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Melanoma patient derived tumorgrafts [PDX] bridge the gap between genomics and molecularly informed medicine

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Abstract

Malignant melanoma (MM) contains thousands of somatic DNA alterations. As affordability and faster turn-around times for identification of druggable targets specific for each patient improves, together with limited number of therapeutic agents available, a growing gap is emerging as to identification of the right drug(s)for the patient at the right time. To further complicate personalized medicine, frequent acquired drug resistance arises, and failure to kill all tumor cells using single agents. Indeed, MM is notorious for resistance to killing. Thus, rational therapeutic combinations promoting rapid onset of apoptosis and preventing drug resistance is highly desirable. Using patient-derived tumorgrafts it is possible to study responses of MM within in-vivo three-dimensional context. Using a collection of such tumorgrafts spanning the genomic landscape, together with agents such as BRAF inhibitors and MEK inhibitors, clinically relevant tumor responses, including acquired drug resistance can be modeled. These models are now being used for identification of drug resistance switches, and ideal combination therapy regimens that prevent drug resistance. As dozens of “avatar” mice can be created from a single patient sample, various drug combinations, scheduling, etc. can be more rapidly tested than would be achievable in a clinical trial setting. We envision results from tumorgraft models actually serving as informative tools for clinical trial design. Ideally, a sufficient number of tumorgraft models genomically characterized, and biologically tested with rationally designed and optimized therapeutic cocktails could be used to “best-fit” models from previous patients aligned with newly diagnosed MM patients approach to guide molecularly informed treatment protocols.

Biography

Brian J. Nickoloff MD, PhD is currently Professor and Director of the Nicholas V. Perricone M.D. Division of Dermatology at Michigan State University College of Human Medicine, and Director (acting) of the Center for Translational Medicine at the Van Andel Institute. He is also Medical Director of Dermatopathology at the Lack Cancer Center, St. Mary’s Hospital, and Trinity Health System in Grand Rapids, MI. He has published over 365 articles and numerous book chapters, as well as editor of three books, and presented lectures worldwide.