Supplementary Materials

- Fig. S1. Phenotype-phenotype associations
- Fig. S2. Volume by mutation.
- Fig. S3. Location and cystic structure VAF separated by individual mutation.
- Fig. S4. Head and neck LM staging system and genotype/stage results.
- Table S1. Phenotype data and sequencing results by individual. (See separate .xlsx file)
- Table S2. Genes included in smMIP panel.
- Table S3. Correlation of variant frequency with cell growth assays from Dogruluk et al. 2015 (31).

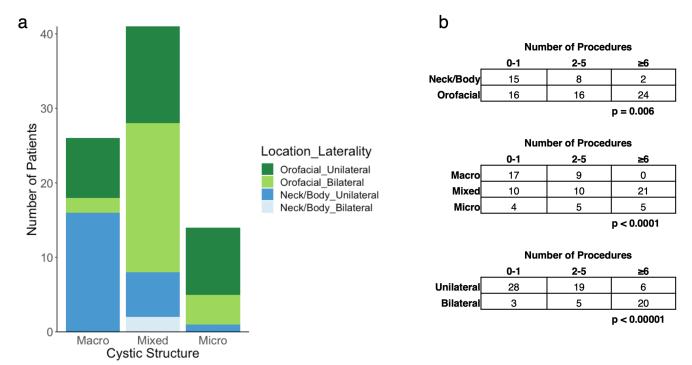


Figure S1: Phenotype-phenotype associations. (a) Histogram demonstrating relationship between location, laterality, and cystic structure. Unilateral neck and body lesions are predominantly macrocystic while microcystic lesions are predominantly in the orofacial region. (b) Contingency tables for number of procedures and location, laterality, and cystic structure demonstrating and increased number of procedures for orofacial, microcystic, and bilateral LMs.

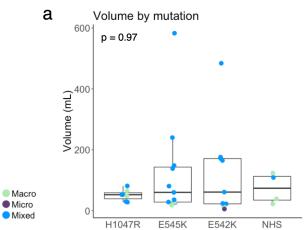


Figure S2: Volume by mutation. (a) Dot-box plot of volume by mutation (n = 31). *P* value indicates result of Kruskal-Wallis comparison. Boxes are defined by the 1st quartile inferiorly, median, and 3rd quartile superiorly with whiskers extending to the farthest non-outlier point (defined as within 3/2 times the interquartile range). Dot colors correspond to cystic structure: green – macrocystic, purple – microcystic, and blue – mixed cystic. Abbreviations: mL – milliliters.

Location separated by mutation a H1047R E545K E542K NHS 0.12 0.09 0.03

Neck/Body

Orofacial

Neck/Body

Orofacial

Orofacial

0.00

Neck/Body

Orofacial

Neck/Body

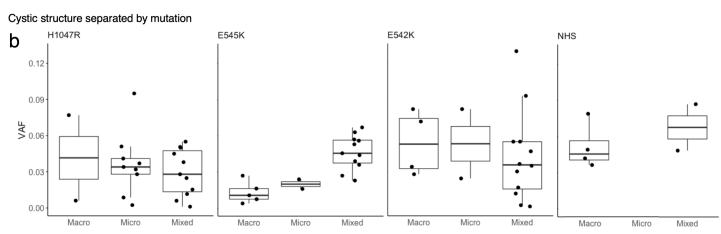


Figure S3: Location and cystic structure VAF separated by individual mutation. Dot-box plots of VAF by (a) location and (b) cystic structure separated by individual mutations (H1047R, n = 22; E545K, n = 18; E542K, n = 18; NHS, n = 6). Boxes are defined by the 1st quartile inferiorly, median, and 3rd quartile superiorly with whiskers extending to the farthest non-outlier point (defined as within 3/2 times the interquartile range). Abbreviations: NHS – non-hotspot mutations. VAF – variant allele fraction.

