Supplemental Table S1: Clinical and Pathologic Characteristics

Pt	Age (yrs)	Sex	Tumor Site	Interval (yrs)	Grade	T	N	M	Stage	MMR IHC	Treatment
1	65	F	Rectosigmoid		2	T3	N2	Mx	IIIB	Not tested	Adjuvant C+R
			RLN								
			Right lung	3.6							
2	58	M	Rectosigmoid		2	T3	N2a	Mx	IIB	No loss	Adjuvant C+R
			RLN								
			Right lung	2.2							
3	52	M	Rectum		N/A	yT3	N2a	Mx	IIB	Not tested	Neoadjuvant C+R
			RLN 1								Adjuvant C
			RLN 2								
			Inguinal LN 1	1.0							
			Inguinal LN 2	1.0							
4	57	M	Distal Transverse		2	T3	N0	Mx	IIA	Not tested	
			Liver	0.5							
			Anastomosis 1	2.0							Adjuvant C
			Abdominal wall implant	2.0							
			Anastomosis 2	2.5		rT3	N1c	M1	IV		
			Small bowel	4.8							
5	65	M	Distal descending		2	T1	N0	Mx	I	Not tested	Adjuvant C+R
			Right presacral soft tissue	1.0							
6	63	F	Proximal Transverse		2-3	T4a	N1a	M1b	IV	MLH1/PMS2 loss	Adjuvant C
			RLN								
			Peritoneum	S							
7	85	F	Ascending		2	T3	N2a	M1b	IV	No loss	Adjuvant C
			RLN								
			Pyloric LN	S							
			Liver	S							
8	33	M	Rectosigmoid		N/A	yT3	N2a	M1	IV	No loss	Neoadjuvant C+R
			Liver	S							?Adjuvant
9	70	M	Rectum		2-3	T3	N1b	M1a	IV	No loss	Adjuvant C
			RLN								
			Liver	S							
10	85	M	Cecum		2-3	T4a	N2b	M1	IV	MLH1/PMS2 loss	Adjuvant C
			RLN								
			Liver	S							
11	33	F	Ascending		1-2	T3	N2a	M1	IV	No loss	Adjuvant C
			RLN								
			Liver	S							
12	74	M	Sigmoid		1-2	mT3	N1b	M1	IV	No loss	?Adjuvant
			Rectum							No loss	
			RLN								
			Liver	S							
13	36	F	Distal sigmoid		2	T3	N2b	M1a	IV	No Loss	Neoadjuvant C
			Liver	S							

Pt = patient, LN = lymph node, RLN = regional LN, S = Same surgery, C = chemotherapy, R = radiotherapy, N/A = not applicable for treated tumors

