

Supplemental Table 1. Institutions and PIs participating in LCMC II.

Institutions Participating in LCMC II	PI
University of Colorado	Paul Bunn, M.D.
The Ohio State University	Gregory Otterson, M.D.
Dana Farber/Brigham and Women's	Bruce Johnson, M.D./David Kwiatkowski, M.D.
Yale University	Katerina Politi, Ph.D
Memorial Sloan Kettering Cancer Center	Mark Kris, M.D.
University of Pittsburgh	Mark Socinski, M.D.
Johns Hopkins University	Charles Rudin, M.D., Ph.D
Emory University	Fadlo Khuri, M.D.
Moffitt Cancer Center	Eric Haura, M.D.
Massachusetts General Hospital	Jeffrey Engelman, M.D.
Washington University in Saint Louis	Saiama Wagar, M.D.
University of Texas Southwestern Medical Center	Joan Schiller, M.D.
MD Anderson	Bonnie Glisson, M.D.
University of California Los Angeles	Edward Garon, M.D.
Oregon Health and Science University	Alan Sadler, M.D.
Vanderbilt University	Yu Shyr, Ph.D

Supplemental Table 2. Overview of mutational profiling platforms employed across 16 LCMC2 testing sites.

Site	MPS*	<u>Genotyping platform</u>				
		Single base** extension**	Mass spectroscopy***	Sanger sequencing	Pyrosequencing	Real time PCR
1	✓		✓	✓	✓	✓
2	✓	✓				
3	✓			✓		
4	✓	✓				
5	✓		✓			
6	✓	✓			✓	
7	✓		✓			
8	✓	✓				
9	✓		✓			
10	✓	✓				
11	✓	✓				
12	✓	✓				
13	✓	✓				
14		✓				
15	✓	✓				
16				✓	✓	✓

\*Massively parallel sequencing; multiple methods were used across different sites

\*\*Single base extension genotyping is commercially known as SNaPshot.

\*\*\*Mass spectroscopy genotyping is commercially known as Sequenom.

Supplemental Table 3. Mutations in the core genes assayed in LCMC II.

<b>Variant</b>	<b>AA</b>
AKT1_c.49G.A	p.E17K
BRAF_c.1397G.T	p.G466V
BRAF_c.1406G.A	p.G469E
BRAF_c.1406G.C	p.G469A
BRAF_c.1406G.T	p.G469V
BRAF_c.1781A.G	p.D594G
BRAF_c.1781A.T	p.D594G
BRAF_c.1789C.G	p.L597V
BRAF_c.1790T.G	p.L597R
BRAF_c.1798G.A	p.V600M
BRAF_c.1799T.A	p.V600E
EGFR_c.2125_2127GAA.CAT	p.E709H
EGFR_c.2125G.A	p.E709K
EGFR_c.2126A.C	p.E709A
EGFR_c.2126A.G	p.E709G
EGFR_c.2126A.T	p.E709V
EGFR_c.2155G.A	p.G719S
EGFR_c.2155G.T	p.G719C
EGFR_c.2156G.A	p.G719D
EGFR_c.2156G.C	p.G719A
EGFR_c.2281G.T	p.D761Y
EGFR_c.2303G.T	p.S768I
EGFR_c.2326C.T	p.R776G
EGFR_c.2327G.A	p.R776H
EGFR_c.2369C.T	p.T790M
EGFR_c.2560A.G	p.T854A
EGFR_c.2572C.A	p.L858M
EGFR_c.2573T.G	p.L858R
EGFR_c.2582T.A	p.L861Q
EGFR_exon.19.del	e19del
EGFR_exon.20.ins	e20ins
ERBB2_c.2264T.C	p.L755S
ERBB2_c.2305G.C	p.D769Y
ERBB2_c.2329G.A	p.V777L
ERBB2_c.2329G.T	p.V777L
ERBB2_ins.A775	e20ins
KRAS_c.181C.A	p.Q61X
KRAS_c.181C.G	p.Q61E
KRAS_c.182A.C	p.Q61P

KRAS_c.182A.G	p.Q61R
KRAS_c.182A.T	p.Q61L
KRAS_c.183A.C	p.Q61H
KRAS_c.183A.T	p.Q61H
KRAS_c.34G.A	p.G12S
KRAS_c.34G.C	p.G12R
KRAS_c.34G.T	p.G12C
KRAS_c.35G.A	p.G12D
KRAS_c.35G.C	p.G12A
KRAS_c.35G.T	p.G12V
KRAS_c.37G.A	p.G13S
KRAS_c.37G.C	p.G13R
KRAS_c.37G.T	p.G13C
KRAS_c.38G.A	p.G13D
KRAS_c.38G.C	p.G13A
KRAS_c.38G.T	p.G13V
KRAS_c.436G.A	p.A146T
KRAS_c.436G.C	p.A146P
KRAS_c.437C.T	p.A146V
KRAS_c.180.181TC.CA	p.Q61K
MAP2K1_c.167A.C	p.Q56P
MAP2K1_c.171G.T	p.K57N
MAP2K1_c.199G.A	p.D67N
NRAS_c.181C.A	p.Q61K
NRAS_c.181C.G	p.Q61R
NRAS_c.182A.C	p.Q61P
NRAS_c.182A.G	p.Q61R
NRAS_c.182A.T	p.Q61L
NRAS_c.183A.C	p.Q61H
NRAS_c.183A.G	p.Q61Q
NRAS_c.183A.T	p.Q61H
NRAS_c.34G.A	p.G12S
NRAS_c.34G.C	p.G12R
NRAS_c.34G.T	p.G12C
NRAS_c.35G.A	p.G12D
NRAS_c.35G.C	p.G12A
NRAS_c.35G.T	p.G12V
NRAS_c.37G.A	p.G13S
NRAS_c.37G.C	p.G13R
NRAS_c.37G.T	p.G13C
NRAS_c.38G.A	p.G13D

