



NEWS RELEASE

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Foundation Medicine and Dana-Farber Cancer Institute Identify Novel Genomic Alterations in Lung and Colorectal Cancer

Findings Published in Nature Medicine Highlight Clinical Application of Next-Generation Sequencing to Suggest Targeted Therapeutic Options for Patients

CAMBRIDGE, Mass. – February 12, 2012 – [Foundation Medicine, Inc.](#), a molecular information company that brings comprehensive cancer gene analysis to routine clinical care, and **[Dana-Farber Cancer Institute](#)** today announced the *Nature Medicine* publication of results from their collaborative next-generation sequencing (NGS) study to assay cancer-relevant genes in 24 non-small cell lung cancer (NSCLC) and 40 colorectal cancer (CRC) cases. In this study, 59% of the samples were found to have genomic alterations directly associated with a clinically-available targeted therapeutic or a relevant clinical trial of a targeted therapy. Two novel gene fusions, *KIF5B-RET* in NSCLC and *C2orf44-ALK* in CRC, were discovered among the potentially druggable alterations identified in the study. Both of these findings may expand therapeutic options for a subset of cancer patients. This publication demonstrates that using targeted NGS to profile patient tumors for molecular alterations associated with therapeutic responses may have an important clinical impact in cancer treatment.

“In this collaboration, we detected clinically-relevant genomic alterations in more than half of the samples profiled, and, because Foundation Medicine’s NGS assay detects all classes of alterations with clinical-grade sensitivity, this research was able to identify both expected as well as completely novel alterations,” said Maureen Cronin, Ph.D., senior vice president, research & product development of Foundation Medicine and co-author of the study. “The discovery of novel rearrangements and fusions, such as *KIF5B-RET* and *C2orf44-ALK*, supports an important role for NGS in the clinical understanding and treatment of cancer.”

“In a common indication like NSCLC, identifying even a small subpopulation of individuals with gene fusions who may be responsive to a targeted therapy has the potential for major therapeutic impact,” said Phil Stephens, Ph.D., executive director, cancer genomics of Foundation Medicine and co-author of the study. “This joint research with Dana-Farber translates genomic research to the clinic and we expect that it may quickly have a positive impact for patients.”

Clinically-relevant alterations, which are defined here as being associated with an available clinical treatment option or ongoing clinical trial investigating a new targeted therapy, were identified in 72% of NSCLC tumor samples and 52.5% of CRC tumor samples.

The novel, recurrent *KIF5B-RET* fusion was identified by the NGS assay in one patient with NSCLC. In subsequent screening, 11 additional *RET* fusions were identified in 561 lung adenocarcinoma samples from a cohort of never or limited former smokers with NSCLC. In common with known oncogenic alterations in *EGFR* and *EML4-ALK*, the *KIF5B-RET* gene fusion was found more than twice as often in NSCLC samples from individuals of Asian descent (0.8% (1/212) of the Caucasian samples and 2% (9/405) of the Asian patient samples). Additionally, none of the fusion-positive tumors contained alterations in any of the other known oncogenes that drive lung cancer (*EGFR*, *ERBB2*, *BRAF* or *KRAS* or rearrangements of *EML4-ALK* or *ROS1*). Tumors with this fusion were specifically sensitive to targeted drugs that inhibit RET, suggesting that prospective clinical trials of RET-targeted therapeutics may benefit individuals with NSCLC with *KIF5B-RET* rearrangements.

The second novel finding in the study was a potentially clinically-relevant gene fusion between *C2orf44* and *ALK* identified in one CRC patient. Additional assays suggest this fusion gene yields 90-fold overexpression of anaplastic lymphoma kinase (ALK), the target of crizotinib, a U.S. FDA approved therapy for NSCLC. Given the structure of the rearrangement that generated the *C2orf44-ALK* fusion, it is unlikely that current clinical detection methods would have detected this alteration. This research thus suggests that a previously unrecognized subset of individuals with CRC may harbor genetic alterations that may make them responsive to ALK-inhibitor treatment.

The assay used for the testing described in this *Nature Medicine* paper is analytically validated to have a false discovery rate of less than 1% with at least 99% sensitivity for base substitutions occurring with at least 10% frequency.

The paper, “Identification of new ALK and RET gene fusions from colorectal and lung cancer biopsies” by Lipson, D. et al. is now available [online](#).

About Foundation Medicine’s Comprehensive Cancer Genomic Test

Foundation Medicine’s [comprehensive cancer genomic test](#) uses next-generation sequencing to analyze routine clinical specimens (i.e., small amounts of formalin fixed, paraffin embedded tumor tissue) for all classes of genomic alterations (point mutations, copy number alterations, insertions/deletions, and select rearrangements) in approximately 200 cancer-related genes. The test is optimized for clinical-grade analysis of tumor tissues, overcoming multiple complexities (such as purity, ploidy and clonality) inherent to tumor genomes. Results are designed to serve as a helpful decision-support tool for physicians to evaluate cancer treatment approaches tailored to each patient’s [molecular subtype](#). Each patient report is reviewed and annotated by a molecular oncologist and consists of scientific and medical literature relevant to that patient’s genomic alterations and includes information on targeted therapies and clinical trials supported by scientific and medical research.

About Foundation Medicine

Foundation Medicine is dedicated to improving cancer care through the development of comprehensive cancer diagnostics that will help physicians inform treatment decisions based on an individual patient's molecular cancer subtype. Foundation Medicine's first laboratory developed test, based on a next-generation sequencing platform, is designed to accommodate a broad landscape of cancer genome information and a growing repertoire of targeted treatments and clinical research opportunities. Foundation Medicine's test will assist physicians to make prompt and informed determinations about the best cancer treatments and clinical trial options for each patient, taking into account each patient's unique cancer-associated alterations alongside publicly available scientific and medical information. The company's founding advisors are world leaders in genome technology, cancer biology and medical oncology; they, alongside clinicians, biotech and molecular diagnostics industry leaders, are working to harness emerging technologies to develop unparalleled tests that will identify and interpret an ever-growing set of actionable genomic alterations, truly enabling personalized cancer medicine. For more information, please visit the company's website at www.foundationmedicine.com.

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