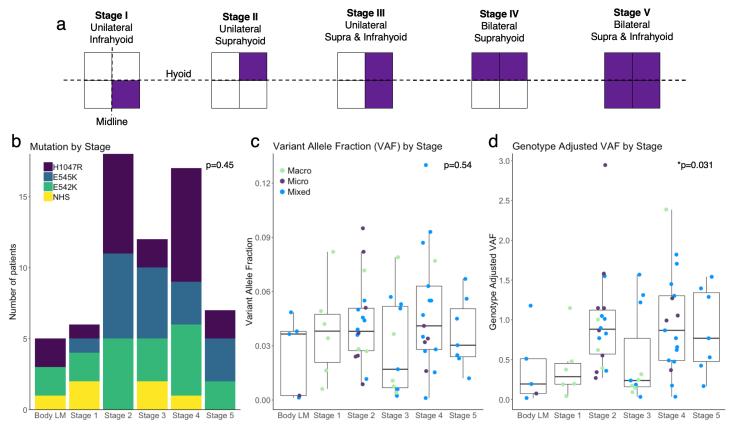


Figure S4: Head and neck LM staging system and genotype/stage results. (a) Schematic exemplifying the five de Serres clinical stages for head and neck LMs. (b) Histogram showing variation of mutations across stage. *P* value is for Fisher exact test. (c) Dot-box plot of VAF plotted by stage and (d) genotype adjusted VAF plotted by stage. *P* values are for Kruskal-Wallis tests. Dot colors correspond to cystic structure (pale green: macrocystic, purple: microcystic, blue: mixed cystic).

Abbreviations: LM – lymphatic malformation. NHS – non-hotspot mutations. VAF – variant allele fraction.

Table S2. Genes included in smMIP panel.