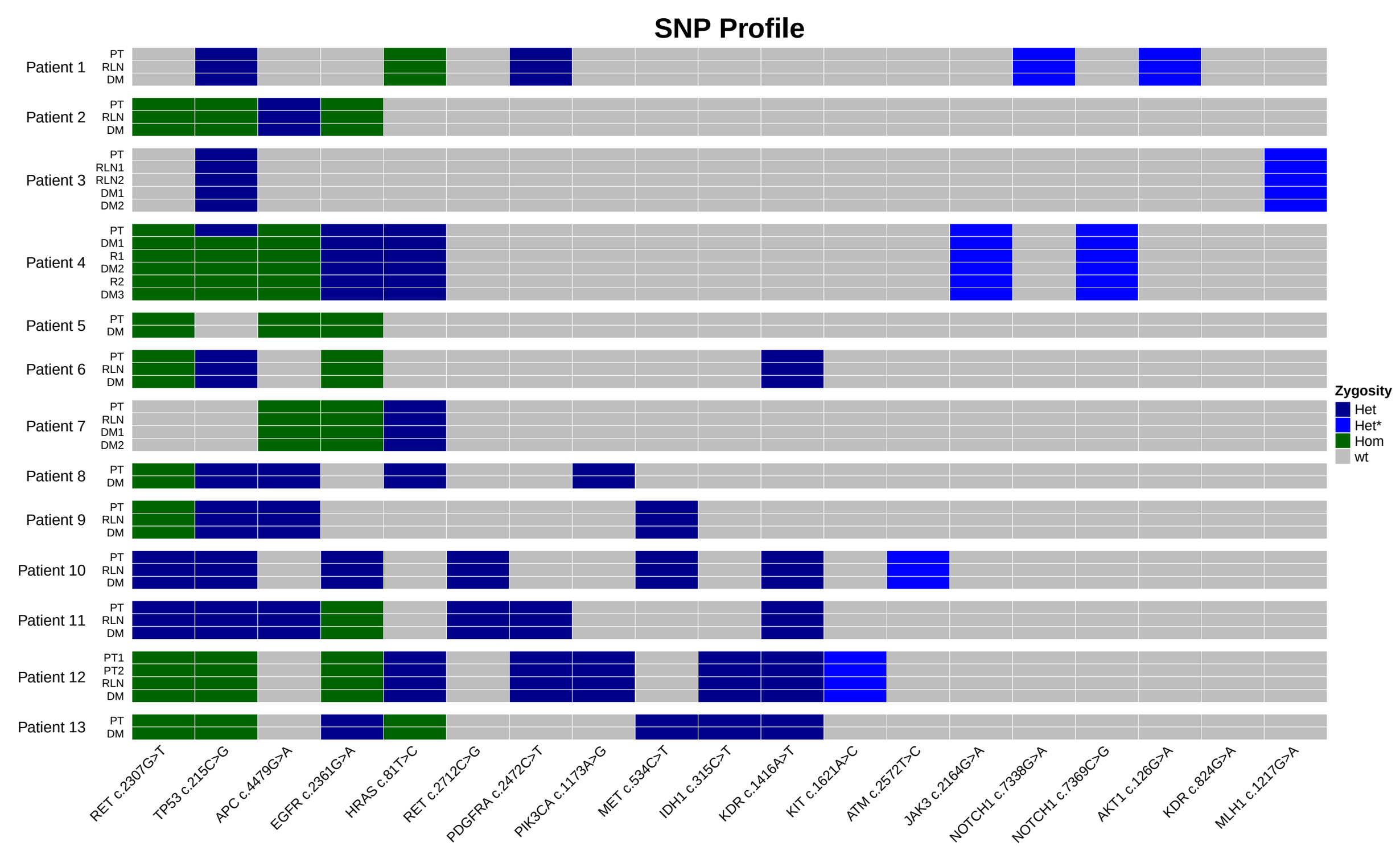
Supplemental Table S2: Number of Discordant Mutations by Gene and by Study

Gene*	Current PT-DM	Current PT-RLN	Goswami et al	Crumley et al	Brannon et al	Kim et al	Total Discor-dances	Number of Studies
Genes showing discordance in multiple samples across multiple studies								
TP53	1	1	4	1	3	2	*12*	*6*
APC	1		2	2	7	2	*14*	*5*
PIK3CA	1	1	6		5		*13*	*4*
SMAD4			3		3	1	*7*	*3*
ERBB4					2	1	*3*	*2*
PIK3CG					2	1	*3*	*2*
NRAS	1		1				*2*	*2*
BRCA2					1	1	*2*	*2*
EPHA5					1	1	*2*	*2*
Genes showing discordance in a single study but in multiple samples								
TTN						5	*5*	*1*
EPHA6					4		*4*	*1*
EPHB1					3		*3*	*1*
KRAS			2				*2*	*1*
AR					2		*2*	*1*
ASXL1					2		*2*	*1*
EPHA7					2		*2*	*1*
FLT1					2		*2*	*1*
MAP2K1					2		*2*	*1*
MTOR					2		*2*	*1*
PIK3CD					2		*2*	*1*
REL					2		*2*	*1*
TET1					2		*2*	*1*
TSHR					2		*2*	*1*
ADAMTS20						2	*2*	*1*
MACF1						2	*2*	*1*
RASA1						2	*2*	*1*
ROBO1						2	*2*	*1*
TRAF4						2	*2*	*1*
WNT2						2	*2*	*1*
Genes showing discordance in a single sample in a single study								
GS			1				*1*	*1*
ALK					1		*1*	*1*
ATM					1		*1*	*1*
ATRX					1		*1*	*1*
BAP1					1		*1*	*1*
BCL6					1		*1*	*1*
CARD11					1		*1*	*1*
CBL					1		*1*	*1*
CEBPA					1		*1*	*1*
EGFR					1		*1*	*1*
EPHA3					1		*1*	*1*
ERBB2					1		*1*	*1*
ERBB3					1		*1*	*1*
FAS					1		*1*	*1*
FH					1		*1*	*1*
FOXL2					1		*1*	*1*

