Recurrently Mutated Genes Differ between Leptomeningeal and Solid Lung Cancer Brain Metastases

Yingmei Li*[1], Boxiang Liu*[2,3,4], Ian David Connolly*[1], Bina Wasunga Kakusa[1], Wenying Pan[5], Seema Nagpal[6], Stephen B. Montgomery[3,4], Melanie Hayden Gephart[1]

Supplementary Information

Table S1. Patient cohort of LMD for WES

| Sample ID	Age	Sex	Smoking Hx	Primary tumor mutations	Tumor/Normal samples
LM1	60	F	former smoker (15 pack-years)	EGFR^{L858R}, CTNNB1^{S37C}	CSF cell
LM2	55	F	never smoker	Weak but reproducible EGFR exon 20 insertion	CSF cell / blood
LM3	26	F	never smoker	Not available	CSF cell
LM4	72	M	never smoker	EGFR exon 19 deletion	CSF cell / saliva
LM5	57	F	never smoker	EGFR^{L858R}	CSF cell / saliva
LM6	63	M	former smoker (12 pack-years)	Not available	CSF cell / blood
LM7	58	M	never smoker	No known mutation	CSF cell
LM8	73	F	never smoker	EGFR exon 19 deletion, TP53^{R248W}	CSF cell / blood
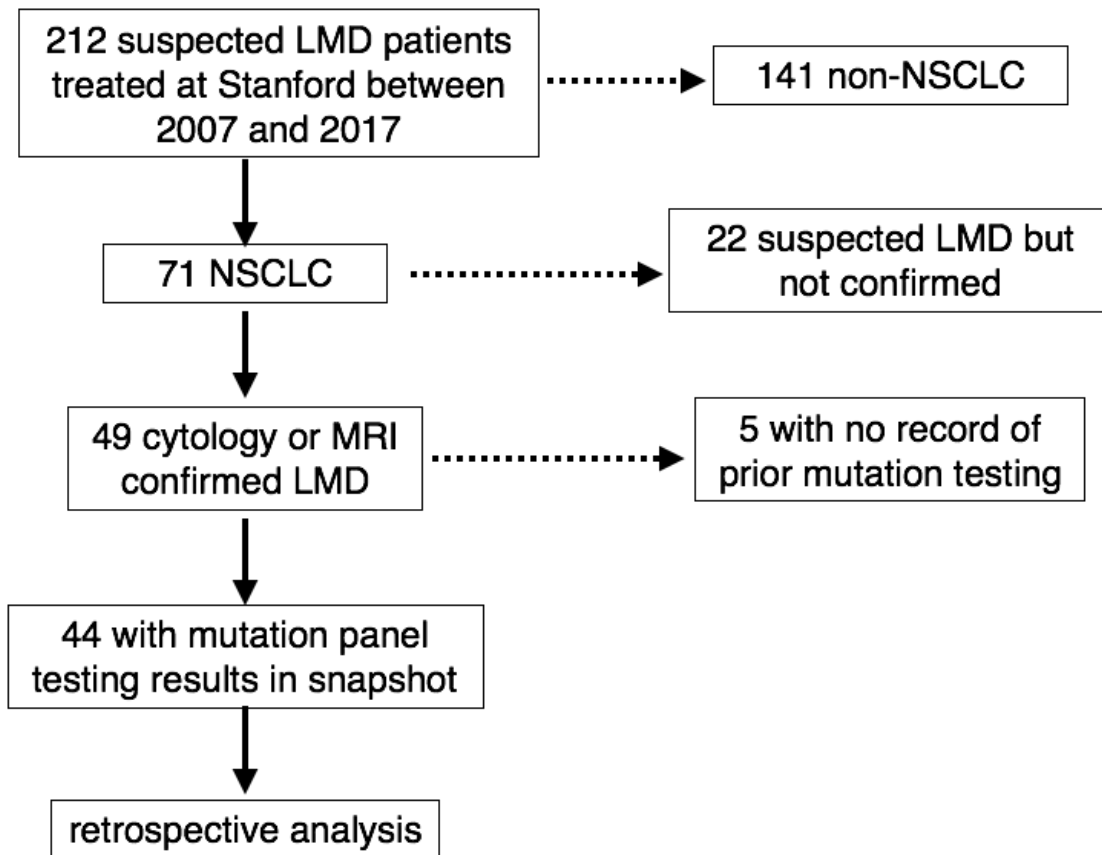
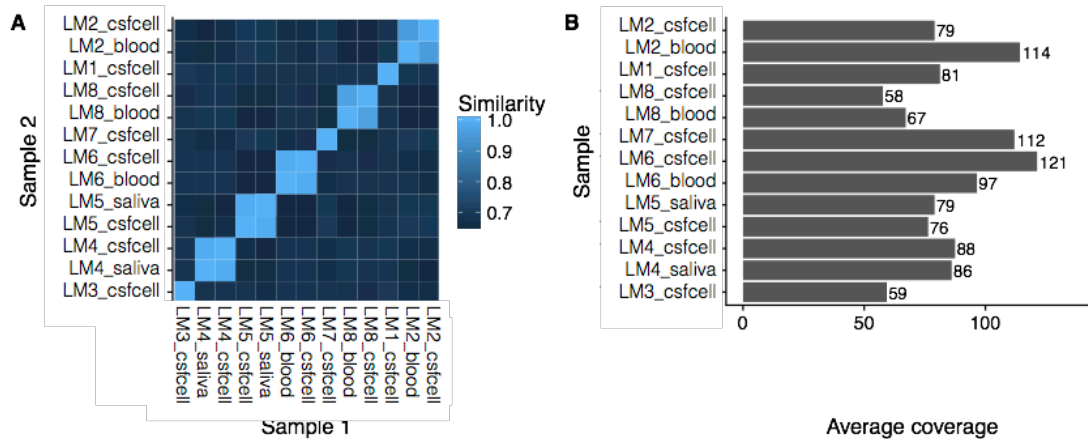Figure S1. Flowchart of retrospective review cohort selection
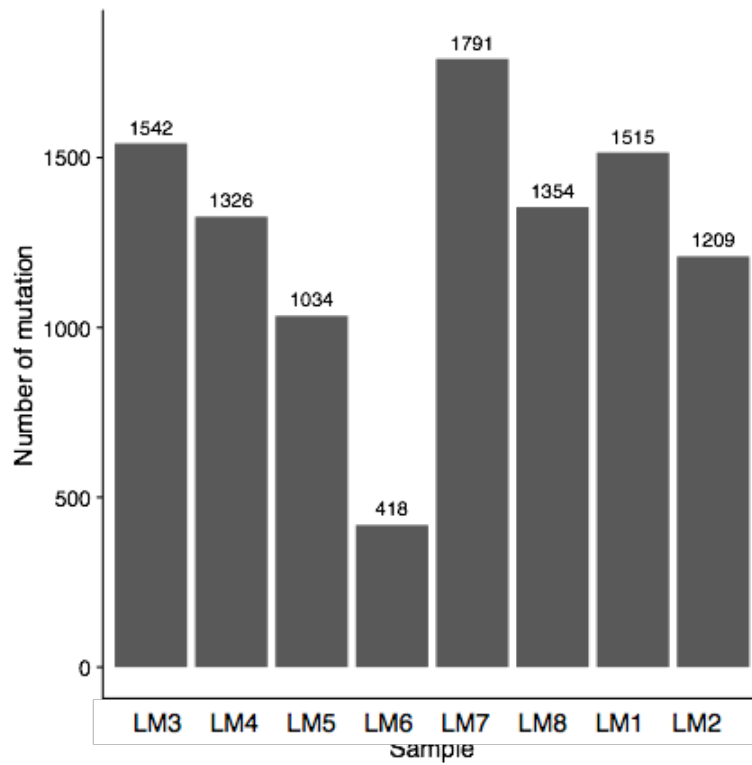