Gene # of MIPs ACVRL1 24 AKT3 23 ARAF 33 CCBE1 20 CCM2 28 CELSR1 127 CTNNB1 31 DCHS1 123 ENG 30 EPHB4 43 FAT4 159 FGFR1 42 FLT4 72 FOXC2 18 GATA2 21 GDF2 14 GJC2 15 GLMN 30 GNA11 18 GNAQ 14 HGF 35 HRAS 13 IDH1 19 IDH2 24 ITGA9 54 KIF11 47 KRAS 10 KRIT1 34 MAP2K1 19 MAP3K3 35 NRAS 8 PDCD10 9	Table S2. Genes	<u>included in</u>
AKT3 ARAF ARAF ARAF ARAF ARAF ARAF ARAF ARA	Gene	# of MIPs
ARAF 20 CCBE1 20 CCM2 28 CELSR1 127 CTNNB1 31 DCHS1 123 ENG 30 EPHB4 43 FAT4 159 FGFR1 42 FLT4 72 FOXC2 18 GATA2 21 GDF2 14 GJC2 15 GLMN 30 GNA11 18 GNAQ 14 HGF 35 HRAS 13 IDH1 19 IDH2 24 ITGA9 54 KIF11 47 KRAS 10 KRIT1 34 MAP2K1 19 MAP3K3 35 NRAS 8 PDCD10 9 PDGFRB 60 PIEZO1 133 PIK3CA 42 PIK3CA 42 PIK3CA 42 PIK3CA 42 PIK3CA 42 PIK3CA 42 PICAT ACCORD 16 PTPN14 48 RASA1 48 SMAD4 23 SOX18 14 TEK 49	ACVRL1	24
CCBE1 20 CCM2 28 CELSR1 127 CTNNB1 31 DCHS1 123 ENG 30 EPHB4 43 FAT4 159 FGFR1 42 FLT4 72 FOXC2 18 GATA2 21 GDF2 14 GJC2 15 GLMN 30 GNA11 18 GNAQ 14 HGF 35 HRAS 13 IDH1 19 IDH2 24 ITGA9 54 KIF11 47 KRAS 10 KRIT1 34 MAP2K1 19 MAP3K3 35 NRAS 8 PDCD10 9 PDGFRB 60 PIEZO1 133 PIK3CA 42 PIK3R6 38 PORCN 26 PTEN 16	AKT3	23
CCM2 28 CELSR1 127 CTNNB1 31 DCHS1 123 ENG 30 EPHB4 43 FAT4 159 FGFR1 42 FLT4 72 FOXC2 18 GATA2 21 GDF2 14 GJC2 15 GLMN 30 GNA11 18 GNAQ 14 HGF 35 HRAS 13 IDH1 19 IDH2 24 ITGA9 54 KIF11 47 KRAS 10 KRIT1 34 MAP2K1 19 MAP3K3 35 NRAS 8 PDCD10 9 PDGFRB 60 PIEZO1 133 PIK3CA 42 PIK3R6 38 PORCN 26 PTEN 16 PTPN14 48	ARAF	33
CELSR1 127 CTNNB1 31 DCHS1 123 ENG 30 EPHB4 43 FAT4 159 FGFR1 42 FLT4 72 FOXC2 18 GATA2 21 GDF2 14 GJC2 15 GLMN 30 GNA11 18 GNAQ 14 HGF 35 HRAS 13 IDH1 19 IDH2 24 ITGA9 54 KIF11 47 KRAS 10 KRIT1 34 MAP2K1 19 MAP3K3 35 NRAS 8 PDCD10 9 PDGFRB 60 PIEZO1 133 PIK3CA 42 PIK3R6 38 PORCN 26 PTEN 16 PTPN14 48 RASA1 48	CCBE1	20
CTNNB1 31 DCHS1 123 ENG 30 EPHB4 43 FAT4 159 FGFR1 42 FLT4 72 FOXC2 18 GATA2 21 GDF2 14 GJC2 15 GLMN 30 GNA11 18 GNAQ 14 HGF 35 HRAS 13 IDH1 19 IDH2 24 ITGA9 54 KIF11 47 KRAS 10 KRIT1 34 MAP2K1 19 MAP3K3 35 NRAS 8 PDCD10 9 PDGFRB 60 PIEZO1 133 PIK3CA 42 PIK3R6 38 PORCN 26 PTEN 16 PTPN14 48 RASA1 48 SMAD4 23	CCM2	28