GRIN2A	1		*1*	*1*
KDM6A	1		*1*	*1*
KDR	1		*1*	*1*
LGR6	1		*1*	*1*
MDM4	1		*1*	*1*
MITF	1		*1*	*1*
NF1	1		*1*	*1*
NFE2L2	1		*1*	*1*
NFKB2	1		*1*	*1*
NOTCH1	1		*1*	*1*
NOTCH3	1		*1*	*1*
NTRK3	1		*1*	*1*
PBRM1	1		*1*	*1*
PDGFRB	1		*1*	*1*
PIK3C2G	1		*1*	*1*
PIK3R1	1		*1*	*1*
PREX2	1		*1*	*1*
PTEN	1		*1*	*1*
PTPRS	1		*1*	*1*
STK11	1		*1*	*1*
SUFU	1		*1*	*1*
TBK1	1		*1*	*1*
TET2	1		*1*	*1*
TGFBR2	1		*1*	*1*
ABCA3		1	*1*	*1*
ADAMTS18		1	*1*	*1*
ADCY1		1	*1*	*1*
BCL9		1	*1*	*1*
CASC5		1	*1*	*1*
CHD5		1	*1*	*1*
CIC		1	*1*	*1*
COL7A1		1	*1*	*1*
CSMD3		1	*1*	*1*
CX3CR1		1	*1*	*1*
DGKB		1	*1*	*1*
ETV4		1	*1*	*1*
FANCG		1	*1*	*1*
FBXW7		1	*1*	*1*
GPC5		1	*1*	*1*
HERC1		1	*1*	*1*
HSP90AB1		1	*1*	*1*
ITGA10		1	*1*	*1*
ITGAL		1	*1*	*1*
JAK1		1	*1*	*1*
KIAA1409/ UNC79		1	*1*	*1*
KNTC1		1	*1*	*1*
LRP1B		1	*1*	*1*
MAGI2		1	*1*	*1*
MAP3K5		1	*1*	*1*
MAPK10		1	*1*	*1*
MARK1		1	*1*	*1*

MAST4	1	*1*	*1*
MGA	1	*1*	*1*
MGMT	1	*1*	*1*
MMP2	1	*1*	*1*
MPL	1	*1*	*1*
MUC16	1	*1*	*1*
NOS1	1	*1*	*1*
NTRK2	1	*1*	*1*
PARP14	1	*1*	*1*
PCM1	1	*1*	*1*
PPM1H	1	*1*	*1*
PREX1	1	*1*	*1*
PRKCZ	1	*1*	*1*
PTPN13	1	*1*	*1*
PTPRC	1	*1*	*1*
PTPRD	1	*1*	*1*
RB1CC1	1	*1*	*1*
RPS6KB2	1	*1*	*1*
SIRT6	1	*1*	*1*
SMAD2	1	*1*	*1*
SMAD3	1	*1*	*1*
SNX13	1	*1*	*1*
STIM1	1	*1*	*1*
SYNE1	1	*1*	*1*
TACR3	1	*1*	*1*
TCF12	1	*1*	*1*
TCF3	1	*1*	*1*
TEX14	1	*1*	*1*
TNKS	1	*1*	*1*
TOP2B	1	*1*	*1*
TOPBP1	1	*1*	*1*
TPO	1	*1*	*1*
VRTN	1	*1*	*1*
ZNF217	1	*1*	*1*
ZNF831	1	*1*	*1*

*Genes with discordant mutations in at least one study are listed, and those with discordant mutations in multiple samples either in the same study or across multiple studies are bolded, if they are frequently mutated in colorectal cancer.


SNP Profile
Patient 1
PT
RLN
DM
Patient 2
PT
RLN
DM
Patient 3
PT
RLN1
RLN2
DM1
DM2
Patient 4
PT
DM1
R1
DM2
R2
DM3
Patient 5
PT
DM
Patient 6
PT
RLN
DM
Patient 7
PT
RLN
DM1
DM2
Patient 8
PT
DM
Patient 9
PT
RLN
DM
Patient 10
PT
RLN
DM
Patient 11
PT
RLN
DM
Patient 12
PT1
PT2
RLN
DM
Patient 13
PT
DM
RET c.2307G>T
TP53 c.215C>G
APC c.4479G>A
EGFR c.2361G>A
HRAS c.81T>C
RET c.2712C>G
PDGFRA c.2472C>T
PIK3CA c.1173A>G
MET c.534C>T
IDH1 c.315C>T
KDR c.1416A>T
KIT c.1621A>C
ATM c.2572T>C
JAK3 c.2164G>A
NOTCH1 c.7338G>A
NOTCH1 c.7369C>G
AKT1 c.126G>A
KDR c.824G>A
MLH1 c.1217G>A
Zygosity
Het
Het*
Hom
wt

SUPPLEMENTAL FIGURE S1: SNP profile. Co-mutation plot shows identical SNPs and zygosity for all samples from a given patient, and no two patients have the same set of SNPs. *Het = heterozygous SNP unique to one patient in this cohort.

