

Precision Oncology: Unlocking Hope for Rare Cancers and Beyond

GROK3 BETA and Melissa Millard Ph.D.

Sandy Scientific LLC

Introduction

Precision oncology, particularly through drug sensitivity testing, is emerging as a gamechanger for patients with rare cancers or cancers lacking a standard of care. These conditions—such as angiosarcomas, certain pediatric tumors, or advanced cancers with no approved therapies—often leave patients with few options due to limited research and treatment guidelines. By testing how a patient’s tumor cells respond to drugs in real time, this approach offers tailored solutions where traditional methods fall short.

Targeting the Untreatable

Rare cancers, which account for about 22% of all cancer diagnoses, and tumors without established protocols often lack actionable genetic mutations or approved targeted therapies. Drug sensitivity testing sidesteps this by directly assessing a tumor’s functional response. Tumor cells, extracted from biopsies, circulating tumor cells (CTCs), or surgical resections, are exposed to a range of drugs, including off-label or experimental options. For instance, a rare cholangiocarcinoma might show unexpected sensitivity to a drug approved for lung cancer, providing a lifeline where genomic sequencing alone offers no answers. This broad screening uncovers viable treatments tailored to the patient’s unique cancer, bypassing the scarcity of disease-specific data.

Adapting to Complexity

The heterogeneity and adaptability of rare cancers make them notoriously hard to treat. A single tumor can contain diverse cell populations, and cancers without standard care often evolve rapidly, resisting conventional therapies. Drug sensitivity testing delivers a current, dynamic profile of the tumor’s vulnerabilities, allowing doctors to pivot as the disease changes. For example, a patient with a rare sarcoma might initially respond to a kinase inhibitor identified through testing, and later, as resistance develops, switch to a different drug pinpointed by retesting—flexibility that’s critical when no roadmap exists.

Empowering Patients with Evidence

For patients facing rare or untreatable cancers, the lack of options can feel hopeless. Precision oncology provides concrete, evidence-based insights, empowering both patients and doctors. Early studies show promise: patients with refractory rare cancers have achieved tumor shrinkage or prolonged stability using therapies identified through drug sensitivity testing. This not only improves outcomes but also offers psychological relief, replacing trial and error guesswork with data-driven decisions. Moreover, AI tools, could amplify this benefit by rapidly analyzing test results against vast drug databases, pinpointing effective treatments faster.

Amplifying Research and Discovery

Beyond individual care, drug sensitivity testing for rare cancers fuels broader discovery. Each test generates data that can inform research, identifying patterns of drug response across similar tumors. Over time, this could build a knowledge base for cancers with little prior study, potentially leading to new standards of care. Collaborative efforts, such as tumor storage hubs preserving samples for ongoing analysis, further enhance this, allowing researchers to test emerging drugs against banked rare tumor cells, accelerating breakthroughs.

Comparison to Traditional Drug Selection

Traditionally, drugs for rare cancers or those without a standard of care are selected based on limited evidence, often extrapolated from similar cancers, physician experience, or small, anecdotal studies. This approach relies heavily on trial and error, using broad-spectrum chemotherapies or drugs approved for more common cancers, with little guarantee of efficacy. Genomic sequencing may guide choices if actionable mutations are found, but for many rare tumors, such targets

are absent or unproven. In contrast, drug sensitivity testing offers a direct, patient-specific evaluation, testing a tumor's actual response to drugs rather than relying on assumptions or population-based data. While traditional methods are faster and more accessible, they lack precision, often leading to ineffective treatments and wasted time—critical losses for patients with aggressive, untreatable cancers.

Traditional Drug Selection:

- Basis: Relies on extrapolation from similar cancers (e.g., using breast cancer drugs for a rare adenocarcinoma), physician intuition, or sparse clinical reports.
- Tools: Often uses broad chemotherapies (e.g., cisplatin) or, if available, genomic sequencing to find rare actionable mutations (e.g., BRAF inhibitors for a matching mutation).
- Limitations: Lacks specificity; many rare tumors have no genetic matches, and efficacy is uncertain, leading to a "best guess" approach. Time is lost on ineffective drugs, critical for fast-progressing cases.
- Advantages: Faster to implement, widely available, and less resource-intensive.

Drug Sensitivity Testing:

- Basis: Directly tests a patient's tumor cells against drugs, providing functional evidence of what works.
- Tools: Screens a range of drugs, including off-label options, tailored to the tumor's response, not just its genetics.
- Advantages: Precision reduces guesswork; identifies unexpected therapies (e.g., a leukemia drug for a rare sarcoma), crucial when no standard exists. Adapts to tumor changes over time.
- Limitations: Slower, costlier, and less accessible due to lab requirements.

Overcoming Obstacles

While challenges like tumor heterogeneity, resource demands, and limited access persist, the benefits for rare and untreatable cancers outweigh these hurdles. The ability to deliver personalized, effective treatments in the absence of conventional options marks precision oncology as a beacon of hope.

Conclusion

For rare cancers and those without a standard of care, precision oncology via drug sensitivity testing offers a transformative edge. It targets the untreatable, adapts to complexity, empowers patients, and drives research—unlocking possibilities where traditional oncology reaches its limits. As technology and infrastructure evolve, this approach could redefine care for the most challenging cancer types.