MY CANCER GENOME

October 2013 Volume 1, Issue 6

In This Issue

New Articles of Interest

Oliver Gautschi, et al. Lung adenocarcinoma with BRAF G469L mutation refractory to vemurafenib. Lung Cancer 2013 Epub Aug 19

F. Stephen Hodi, et al. Imatinib for melanomas harboring mutationally activated or amplified KIT arising on mucosal, acral, and chronically sun-damaged skin. J. Clin. Oncol. 2013 Sep 10;31(26):3182-90

Newsletter-Related Content on MCG.org

Overview of Targeted Therapies for Cancer

What's New on MCG: Types of Molecular Tumor Testing

As the field of molecular medicine continues to move forward quickly, the My Cancer Genome team has expanded the molecular medicine content available on the website. Our newest page in the Molecular Medicine section is a description of the types of molecular tumor testing, contributed by Cindy L. Vnencak-Jones, Ph.D., Michael F. Berger, Ph.D., and William Pao, M.D., Ph.D.

This review covers eleven types of molecular tumor tests and includes information on the variants detected, a description of the method, the time required to complete the test, and a summary of the pros and cons of each method. For example, the review covers a comparison of four types of next generation sequencing: whole exome sequencing, whole genome sequencing, and two types of custom panels. The information is also summarized in a reference table displaying the types of variants detected in each test.

The new content on molecular tumor testing is an expansion of our molecular medicine section, which includes Detecting Gene Alterations in Cancers, an Overview of Targeted Therapies for Cancer, and a comprehensive list of anticancer agents.

Contributor Highlight: Michael F. Berger, Ph.D.

Michael F. Berger, Ph.D.

Assistant Professor, Department of Pathology, Department of Medicine and Human Oncology and Pathogenesis Program, Memorial Sloan-Kettering Cancer Center, New York, New York

Molecular Medicine Contributing Editor, My Cancer Genome

Dr. Berger is a contributing editor for the Molecular Medicine section of My Cancer Genome. Dr. Berger is an assistant professor and research scientist in

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the field of cancer genomics and computational biology, and his research has been pivotal in demonstrating the genetic complexity and identifying resistance mutations in several cancers, including prostate cancer and melanoma. Dr. Berger, mentored by Dr. David Solit, recently received the Danny Fund-MRA Young Investigator award from the Melanoma Research Alliance for research investigating genomic alterations that underlie variation in drug response in melanoma.

Contributor Highlight: Nicolas Girard, M.D., Ph.D.

Nicolas Girard, M.D., Ph.D.

Professor, Louis Pradel Hospital, Claude-Bernard University, Lyon, France

Thymic Carcinoma Section Editor, My Cancer Genome

Pr. Girard is the section editor for the thymic carcinoma section of My Cancer Genome. Pr. Girard is the Vice President of the International Thymic Malignancy Interest Group, ITMIG, and the Chair of the Research and Infrastructure section. Thymic malignancies present a challenge for basic science and clinical research due to the rarity of the disease. ITMIG addresses this challenge by providing resources for collaborative research between institutions. Initiatives include the Virtual Tumor Bank, which holds standardized annotated data from thymic tissue specimens from around the world, and retrospective and prospective case databases that house data from more than 6000 cases. In France, Pr. Girard, together with collaborators from the Gustave Roussy Institute, has launched a nation-wide network for thymic malignancies, in which all patients with thymic tumors are enrolled through support of the French NCI.

Contributor Highlight: Roger Lo, M.D., Ph.D.

Roger Lo, M.D., Ph.D.

Associate Professor and Director, Melanoma Clinic in Dermatology, UCLA Jonsson Comprehensive Cancer Center, Los Angeles, California

Melanoma Consulting Editor, My Cancer Genome

Dr. Lo is a consulting editor for the melanoma section of My Cancer Genome. In April 2013, Dr. Lo was awarded the AACR Outstanding Achievement in Cancer Research Award for his contributions in elucidating the molecular mechanisms behind acquired resistance to BRAF-inhibitors in *BRAF*-mutated melanoma, and understanding why squamous cell carcinoma can develop as a side effect of BRAF inhibition. The clinical impact of the Lo Lab's research is important, as three phase III trials combining several different MEK and BRAF inhibitors for patients with melanoma have opened since June 2012: NCT01597908, NCT01682083, NCT01689519.

Article of Interest Highlight:

Imatinib for Melanomas Harboring Mutationally Activated or Amplified *KIT* Arising on Mucosal, Acral, and Chronically Sun-Damaged Skin

Authors: Hodi FS, Corless CL, Giobbie-Hurder A, Fletcher JA, Zhu M, Marino-Enriquez A, Friedlander P, Gonzalez R, Weber JS, Gajewski TF, O'Day SJ, Kim KB, Lawrence D, Flaherty KT, Luke JJ, Collichio FA, Ernstoff MS, Heinrich MC, Beadling C, Zukotynski KA, Yap JT, Van den Abbeele AD, Demetri GD, Fisher DE.

Study Type: Phase II, multi-center study at nine medical centers

Eligibility: Patients with metastatic mucosal, acral, or chronically sun-damaged melanoma with *KIT* mutations (8 pts), *KIT* amplification (11 pts) or both (5 pts) were enrolled.

Screening and Enrollment period: 4 years, 8 months (July 2006-March 2011)

Study Treatment: imatinib (Gleevec) 400 mg orally daily until first incidence of disease progression; allowed dose escalation to twice daily until second incidence of disease progression

Statistical Considerations: A sample size of 24 allowed for 83% power to detect a response rate of 20% against the null hypothesis of 5% with one-sided type I error of 11%

Results: Response rate was 29.2% including confirmed (2 restagings) and unconfirmed (1 restaging) responses; in only confirmed responses the rate was 20.8%. Response rate for *KIT*-mutated patients was 53.8%. Median time-to-progression for all patients was 3.7 months.

***KIT* Mutations**: **Exon 11**: L576P (4 pts), insPYD577-582 (1 pt), V559A (1 pt), V560D (1 pt), delWKVVE557-560 (1 pt) and W557R (1 pt). **Exon 17**: D820Y (1 pt). **Exon 13**: K642E (3 pts).

See My Cancer Genome content for context: *KIT* mutations in melanoma

Related Article: Targeting Activated *KIT* Signaling for Melanoma Therapy