

CASE STUDY

Discovering resistance mechanisms of ^{MUT}NRAS melanoma towards MEK inhibitor treatment from patient derived tumors

Who: Gatien Moriceau, PhD - UCLA, Department of Medicine - Dermatology Division

Gatien Moriceau, PhD, is currently Project Scientist in Roger Lo's laboratory at UCLA. His work focuses on studying the biology of response and resistance of ^{MUT}NRAS melanoma under MEK inhibitor (MEKi), treatment and proposes to investigate the genetic/non-genetic and immune mechanisms of acquired MEKi resistance in ^{MUT}NRAS melanoma and therapeutic implications. He received his PhD in Bone Biology and Medical Science at the University of Nantes, France.

Why 3D Biology™ technology?

Performing the nCounter® Vantage 3D™ Assays on actual ^{MUT}NRAS melanoma patient tumors and Patient Derived Xenograft (PDX) models will elucidate the genetic, transcriptomic, and proteomic heterogeneity and mechanisms associated with MEKi resistance. Most importantly, the assay is highly parallelized and is amenable for limited amounts of patient tumor samples, which is typical for any clinical trial derived biopsies.

Aim of the project:

We propose to investigate the genetic/non-genetic and immune mechanisms of acquired MEKi resistance in ^{MUT}NRAS melanoma through analyzing pre- and post-treatment tumors (with a total of 15 tumors) from seven ^{MUT}NRAS melanoma patients. To enable a mechanistic study, we also generated >20 patient derived xenograft (PDX) MEKi-resistant tumors from two different ^{MUT}NRAS melanoma patients. These PDX tumors were treated with MEKi at three different dosages to study the correlates of different resistance mechanisms with multiple MEKi dosing.

Methods:

We will utilize the 36 sample assays provided by the nCounter Vantage 3D Assay Grant to analyze slides from each patient-derived and PDX tumor FFPE sample. We will combine the data from this analysis with whole exome data (with patient-matched normals) from the same set of tumor tissues.

A cross-sample comparison using the nCounter Vantage 3D Assays will allow for systematic assessment of genetic and proteomic changes associated with MEKi resistance within actual patient tumors. Most importantly, any observation from the Vantage 3D™ Assay will be validated both *in vitro* (using isogenic pairs of ^{MUT}NRAS cell lines pre-/post-MEKi resistance) and *in vivo* (using the PDX and PDX derived cell lines).

nCounter® Vantage 3D™ Assay selection:

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

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UCLA, Department of Medicine
Dermatology Division



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JUN 2017 GLSC_PM0058

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