DCHS1 123 ENG 30 EPHB4 43 FAT4 159 FGFR1 42 FLT4 72 FOXC2 18 GATA2 21 GDF2 14 GJC2 15 GLMN 30 GNA11 18 GNAQ 14 HGF 35 HRAS 13 IDH1 19 IDH2 24 ITGA9 54 KIF11 47 KRAS 10 KRIT1 34 MAP2K1 19 MAP3K3 35 NRAS 8 PDCD10 9 PDGFRB 60 PIEZO1 133 PIK3CA 42 PIK3R6 38 PORCN 26 PTEN 16 PTPN14 48 RASA1 48 SMAD4 23 SOX18 14	CELSR1	127
ENG 30 EPHB4 43 FAT4 159 FGFR1 42 FLT4 72 FOXC2 18 GATA2 21 GDF2 14 GJC2 15 GLMN 30 GNA11 18 GNAQ 14 HGF 35 HRAS 13 IDH1 19 IDH2 24 ITGA9 54 KIF11 47 KRAS 10 KRIT1 34 MAP2K1 19 MAP3K3 35 NRAS 8 PDCD10 9 PDGFRB 60 PIEZO1 133 PIK3CA 42 PIK3R6 38 PORCN 26 PTEN 16 PTPN14 48 RASA1 48 SMAD4 23 SOX18 14 TEK 49	CTNNB1	31
EPHB4 43 FAT4 159 FGFR1 42 FLT4 72 FOXC2 18 GATA2 21 GDF2 14 GJC2 15 GLMN 30 GNA11 18 GNAQ 14 HGF 35 HRAS 13 IDH1 19 IDH2 24 ITGA9 54 KIF11 47 KRAS 10 KRIT1 34 MAP2K1 19 MAP3K3 35 NRAS 8 PDCD10 9 PDGFRB 60 PIEZO1 133 PIK3CA 42 PIK3R6 38 PORCN 26 PTEN 16 PTPN14 48 RASA1 48 SMAD4 23 SOX18 14 TEK 49	DCHS1	123
FAT4 159 FGFR1 42 FLT4 72 FOXC2 18 GATA2 21 GDF2 14 GJC2 15 GLMN 30 GNA11 18 GNAQ 14 HGF 35 HRAS 13 IDH1 19 IDH2 24 ITGA9 54 KIF11 47 KRAS 10 KRIT1 34 MAP2K1 19 MAP3K3 35 NRAS 8 PDCD10 9 PDGFRB 60 PIEZO1 133 PIK3CA 42 PIK3R6 38 PORCN 26 PTEN 16 PTPN14 48 RASA1 48 SMAD4 23 SOX18 14 TEK 49	ENG	30
FGFR1 42 FLT4 72 FOXC2 18 GATA2 21 GDF2 14 GJC2 15 GLMN 30 GNA11 18 GNAQ 14 HGF 35 HRAS 13 IDH1 19 IDH2 24 ITGA9 54 KIF11 47 KRAS 10 KRIT1 34 MAP2K1 19 MAP3K3 35 NRAS 8 PDCD10 9 PDGFRB 60 PIEZO1 133 PIK3CA 42 PIK3R6 38 PORCN 26 PTEN 16 PTPN14 48 RASA1 48 SMAD4 23 SOX18 14 TEK 49	EPHB4	43
FLT4 72 FOXC2 18 GATA2 21 GDF2 14 GJC2 15 GLMN 30 GNA11 18 GNAQ 14 HGF 35 HRAS 13 IDH1 19 IDH2 24 ITGA9 54 KIF11 47 KRAS 10 KRIT1 34 MAP2K1 19 MAP3K3 35 NRAS 8 PDCD10 9 PDGFRB 60 PIEZO1 133 PIK3CA 42 PIK3R6 38 PORCN 26 PTEN 16 PTPN14 48 RASA1 48 SMAD4 23 SOX18 14 TEK 49	FAT4	159
FOXC2 18 GATA2 21 GDF2 14 GJC2 15 GLMN 30 GNA11 18 GNAQ 14 HGF 35 HRAS 13 IDH1 19 IDH2 24 ITGA9 54 KIF11 47 KRAS 10 KRIT1 34 MAP2K1 19 MAP3K3 35 NRAS 8 PDCD10 9 PDGFRB 60 PIEZO1 133 PIK3CA 42 PIK3R6 38 PORCN 26 PTEN 16 PTPN14 48 RASA1 48 SMAD4 23 SOX18 14 TEK 49	FGFR1	42