A. Omnibus Fisher Exact Test for Independence of Tumor Pair Classification Across Studies

	Concordant	Overlapping	Discordant	Row Totals
current PT-DM	10	1	1	12
current PT-RLN	7	1	1	9
Goswami et al	73	12	1	86
Crumley et al	13	2	1	16
Brannon et al	44	25	0	69
Kim et al	14	5	0	19
Lee et al	0	12	3	15
Column Totals	161	58	7	226

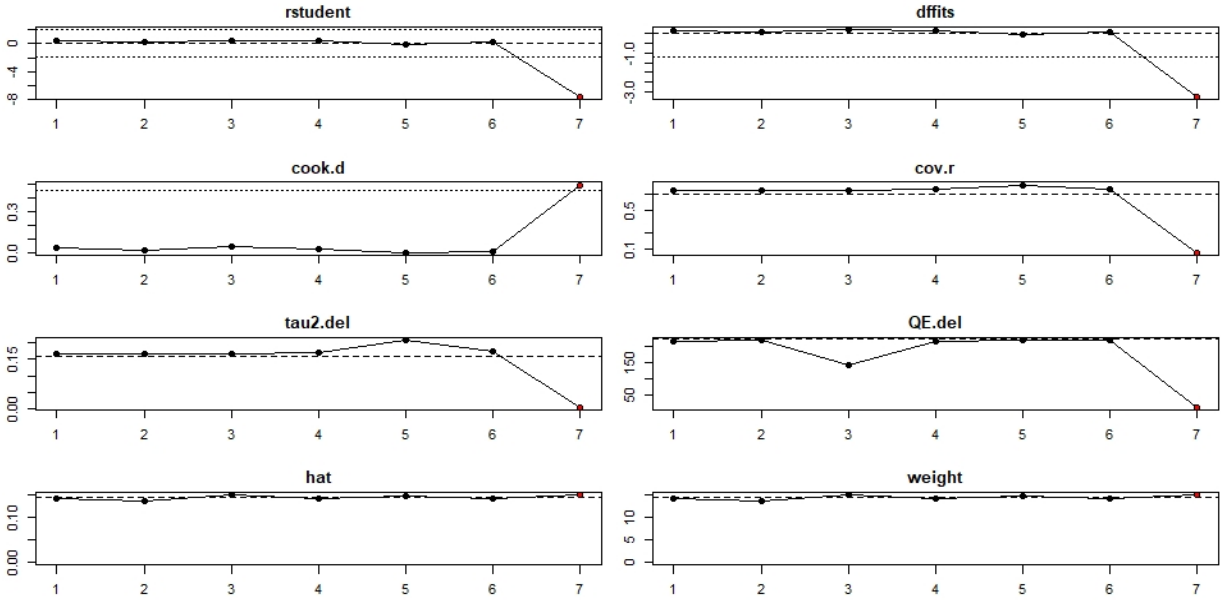
Fisher's Exact Test for Count Data
p-value = **7.013e-10**
alternative hypothesis: two.sided