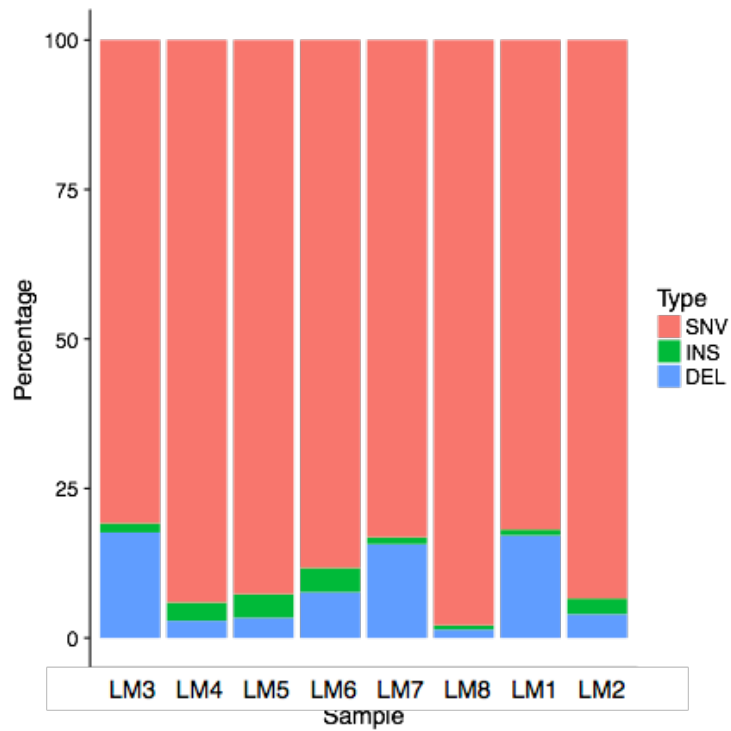Figure S2. Sequencing QC for each LMD sample