GATA2 21 GDF2 14 GJC2 15 GLMN 30 GNA11 18 GNAQ 14 HGF 35 HRAS 13 IDH1 19 IDH2 24 ITGA9 54 KIF11 47 KRAS 10 KRIT1 34 MAP2K1 19 MAP3K3 35 NRAS 8 PDCD10 9 PDGFRB 60 PIEZO1 133 PIK3CA 42 PIK3R6 38 PORCN 26 PTEN 16 PTPN14 48 RASA1 48 SMAD4 23 SOX18 14 TEK 49	FLT4	72
GDF2 14 GJC2 15 GLMN 30 GNA11 18 GNAQ 14 HGF 35 HRAS 13 IDH1 19 IDH2 24 ITGA9 54 KIF11 47 KRAS 10 KRIT1 34 MAP2K1 19 MAP3K3 35 NRAS 8 PDCD10 9 PDGFRB 60 PIEZO1 133 PIK3CA 42 PIK3R6 38 PORCN 26 PTEN 16 PTPN14 48 RASA1 48 SMAD4 23 SOX18 14 TEK 49	FOXC2	18
GJC2 15 GLMN 30 GNA11 18 GNAQ 14 HGF 35 HRAS 13 IDH1 19 IDH2 24 ITGA9 54 KIF11 47 KRAS 10 KRIT1 34 MAP2K1 19 MAP3K3 35 NRAS 8 PDCD10 9 PDGFRB 60 PIEZO1 133 PIK3CA 42 PIK3R6 38 PORCN 26 PTEN 16 PTPN14 48 RASA1 48 SMAD4 23 SOX18 14 TEK 49	GATA2	21
GLMN 30 GNA11 18 GNAQ 14 HGF 35 HRAS 13 IDH1 19 IDH2 24 ITGA9 54 KIF11 47 KRAS 10 KRIT1 34 MAP2K1 19 MAP3K3 35 NRAS 8 PDCD10 9 PDGFRB 60 PIEZO1 133 PIK3CA 42 PIK3R6 38 PORCN 26 PTEN 16 PTPN14 48 RASA1 48 SMAD4 23 SOX18 14 TEK 49	GDF2	14
GNA11 18 GNAQ 14 HGF 35 HRAS 13 IDH1 19 IDH2 24 ITGA9 54 KIF11 47 KRAS 10 KRIT1 34 MAP2K1 19 MAP3K3 35 NRAS 8 PDCD10 9 PDGFRB 60 PIEZO1 133 PIK3CA 42 PIK3R6 38 PORCN 26 PTEN 16 PTPN14 48 RASA1 48 SMAD4 23 SOX18 14 TEK 49	GJC2	15
GNAQ 14 HGF 35 HRAS 13 IDH1 19 IDH2 24 ITGA9 54 KIF11 47 KRAS 10 KRIT1 34 MAP2K1 19 MAP3K3 35 NRAS 8 PDCD10 9 PDGFRB 60 PIEZO1 133 PIK3CA 42 PIK3R6 38 PORCN 26 PTEN 16 PTPN14 48 RASA1 48 SMAD4 23 SOX18 14 TEK 49	GLMN	30
HGF 35 HRAS 13 IDH1 19 IDH2 24 ITGA9 54 KIF11 47 KRAS 10 KRIT1 34 MAP2K1 19 MAP3K3 35 NRAS 8 PDCD10 9 PDGFRB 60 PIEZO1 133 PIK3CA 42 PIK3R6 38 PORCN 26 PTEN 16 PTPN14 48 RASA1 48 SMAD4 23 SOX18 14 TEK 49	GNA11	18
HRAS 13 IDH1 19 IDH2 24 ITGA9 54 KIF11 47 KRAS 10 KRIT1 34 MAP2K1 19 MAP3K3 35 NRAS 8 PDCD10 9 PDGFRB 60 PIEZO1 133 PIK3CA 42 PIK3R6 38 PORCN 26 PTEN 16 PTPN14 48 RASA1 48 SMAD4 23 SOX18 14 TEK 49	GNAQ	14
IDH1 19 IDH2 24 ITGA9 54 KIF11 47 KRAS 10 KRIT1 34 MAP2K1 19 MAP3K3 35 NRAS 8 PDCD10 9 PDGFRB 60 PIEZO1 133 PIK3CA 42 PIK3R6 38 PORCN 26 PTEN 16 PTPN14 48 RASA1 48 SMAD4 23 SOX18 14 TEK 49	HGF	35