B. Pairwise Comparison of Proportions of Tumor Pairs Classified as Concordant, Overlapping, or Discordant

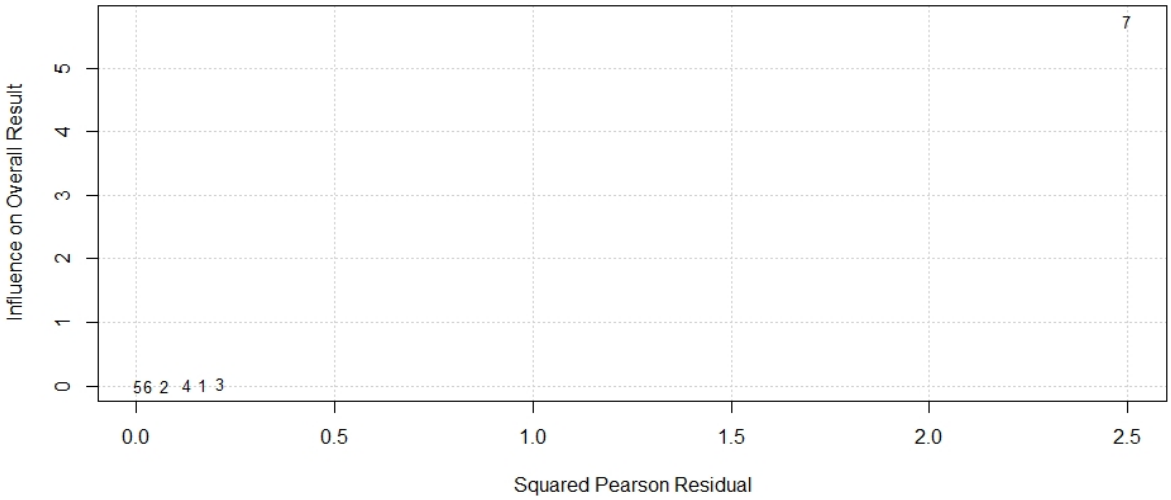
	current PT-DM	current PT-RLN	Goswami et al	Crumley et al	Brannon et al	Kim et al	Lee et al
current PT-DM		1.000	1.000	1.000	0.562	1.000	**1.88E-04**
current PT-RLN			1.000	1.000	0.722	1.000	**1.72E-03**
Goswami et al				1.000	**0.045**	1.000	**1.59E-09**
Crumley et al					0.776	1.000	**7.77E-05**
Brannon et al						1.000	**2.63E-06**
Kim et al							**2.49E-04**
Lee et al							

SUPPLEMENTAL FIGURE S2: Study comparison. (A) An omnibus Fisher exact test was performed to test whether there are any differences in the proportion of tumor pairs classified as concordant, overlapping, or discordant among the different studies. Results show that not all studies were the same in how they classified tumor pairs. (B) Because the omnibus test showed that there was a significant difference in at least one study, a pairwise comparison was performed. Lee *et al* was significantly different from all other studies in the proportions of patient-matched tumor pairs that were classified as concordant, overlapping, or discordant. P-values are shown for 2-tailed Fisher exact tests adjusted with Bonferroni correction. Significant differences are in bold ($\alpha = 0.05$).

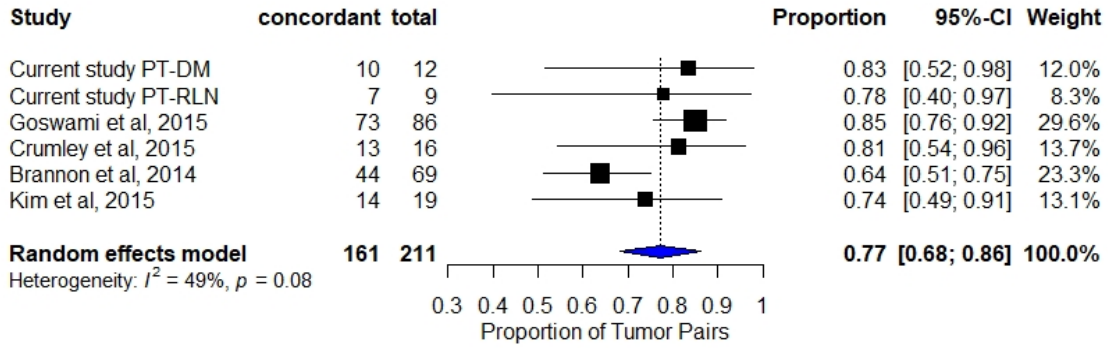
A. Diagnostic plots showing disproportionate influence of Lee et al study



B. Lee et al study has overly large contribution to heterogeneity and influence on pooled effect size



C. Primary and metastatic pairs are highly concordant for mutations in common cancer genes



SUPPLEMENTAL FIGURE S3: Meta-analysis for proportion of tumor pairs concordant for mutations in 50 common cancer genes. (A) Diagnostic plots showing the influence each study (x-axis) has on the studentized residual (rstudent), DIFFITS (dffits), Cook's distance (cook.d), covariance ratio (cov.r), τ^2 (tau2.del), Q_E (QE.del), hat matrix diagonals (hat), and weight. (B) Baujat plot showing that relative to the other studies, Lee et al (Study 7 on top right) unduly influences the pooled effect size (y-axis) and overly contributes to the overall heterogeneity among the studies as measured by Cochran's Q (x-axis). (C) About three quarters of tumor pairs can be expected to be genetically identical with respect to 50 genes. Lee et all was left out of this analysis. Still, however, about half the heterogeneity can be explained by the heterogeneity between studies (I^2 = 49%).