NRAS_c.38G.C	p.G13A
NRAS_c.38G.T	p.G13V
PIK3CA_c.1035T.A	p.N245K
PIK3CA_c.1035T.G	p.N245K
PIK3CA_c.1258T.C	p.N245K
PIK3CA_c.1624G.A	p.E542K
PIK3CA_c.1624G.C	p.E542Q
PIK3CA_c.1633G.A	p.E545K
PIK3CA_c.1633G.C	p.E545Q
PIK3CA_c.1634A.C	p.E545A
PIK3CA_c.1634A.G	p.E545G
PIK3CA_c.1635G.T	p.E545D
PIK3CA_c.263G.A	p.R88Q
PIK3CA_c.3129G.T	p.M1043I
PIK3CA_c.3139C.T	p.H1047Y
PIK3CA_c.3140A.G	p.H1047R
PIK3CA_c.3140A.T	p.H1047L

Supplemental Table 4. Massively parallel sequencing (MPS) assays employed by LCMCII institutions.

Institution	NGS Test Name	NGS Methodology	Reference
MSKCC	MSK-IMPACT	Custom_Hybrid Capture_HiSeq	[1]
Brigham and Women's Hospital/Dana Farber	OncoPanel	Custom_Hybrid Capture_HiSeq	[2]
Wash U	WUCaMP	ClearSeq Comprehensive Cancer?_Hybrid Capture_HiSeq	[3]
U of Colorado	Not specified	TST26_Amplicon_MiSeq/NextSeq	
Emory	CMP26	TST26_Amplicon_MiSeq/NextSeq	[4]
Moffitt	Not specified	TST26_Amplicon_MiSeq/NextSeq	
UTSW	Not specified	TST26_Amplicon_MiSeq/NextSeq	
MD Anderson	Not specified	AmpliSeq Cancer HotSpot v2_Amplicon_PGM	[5, 6]
Mass General	SNaPshot Cancer Genotyping	AmpliSeq Cancer HotSpot v2_Amplicon_PGM	
Ohio State	PULMOL	AmpliSeq Colon and Lung v2_Amplicon_PGM	
Oregon Health & Sciences	GeneTrails® NSCLC Genotyping Panel	Custom Amplicon_PGM	Described in Suppl Data of [7]
Johns Hopkins	Lung Cancer Mutation Panel	AmpliSeq Cancer HotSpot v2_Amplicon_PGM	
UCLA	Lung Cancer Mutation Panel	AmpliSeq Cancer HotSpot v2_Amplicon_PGM	
Pitt	OncoSeq	AmpliSeq Cancer HotSpot v2_Amplicon_PGM	
Yale	Not specified	Amplicon_PGM	

1. Cheng, D.T., et al., *Memorial Sloan Kettering-Integrated Mutation Profiling of Actionable Cancer Targets (MSK-IMPACT): A Hybridization Capture-Based Next-Generation Sequencing Clinical Assay for Solid Tumor Molecular Oncology*. J Mol Diagn, 2015. **17**(3): p. 251-64.
2. Sholl, L.M., et al., *Institutional implementation of clinical tumor profiling on an unselected cancer population*. JCI Insight, 2016. **1**(19): p. e87062.
3. Cottrell, C.E., et al., *Validation of a next-generation sequencing assay for clinical molecular oncology*. J Mol Diagn, 2014. **16**(1): p. 89-105.
4. Fisher, K.E., et al., *Clinical Validation and Implementation of a Targeted Next-Generation Sequencing Assay to Detect Somatic Variants in Non-Small Cell Lung, Melanoma, and Gastrointestinal Malignancies*. J Mol Diagn, 2016. **18**(2): p. 299-315.
5. Singh, R.R., et al., *Clinical validation of a next-generation sequencing screen for mutational hotspots in 46 cancer-related genes*. J Mol Diagn, 2013. **15**(5): p. 607-22.
6. Goswami, R.S., et al., *Identification of Factors Affecting the Success of Next-Generation Sequencing Testing in Solid Tumors*. Am J Clin Pathol, 2016. **145**(2): p. 222-37.

7. Lopez-Chavez, A., et al., *Molecular profiling and targeted therapy for advanced thoracic malignancies: a biomarker-derived, multiarm, multihistology phase II basket trial*. *J Clin Oncol*, 2015. **33**(9): p. 1000-7.