IDH2 24 ITGA9 54 KIF11 47 KRAS 10 KRIT1 34 MAP2K1 19 MAP3K3 35 NRAS 8 PDCD10 9 PDGFRB 60 PIEZO1 133 PIK3CA 42 PIK3R6 38 PORCN 26 PTEN 16 PTPN14 48 RASA1 48 SMAD4 23 SOX18 14 TEK 49	HRAS	13
ITGA9 54 KIF11 47 KRAS 10 KRIT1 34 MAP2K1 19 MAP3K3 35 NRAS 8 PDCD10 9 PDGFRB 60 PIEZO1 133 PIK3CA 42 PIK3R6 38 PORCN 26 PTEN 16 PTPN14 48 RASA1 48 SMAD4 23 SOX18 14 TEK 49	IDH1	19
KIF11 47 KRAS 10 KRIT1 34 MAP2K1 19 MAP3K3 35 NRAS 8 PDCD10 9 PDGFRB 60 PIEZO1 133 PIK3CA 42 PIK3R6 38 PORCN 26 PTEN 16 PTPN14 48 RASA1 48 SMAD4 23 SOX18 14 TEK 49	IDH2	24
KRAS 10 KRIT1 34 MAP2K1 19 MAP3K3 35 NRAS 8 PDCD10 9 PDGFRB 60 PIEZO1 133 PIK3CA 42 PIK3R6 38 PORCN 26 PTEN 16 PTPN14 48 RASA1 48 SMAD4 23 SOX18 14 TEK 49	ITGA9	54
KRIT1 34 MAP2K1 19 MAP3K3 35 NRAS 8 PDCD10 9 PDGFRB 60 PIEZO1 133 PIK3CA 42 PIK3R6 38 PORCN 26 PTEN 16 PTPN14 48 RASA1 48 SMAD4 23 SOX18 14 TEK 49	KIF11	47
MAP2K1 19 MAP3K3 35 NRAS 8 PDCD10 9 PDGFRB 60 PIEZO1 133 PIK3CA 42 PIK3R6 38 PORCN 26 PTEN 16 PTPN14 48 RASA1 48 SMAD4 23 SOX18 14 TEK 49	KRAS	10
MAP3K3 35 NRAS 8 PDCD10 9 PDGFRB 60 PIEZO1 133 PIK3CA 42 PIK3R6 38 PORCN 26 PTEN 16 PTPN14 48 RASA1 48 SMAD4 23 SOX18 14 TEK 49	KRIT1	34
NRAS 8 PDCD10 9 PDGFRB 60 PIEZO1 133 PIK3CA 42 PIK3R6 38 PORCN 26 PTEN 16 PTPN14 48 RASA1 48 SMAD4 23 SOX18 14 TEK 49	MAP2K1	19
PDCD10 9 PDGFRB 60 PIEZO1 133 PIK3CA 42 PIK3R6 38 PORCN 26 PTEN 16 PTPN14 48 RASA1 48 SMAD4 23 SOX18 14 TEK 49	MAP3K3	35
PDGFRB 60 PIEZO1 133 PIK3CA 42 PIK3R6 38 PORCN 26 PTEN 16 PTPN14 48 RASA1 48 SMAD4 23 SOX18 14 TEK 49	NRAS	8
PIEZO1 133 PIK3CA 42 PIK3R6 38 PORCN 26 PTEN 16 PTPN14 48 RASA1 48 SMAD4 23 SOX18 14 TEK 49	PDCD10	9
PIK3CA 42 PIK3R6 38 PORCN 26 PTEN 16 PTPN14 48 RASA1 48 SMAD4 23 SOX18 14 TEK 49	PDGFRB	60
PIK3R6 38 PORCN 26 PTEN 16 PTPN14 48 RASA1 48 SMAD4 23 SOX18 14 TEK 49	PIEZO1	133
PORCN 26 PTEN 16 PTPN14 48 RASA1 48 SMAD4 23 SOX18 14 TEK 49	PIK3CA	42
PTEN 16 PTPN14 48 RASA1 48 SMAD4 23 SOX18 14 TEK 49	PIK3R6	38
PTPN14 48 RASA1 48 SMAD4 23 SOX18 14 TEK 49	PORCN	26
RASA1 48 SMAD4 23 SOX18 14 TEK 49	PTEN	16
SMAD4 23 SOX18 14 TEK 49	PTPN14	48
SOX18 14 TEK 49	RASA1	48
TEK 49	SMAD4	23
	SOX18	14
VEGFC 17	TEK	49
	VEGFC	17