Figure S3. Mutations per samples

Figure S4. Mutation percentage by type

Figure S5. Mutation distribution
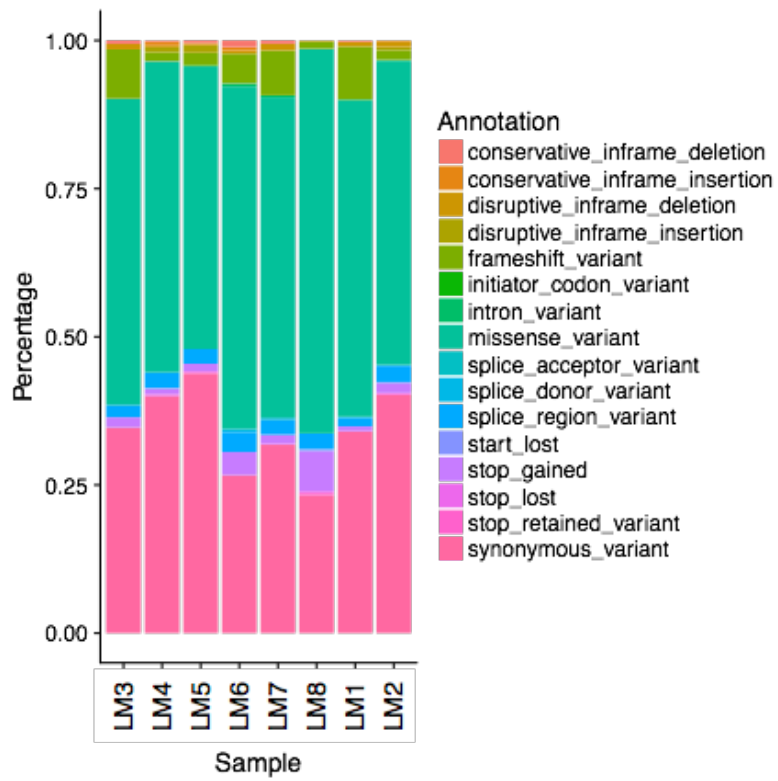
Query

Protein Acc	Position	AA₁	AA₂	Description
P08581	1162	H	L	Canonical; RecName: Full=Hepatocyte growth factor receptor; Short=HGF receptor; EC=2.7.10.1; AltName: Full=HGF/SF receptor; AltName: Full=Proto-oncogene c-Met; AltName: Full=Scatter factor receptor; Short=SF receptor; AltName: Full=Tyrosine-protein kinase Met; Flags: Precursor; Length: 1390

Results

⊞ **Prediction/Confidence**   *PolyPhen-2 v2.2.2r398*

HumDiv

This mutation is predicted to be **PROBABLY DAMAGING** with a score of **1.000** (sensitivity: **0.00**; specificity: **1.00**)

0.00 0.20 0.40 0.60 0.80 1.00

⊟ **HumVar**

This mutation is predicted to be **PROBABLY DAMAGING** with a score of **0.999** (sensitivity: **0.09**; specificity: **0.99**)

0.00 0.20 0.40 0.60 0.80 1.00

Details

⊟ **Multiple sequence alignment**   *UniProtKB/UniRef100 Release 2011_12 (14-Dec-2011)*

Shown are 75 amino acids surrounding the mutation position (marked with a black box). An interactive version of the complete alignment is also available.
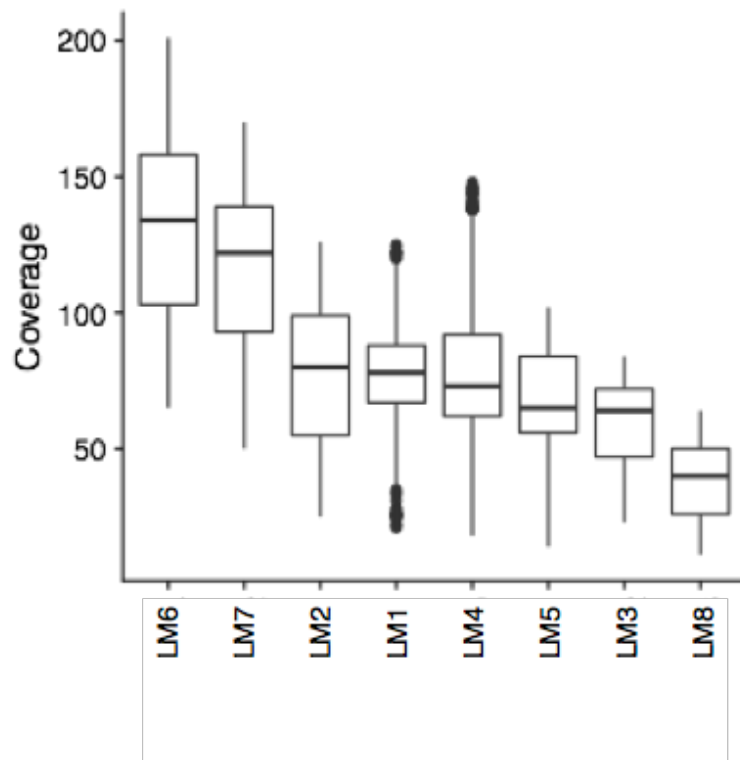
Figure S6 MET p.His1180Leu mutation

Figure. S7 WES coverage of *KRAS* gene