CASE STUDY

Identification and verification of druggable target(s) in cutaneous melanoma without BRAF or RAS mutations

Who: Holly Yin, PhD - City of Hope National Medical Center

Holly Yin received her PhD in Molecular Biology and Genetics from Cornell University, followed by her postdoc training in the Genomics Institute of the Novartis Research Foundation (GNF), San Diego where she worked on developing new anticancer drugs by combining high-throughput small molecule screening with other genomic approaches. She also worked as Research Scientist in the field of infectious disease to identify novel targets and small molecule inhibitors for Hepatitis C virus (HCV) at ItherX/Immusol. Dr. Yin started her appointment with the Translational Genomics Research Institute (TGen) as an Assistant Professor in 2005, where she focuses on novel target identification, drug discovery, and drug development using high throughput RNAi and small molecule screening. Recently, Dr. Yin joined City of Hope in the Department of Pathology working in precision medicine by applying NanoString and other genomic technologies to identify biomarkers for accurate treatment. Dr. Yin has published over 30 peer-reviewed publications, reviews, and book chapters and has been invited to speak both nationally and internationally.

Why 3D Biology™ Technology?

By using 3D Biology technology, we expect to identify genes and pathways that have drastic changes at the DNA, RNA, or protein levels (with significant p-values) between the wild-type and mutant groups. Therefore, when combined with our previous unpublished studies, we will be able to (1) Prioritize our cell line RNAi data into a handful of targets for BRAF and RAS wild-type background; (2) Validate the findings using melanoma samples; (3) Potentially advance the targets to be druggable by comparing with our previous cell line drug screen data; (4) Contribute to future personalized therapeutics for patients wild-type for BRAF.

Aim of the project:

This project aims to identify and verify novel genes and pathways involved in the survival of melanoma cells without BRAF and RAS mutations. Importantly, a significant proportion of tumors harbor neither the BRAF nor RAS mutations typically associated with constitutive MAPK pathway signaling (estimated to be 30-40% of melanomas), and thus the development of novel targeted approaches for the treatment of these patients is a critical need.

Methods:

In order to prioritize and validate the findings from two previous genomic studies from melanoma cell lines, we would like to take the advantage of the nCounter® Vantage 3D™ assay, which enables detection of DNA, RNA, and protein alterations simultaneously in a single assay, particularly for the FFPE samples. We have a large collection of melanoma FFPE samples with molecular characterization of BRAF and RAS mutation status (100 samples in total). We will curate patient samples that are all treatment-naïve and pair with 6 samples of wild-type BRAF and RAS versus BRAF V600E mutants.

nCounter® Vantage 3D™ Assay selection:

nCounter Vantage 3D DNA SNV Solid Tumor Panel + RNA:Protein Solid Tumor Assay for FFPE

"People can do RNA, but for protein we are doing ELISA or Western Blot, one at a time. Or IHC, which is also only one at a time. Adding protein in a more multiplex style is definitely adding value. The best is you can do all three [analytes] in one shot. I'm really hoping this will help me to identify the target for BRAF wild-type patients in melanoma."

Holly Yin, PhD
City of Hope National Medical Center

To learn more about 3D Biology Technology visit 3d.nanostring.com

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