Table S3. Correlation of variant frequency with cell growth assays from Dogruluk et al., 2015 (31).

Count (COSMIC, all (all (COSMIC, all (all (COSMIC, all (all (cosmic, all (cosmic, ali)
PIK3CA Variant (COSMIC, all cancers) (total PIK3CA variants = 13969) change (mean) [Fig.2b (29)] change (mean) [Fig.2d (29)] H1047R 4266 30.54 48.4 16.5 E545K 3174 22.72 52.3 10.8 E542K 1953 13.98 51.2 6.1 H1047L 583 4.17 46.0 5.9 E545A 269 1.93 20.9 5.3 Q546K 241 1.73 30.1 7.1 E545G 204 1.46 21.0 5.7 N345K 202 1.45 36.2 4.2 C420R 168 1.20 32.7 5.3 H1047Y 119 0.85 5.5 2.3 M1043I 106 0.76 2.7 1.6 G1049R 102 0.73 20.8 9.0 Q546R 102 0.73 24.1 5.5 E545Q 73 0.52 6.1 2.8
PIK3CA Variant cancers) variants = 13969) [Fig.2b (29)] [Fig.2d (29)] H1047R 4266 30.54 48.4 16.5 E545K 3174 22.72 52.3 10.8 E542K 1953 13.98 51.2 6.1 H1047L 583 4.17 46.0 5.9 E545A 269 1.93 20.9 5.3 Q546K 241 1.73 30.1 7.1 E545G 204 1.46 21.0 5.7 N345K 202 1.45 36.2 4.2 C420R 168 1.20 32.7 5.3 H1047Y 119 0.85 5.5 2.3 M1043I 106 0.76 2.7 1.6 G1049R 102 0.73 20.8 9.0 Q546R 102 0.73 24.1 5.5 E545Q 73 0.52 6.1 2.8 M1043V 62 0.44
H1047R 4266 30.54 48.4 16.5 E545K 3174 22.72 52.3 10.8 E542K 1953 13.98 51.2 6.1 H1047L 583 4.17 46.0 5.9 E545A 269 1.93 20.9 5.3 Q546K 241 1.73 30.1 7.1 E545G 204 1.46 21.0 5.7 N345K 202 1.45 36.2 4.2 C420R 168 1.20 32.7 5.3 H1047Y 119 0.85 5.5 2.3 M1043I 106 0.76 2.7 1.6 G1049R 102 0.73 20.8 9.0 Q546R 102 0.73 24.1 5.5 E545Q 73 0.52 6.1 2.8 M1043V 62 0.44 5.7 3.1 E453K 61 0.44 8.4 3.4
E542K 1953 13.98 51.2 6.1 H1047L 583 4.17 46.0 5.9 E545A 269 1.93 20.9 5.3 Q546K 241 1.73 30.1 7.1 E545G 204 1.46 21.0 5.7 N345K 202 1.45 36.2 4.2 C420R 168 1.20 32.7 5.3 H1047Y 119 0.85 5.5 2.3 M1043I 106 0.76 2.7 1.6 G1049R 102 0.73 20.8 9.0 Q546R 102 0.73 24.1 5.5 E545Q 73 0.52 6.1 2.8 M1043V 62 0.44 5.7 3.1 E453K 61 0.44 8.4 3.4 Q546P 46 0.33 23.0 5.8 N1044K 41 0.29 8.0 3.1
H1047L 583 4.17 46.0 5.9 E545A 269 1.93 20.9 5.3 Q546K 241 1.73 30.1 7.1 E545G 204 1.46 21.0 5.7 N345K 202 1.45 36.2 4.2 C420R 168 1.20 32.7 5.3 H1047Y 119 0.85 5.5 2.3 M1043I 106 0.76 2.7 1.6 G1049R 102 0.73 20.8 9.0 Q546R 102 0.73 24.1 5.5 E545Q 73 0.52 6.1 2.8 M1043V 62 0.44 5.7 3.1 E453K 61 0.44 8.4 3.4 Q546P 46 0.33 23.0 5.8 N1044K 41 0.29 8.0 3.1 K111N 39 0.28 2.4 1.1
E545A 269 1.93 20.9 5.3 Q546K 241 1.73 30.1 7.1 E545G 204 1.46 21.0 5.7 N345K 202 1.45 36.2 4.2 C420R 168 1.20 32.7 5.3 H1047Y 119 0.85 5.5 2.3 M1043I 106 0.76 2.7 1.6 G1049R 102 0.73 20.8 9.0 Q546R 102 0.73 24.1 5.5 E545Q 73 0.52 6.1 2.8 M1043V 62 0.44 5.7 3.1 E453K 61 0.44 8.4 3.4 Q546P 46 0.33 23.0 5.8 N1044K 41 0.29 8.0 3.1 K111N 39 0.28 2.4 1.1
