

In Vitro and in Vivo Assays and Models: Poster Presentations - Proffered Abstracts

Moving towards clinically relevant preclinical models: Establishment, molecular characterization and in vivo evaluation of patient-derived low passage human tumor models

Michael Wick, Francis Nieves, Mitchell Moore, David Sidransky, Kyriakos Papadopoulos and Manuel Hidalgo

South Texas Accelerated Research Therapeutics (START), San Antonio, TX, Champions Biotechnology Incorporated, Arlington, VA

Abstract

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Standard human tumor xenograft models in preclinical oncology drug development typically originate from high passage number immortalized cell lines. While information from these models is useful in discovery and initial proof-of-concept studies, their clinical relevance is often limited due to alterations and adaptations from successive passages in tissue culture and animals. Preclinical models established from donor patient tumor fragments passaged only a few times in vivo may better represent clinical disease. In addition, genetic and molecular characterization of these models may aid in determining the models most useful for evaluating novel agents including targeted therapies.

We have developed the Tumorgraft™ platform, establishing low passage models of human cancer including lung, pancreas, colon, ovarian and gastric malignancies and various sarcomas. Following establishment, models were characterized at a molecular level using DNA and RNA-based assays. In addition, in vivo sensitivities of various agents were evaluated based on clinical information from patient donors as well as current standards of care.

Molecular characterization studies identified polymorphisms in some models, as well as known mutations in several signaling molecules important in cancer progression including the epidermal growth factor receptor (EGFR), B-raf, and Ras proteins. In vivo evaluation identified a range of activity towards standard agents tested, as well as clinically correlative drug sensitivities. Overall, these low passage models offer an alternative to standard xenografts and may be more representative of clinical disease. Data collected from molecular characterization and in vivo evaluation of these models confirm their utility for development of novel agents especially targeted therapies.