ONCOLOGY

For many individuals with cancer, especially those with recalcitrant, recurrent, or metastatic cancers, undergoing treatment is an exercise in trial and error. When first-line cancer treatment fails, stops working, or has side effects that are not tolerated, individuals typically undergo second- and third-line treatments, and oftentimes many more over the course of their disease. Because treatment guidelines for advanced cancer are often lacking or non-existent, people with complex cancers often endure the side effects and financial burden of treatment that provides little or no clinical benefit, while at the same time losing precious time.

While genetic profiling of patient tumor tissue can provide directional information about which molecular-targeting drugs to try, clinical failure rates for treatment guided solely by genomics remain dismally high. Unlike genetic profiling, personalized functional testing captures biological complexities of human cancer in a living system.[1, 2]

To perform the YourPDX™ test, Certis uses personalized orthotopic patient-derived xenograft (O-PDX) models–an advanced type of mouse avatar developed by engrafting human donor tumor tissue into the site of origin in immune-compromised research mice. O-PDX models closely mimic human donor cancer genetics, biology, morphology, metastases, and drug response, making them clinically relevant tools for predicting therapeutic effects in human patients. O-PDX models have been shown to be predictive of clinical outcomes and are used for preclinical drug evaluation, biomarker identification, biologic studies, and personalized medicine.[4, 5]

ELIGIBILITY CRITERIA

- Any US adult (18+ years or older) diagnosed with a solid tumor cancer.
- Participating individuals must obtain a physician-ordered biopsy or resection surgery; a fresh tumor tissue specimen is required to perform testing.
- Tissue from tumors treated with radiation within 10 weeks prior to biopsy or resection surgery cannot be accepted.

TESTING PROCESS

In vivo functional testing is a multi-step process as outlined below.

1. **Test Ordering and Consent.** YourPDX™ testing must be ordered by an oncologist. Individuals who elect YourPDX™ testing must consent a fresh tumor tissue specimen to Certis Oncology, complete the necessary consent forms, and agree to share relevant protected health information (PHI) including diagnosis, treatment history, and any available genetic/molecular profiling data.

2. **Sample Collection.** Certis will coordinate with the clinical care team and provide them with the Certis Specimen Transport Kit including instructions for use and express shipping. A fresh tissue specimen from a physician-ordered biopsy or surgical resection must be received by Certis within 24 hours of the procedure. The ideal tumor tissue sample size is at least three cubic centimeters.

3. **Initiation Study**. The goals of this first phase of the testing process are to (1) stabilize human tumor tissue in first-generation mice and (2) expand tumor tissue volume in preparation for the pharmacology study. To maximize engraftment success, fragments of human tumor tissue will be surgically implanted into various locations in up to five mice, depending on the size of specimen received. Note that success of the Initiation Study is dependent on biological variables and cannot be guaranteed.[3]

4. **Test Agent Selection.** The treating oncologist, along with the study participant, must decide how many and which treatment options to test in the pharmacolgy study. To avoid delays with the second phase of the testing process, it's important to make these decisions early, as procuring these test agents can take time.

TESTING PROCESS (CONT.)

5. **Mouse Avatar Development.** If the Initiation Study is successful, Certis will orthotopically engraft expanded tumor tissue from first-generation mice into a second-generation of mice to develop the large number of personalized mouse avatars required for each test. For each treatment option to be tested, we require five fully tumored mice, plus five more for the control arm, in which animals receive no treatment. We typically implant about 25% more mice than will ultimately be required to ensure we have enough well-developed avatars for each study. To be eligible for testing, mice must have tumors that measure between 50-100mm.[3]

6. **Dosing Phase.** Certis scientists will randomize fully tumored avatars into study arms of 5 mice each, and each cohort will receive one of the chosen treatment options over a 28-day dosing period. We will use MRI and quantitative three-dimensional tumor volume measurement (TVM) to record changes in tumor size in each of the mice.

7. **Results.** When a participant's study is complete, we'll provide their treating oncologist with a full report, detailing a visual account of the study and results. It will include before-and-after MRI images of tumors from mice in each arm—as well as images of histology stains, which illustrate the cellular structure of tissues and provide additional confirmation of tumor response in each mouse avatar. The Certis Laboratory Director, an experienced medical pathologist, independently reviews all results before they are delivered as a final report.

TESTING FEES

Fees associated with YourPDX™ functional testing are not typically covered by insurance and are dependent upon the number of treatment options tested. Certis will work directly with the study participant or other financially responsible person to put in place a Patient Services Agreement, which will detail fees. Standard fees are as follows:

Phase One - Study Initiation: The standard fee is $10,000, which includes next-generation sequencing (NGS) on the primary tumor tissue. If engraftment is not successful and the Initiation Study fails, we cannot issue a refund.

Phase Two - Pharmacology Study: Fees are based on the number of treatment options included in the study design.

- Each study requires one control arm (this is the group of untreated mice required to compare tumor response): $7,500.
- Each therapy or combination therapy to be tested represents one arm. For each study arm, we enroll five fully tumored mice to ensure reliable data. The fee is $7,500 per arm. A drug recovery fee may be assessed for test agents that cost over $250 per arm.

EXAMPLE: An individual elects to test four different treatment options.

Initiation Study: $10,000
Pharmacology Study to Test Four Treatment Options:
$7,500 x 4 ($30,000) + $7,500 (control arm) = $37,500

Total: $47,500

QUESTIONS?

Contact us:

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YOURPDX IS A FUNCTIONAL DRUG SENSITIVITY TEST THAT MEASURES THERAPEUTIC RESPONSE IN ORTHOTOPIC PATIENT-DERIVED XENOGRAFT MODELS. TEST RESULTS ARE NOT A REPLACEMENT FOR MEDICAL ADVICE. TREATMENT DECISIONS ARE THE RESPONSIBILITY OF PATIENTS AND THEIR PHYSICIANS. YOURPDX TESTING REQUIRES FRESH TUMOR TISSUE. IT IS ESSENTIAL TO CONTACT US PRIOR TO BIOPSY OR RESECTION SURGERY.

CERTIS™ ONCOLOGY INTELLIGENCE

References: 1. Letai A. Functional Precision Cancer Medicine-Moving Beyond Pure Genomics. *Nat Med.* Sep. 8, 2017;23(9):1028-1035. **2.** Letai A, Bhola P, Welm AL. Functional Precision Oncology: Testing Tumors with Drugs to Identify Vulnerabilities and Novel Combinations. *Cancer Cell.* Jan. 10, 2022;40(1):26-35. **3.** Published literature reports engraftment rates vary by cancer type. **4.** Liu, Y., Wu, W., Cai, C. et al. Patient-derived Xenograft Models in Cancer Therapy: Technologies and Applications. *Sig Transduct Target* Ther 8, 160 (2023). **5.** Yoshida GJ. Applications of Patient-Derived Tumor Xenograft Models and Tumor Organoids. **J Hematol Oncol**. 2020 Jan 7;13(1):4. doi: 10.1186/s13045-019-0829-z. PMID: 31910904; PMCID: PMC6947974.