Q546K 241 1.73 30.1 7.1 E545G 204 1.46 21.0 5.7 N345K 202 1.45 36.2 4.2 C420R 168 1.20 32.7 5.3 H1047Y 119 0.85 5.5 2.3 M1043I 106 0.76 2.7 1.6 G1049R 102 0.73 20.8 9.0 Q546R 102 0.73 24.1 5.5 E545Q 73 0.52 6.1 2.8 M1043V 62 0.44 5.7 3.1 E453K 61 0.44 8.4 3.4 Q546P 46 0.33 23.0 5.8 N1044K 41 0.29 8.0 3.1 K111N 39 0.28 2.4 1.1
E545G 204 1.46 21.0 5.7 N345K 202 1.45 36.2 4.2 C420R 168 1.20 32.7 5.3 H1047Y 119 0.85 5.5 2.3 M1043I 106 0.76 2.7 1.6 G1049R 102 0.73 20.8 9.0 Q546R 102 0.73 24.1 5.5 E545Q 73 0.52 6.1 2.8 M1043V 62 0.44 5.7 3.1 E453K 61 0.44 8.4 3.4 Q546P 46 0.33 23.0 5.8 N1044K 41 0.29 8.0 3.1 K111N 39 0.28 2.4 1.1
N345K 202 1.45 36.2 4.2 C420R 168 1.20 32.7 5.3 H1047Y 119 0.85 5.5 2.3 M1043I 106 0.76 2.7 1.6 G1049R 102 0.73 20.8 9.0 Q546R 102 0.73 24.1 5.5 E545Q 73 0.52 6.1 2.8 M1043V 62 0.44 5.7 3.1 E453K 61 0.44 8.4 3.4 Q546P 46 0.33 23.0 5.8 N1044K 41 0.29 8.0 3.1 K111N 39 0.28 2.4 1.1
C420R 168 1.20 32.7 5.3 H1047Y 119 0.85 5.5 2.3 M1043I 106 0.76 2.7 1.6 G1049R 102 0.73 20.8 9.0 Q546R 102 0.73 24.1 5.5 E545Q 73 0.52 6.1 2.8 M1043V 62 0.44 5.7 3.1 E453K 61 0.44 8.4 3.4 Q546P 46 0.33 23.0 5.8 N1044K 41 0.29 8.0 3.1 K111N 39 0.28 2.4 1.1
H1047Y 119 0.85 5.5 2.3 M1043I 106 0.76 2.7 1.6 G1049R 102 0.73 20.8 9.0 Q546R 102 0.73 24.1 5.5 E545Q 73 0.52 6.1 2.8 M1043V 62 0.44 5.7 3.1 E453K 61 0.44 8.4 3.4 Q546P 46 0.33 23.0 5.8 N1044K 41 0.29 8.0 3.1 K111N 39 0.28 2.4 1.1
M1043I 106 0.76 2.7 1.6 G1049R 102 0.73 20.8 9.0 Q546R 102 0.73 24.1 5.5 E545Q 73 0.52 6.1 2.8 M1043V 62 0.44 5.7 3.1 E453K 61 0.44 8.4 3.4 Q546P 46 0.33 23.0 5.8 N1044K 41 0.29 8.0 3.1 K111N 39 0.28 2.4 1.1
G1049R 102 0.73 20.8 9.0 Q546R 102 0.73 24.1 5.5 E545Q 73 0.52 6.1 2.8 M1043V 62 0.44 5.7 3.1 E453K 61 0.44 8.4 3.4 Q546P 46 0.33 23.0 5.8 N1044K 41 0.29 8.0 3.1 K111N 39 0.28 2.4 1.1
Q546R 102 0.73 24.1 5.5 E545Q 73 0.52 6.1 2.8 M1043V 62 0.44 5.7 3.1 E453K 61 0.44 8.4 3.4 Q546P 46 0.33 23.0 5.8 N1044K 41 0.29 8.0 3.1 K111N 39 0.28 2.4 1.1
E545Q 73 0.52 6.1 2.8 M1043V 62 0.44 5.7 3.1 E453K 61 0.44 8.4 3.4 Q546P 46 0.33 23.0 5.8 N1044K 41 0.29 8.0 3.1 K111N 39 0.28 2.4 1.1
M1043V 62 0.44 5.7 3.1 E453K 61 0.44 8.4 3.4 Q546P 46 0.33 23.0 5.8 N1044K 41 0.29 8.0 3.1 K111N 39 0.28 2.4 1.1
E453K 61 0.44 8.4 3.4 Q546P 46 0.33 23.0 5.8 N1044K 41 0.29 8.0 3.1 K111N 39 0.28 2.4 1.1
Q546P 46 0.33 23.0 5.8 N1044K 41 0.29 8.0 3.1 K111N 39 0.28 2.4 1.1
N1044K 41 0.29 8.0 3.1 K111N 39 0.28 2.4 1.1
K111N 39 0.28 2.4 1.1
P539R 32 0.23 6.1 2.6
Q546E 24 0.17 12.6 3.2
T1025T 22 0.16 1.4 1.6
E542V 18 0.13 7.3 3.6
N345I 15 0.11 3.9 2.6
H701P 8 0.06 1.1 0.5
A1020V 4 0.03 0.9 1.3
131M 2 0.01 1.2 1.4

Pearson correlation with COSMIC frequency

r = 0.72 P = 2.45E-5

r = 0.82 P = 1.33E-7