

Translational Genomics and Precision Medicine in Metastatic Breast Cancer

Abstract: Over the past decade, genomic characterization of tumors from cancer patients obtained through large-scale sequencing projects has shed enormous light on the molecular underpinnings of cancer. These discoveries have, in turn, led to the development of novel therapies and preventive measures that have already revolutionized cancer care. Despite this tremendous progress, there remains much more that we need to develop better treatments for metastatic cancer. In this presentation, we will discuss translational genomics approaches and precision medicine strategies for metastatic breast cancer. We will focus on how genomic and molecular characterization of metastatic tumor samples from patients sheds light on the biology of metastatic breast cancer and enables the development of strategies to overcome or prevent drug resistance. We will discuss the landscape of mutations in metastatic breast cancer, the potential clinical impact of genomic profiling, and the incorporation of genomic information into clinical care and clinical trials. We will also discuss how partnering directly with patients, in projects such as The Metastatic Breast Cancer Project (mbcproject.org), enables rapid identification of large numbers of patients willing to share tumors, saliva, and medical records to accelerate this research.

Papers:

1. Ghazani AA, Oliver NM, St. Pierre JP, Garofalo A, Rainville I, Hiller E, Treacy DJ, Rojas-Rudilla V, Sam Wood, Bair E, Parello M, Huang F, Giannakis M, Wilson F, Stover E, Corsello S, Nguyen T, Rana HQ, Church A, Lowenstein C, Sougnez C, Amin-Mansour A, Heng J, Brais L, Santos A, Bauer P, Waldron A, Lo P, Gorman M, Lydon C, Welch M, McNamara P, Gabriel S, Sholl LM, Lindeman NI, Garber JE, Joffe S, Van Allen EM; Gray SW, Jänne PA, Garraway LA, **Wagle N**. Assigning Clinical Meaning to Somatic and Germline Whole Exome Sequencing Data in a Prospective Cancer Precision Medicine Study. *Genetics in Medicine*, 2017 Jan 26.
2. Stover DG and **Wagle N**. Precision medicine in breast cancer: genes, genomes, and the future of genomically driven treatments. *Curr Oncol Rep*. 2015 Apr;17(4):438
3. Van Allen E, **Wagle N**, and Levy MA. The clinical analysis and interpretation of cancer genome data. *Journal of Clinical Oncology*. 2013 May 20;31(15):1825-33. Epub 2013 Apr 15.
4. **Wagle N**, Grabiner BC, Van Allen EM, Amin-Mansour A, Taylor-Weiner A, Rosenberg M, Gray N, Barletta JA, Guo Y, Swanson SJ, Ruan D, Hanna GJ, Haddad RI, Getz G, Kwiatkowski DJ, Carter SL, Sabatini DM, Janne PA, Garraway LA, Lorch JH. Response and Acquired Resistance to Everolimus in Anaplastic Thyroid Cancer. *New England Journal of Medicine* 2014 Oct 9; 371(15): 1426-33
5. **Wagle N***, Emery C*, Berger MF, Davis MJ, Sawyer A, Pochanard P, Kehoe S, Johannessen CM, MacConaill LE, Hahn WC, Meyerson M, and Garraway LA. Dissecting therapeutic resistance to RAF inhibition in melanoma by tumor genomic profiling. *Journal of Clinical Oncology*. 2011 Aug 1;29(22):3085-96. Epub 2011 Mar 7.

Bio: Nikhil Wagle is an Assistant Professor of Medicine at Harvard Medical School, a medical oncologist at Dana-Farber Cancer Institute, and an associate member of the Broad Institute of MIT and Harvard. He is the Deputy Directory of the Center for Cancer Precision Medicine at Dana-Farber Cancer Institute. He received his MD from Harvard Medical School and completed his residency training in internal medicine at Brigham and Women's Hospital, where he also served as chief medical resident, and completed his fellowship training in hematology/oncology in the Dana-Farber/Partners program.

Dr. Wagle leads a translational research program in the field of breast cancer genomics and precision cancer medicine. The major goals of his work are to better understand the biology of metastatic breast cancer and to develop new ways to overcome or prevent drug resistance in patients with advanced breast cancer. Ultimately, his research aims to identify characteristics of tumors that might improve clinical decision-making for patients.

He also leads The Metastatic Breast Cancer Project (mbcproject.org), a nationwide patient-driven research initiative that engages patients with advanced breast cancer through social media and seeks to empower them to accelerate cancer research through sharing their samples and clinical information. The project's outreach program, developed in collaboration with advocacy organizations and patients, serves to connect thousands of patients around the U.S. with metastatic breast cancer research, allowing them to participate regardless of where they live.

Dr. Wagle has received grant funding from Susan G. Komen, the Breast Cancer Research Foundation, the V Foundation, the Breast Cancer Research Alliance, and the Department of Defense. He is a recipient several awards and honors, including a Young Investigator Award from the Conquer Cancer Foundation of the American Society of Clinical Oncology, the 2013 Landon Foundation-AACR INNOVATOR Award for Research in Personalized Cancer Medicine, and the inaugural 2016 AACR NextGen Award for Transformative Cancer Research. His work has been published in the *New England Journal of Medicine*, the *Journal of Clinical Oncology*, *Cancer Discovery*, and *Nature Medicine*.

Dr. Wagle is also co-founder of *Doctors for America*, a grassroots organization of over 18,000 doctors and medical student in the United States who are working to build a better health care system for all Americans.