

**Bioinformatics and Experimental Validation for Identifying Biomarkers  
Associated with AMG510 (Sotorasib) Resistance in  
KRAS<sup>G12C</sup>-Mutated Lung adenocarcinoma**

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**GO and KEGG Functional Annotation**

The annotation and visualization processes were performed utilizing the Metascape database ([www.metascape.org](http://www.metascape.org)). Our analysis focused on assessing the enrichment of differentially expressed genes in the Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways and Gene Ontology (GO) terms. To establish statistical significance, we set criteria that included at least three overlaps and a P-value at or below 0.01.

**Table S1.** Primer sequences for RT-qPCR

SLC2A1	F:5'-GAGCAGCTACCCTGGATGTC-3'
	R:5'-GGCCACAAAGCCAAAGATGG-3'
TLE1	F:5'-GGCTGCACTCTCATAGTGGG-3'
	R:5'-AAGCAGACCTTGAATCGGG-3'
FAM83A	F:5'-GTGGAGCTGTTTGACGAGGA-3'
	R:5'-CATCACAGGCTTGGAGGAGG-3'
HMGA2	F:5'-CCACTTCAGCCCAGGGACAA-3'
	R:5'-TCCTCTCTTCTGAGGCGCTG-3'
FBX044	F:5'-ATCCTGCTGGAGCTGTTCAC-3'
	R:5'-GTTTCCAGAGGGTCACGAGG-3'

**Table S2.** Differentially expressed genes (up- and down-regulated)

DEGs	Gene name
<b>Upregulated (431)</b>	CD24, SLC16A7, BPIFB1, LGALS9, MAP2, TMEM176B, SLC44A4, TMC5, PROM1, ITM2A, CTSS, FAM3D, SLPI, LITAF, CLDN3, ALDH1A1, TTR, CREB3L1, TOX3, SORBS2, CDS1, FER1L6, PDZK1IP1, PLA2G10, ELAPOR1, GSTA1, CEACAM5, RETREG1, DHRS3, F2RL2, GALNTL6, MUC16, LINC00942, NPNT, GMDS, VTCN1, TC2N, MACC1, PLCL2, SCGB2A1, KRTCAP3, PSMB9, HLA-B, OCLN, SPINK1, ASRGL1, KIAA0319, ST6GAL1, VDR, DSTN, C2orf72, GDF15, CDR2L, PLAAT4, ANG, ARFGEF3, ZNF703, WFDC2, ELF3, CYP4F3, HRH2, AGT, TP53I11, CYB5A, SHROOM1, LINC02532, AP1M2, ONECUT2, TMED6, C5, SEMA5A, FOSL2, NCOA7, KCNS3, TRIM16L, SMIM31, THSD7A, MUC4, GALNT7, RASSF5, APOD, LYPD6B, VWA5A, MARCHF3, ITGB6, XBP1, MAST4, PTGR1, PHEX, CLDN7, MIR9-1HG, RCAN2, PGGHG, MECOM, CCL28, CFB, AL121839.2, CLDN1, ABCA12, LINC02381, CXCL16, NQO1, F5, MITF, CFH, NFKBIZ, ARRB2, MATN2, FAM102A, RNASE4, GOLPH3L, ARHGDIB, ECI2, CNR1, PLA1A, CHCHD7, MLXIP, EMBP1, ATP2C2, ADGRF1, CFI, BEX4, PIP, NCF2, TSPAN13, GSTP1, B2M, CXCL1, SEMA6A, FUT2, CCDC198, MTUS1, ADGRV1, C4orf19, AC131206.1, BAAT, CTDSP2,

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NUCB2, RHBDL2, OPHN1, ERMP1, FTH1, RNF217-AS1, EDN1, SLC29A1, SLC35C1, BMP2, CCDC18-AS1, UCHL1, SCRN1, SLC1A1, HOXA-AS2, GADD45G, CPLX2, CHP1, CLIC6, DCPS, HLA-E, GOLM1, CBR1, LCP1, AC006230.1, ACSS1, MPLKIP, BMP3, GLTPD2, ARHGEF17, DRAIC, AQP1, CPS1, REPIN1, COL4A4, SLC38A10, RND3, FXYD3, ADH1C, PLCXD2, RABGAP1L, GALM, MX1, GALNT3, ALOX5, IFNAR2, YIPF2, DMKN, NSF, SUSL6, LCN2, CRABP2, TPP2, BACE2, KIF26B, EMP2, KRT7, SORT1, MGAT1, SCN2A, HLA-A, TM7SF2, ARHGAP23, HS3ST1, FOXA1, NFIA, SPSB2, ABHD17A, CYP2B7P, AHSA2P, FAM133A, AC009407.1, KRT4, AKR1C4, ANKFN1, TRIP6, CBX6, SCAMP2, IRF2BP2, MMP7, TTC39A, IGFBP4, C1S, FTL, ZNF572, ANKRD36C, IFI27, RNF103, CACNA1H, MBOAT1, SLC22A17, PDE1B, FAM214A, VPS45, HES1, CYP4F11, COL4A3, C2orf15, SRGAP3, ABCA5, RRNAD1, TMEM125, BICDL2, EPB41L5, SLC25A29, QPRT, TMEM106C, ABHD11, GCLM, H2BC21, PAK1, PI3R, EPB41L1, PLCB2, DAPK1, EPB41L4A, CBR3, PARM1, LIMK2, SH3BGRL2, CCDC170, FOXP2, RAB40B, SMOC1, AL033397.1, C1orf216, ALDH3B1, AC019322.4, MGAT4A, HOXC6, TMEM9B, PHLDB2, GABARAPL1, UNC93B1, RPRML, CEBPA, VSTM2L, ZNF12, GLIS3, TLE1, PTPRF, AKR1C1, AR, PIK3C2B, CLDN4, BLCAP, CAT, ZER1, HLA-F, FILIP1L, AKR1C3, POU4F1, AC135050.6, KCNK5, GATM, NMRAL2P, ARMH4, PROC, IRF1, TALDO1, TNS3, TCEA3, SEPHS2, TMEM59, SYTL2, FRK, SLC40A1, SMIM4, PRR15L, IRF6, COL27A1, EFNA1, NRARP, SECTM1, AC010168.2, RAB11FIP5, AC004951.1, AC004870.2, ST14, PSMD11, CAMK1D, SAMD9L, PCED1B, TNRC6C, TRAPPC4, AL591895.1, ZNF277, ABL1, MBNL3, ADAR, TM4SF5, MYLIP, CLTRN, PLCB1, UBE2L6, CCDC7, RBM47, PDE5A, SLC48A1, AOC1, CD38, CD63, PCAT7, TMC4, LINC00632, MAP1A, RTN3, JUP, AC027117.1, PSMB8, TMEM230, TSPAN7, PSMB8-AS1, PARD3B, CCPG1, OSGIN1, SGSM1, IFIT3, CCNJL, AQP3, FSTL1, PRKAB1, LRIG1, DHRS7B, CDH1, SELL, LINC00342, PRRG4, PRKCB, SLC1A5, LASP1, HMGB3, NEURL1B, BLOC1S4, PRSS16, TACSTD2, RARRES2, GALNT6, NAA20, NCALD, SDCBP2, NORAD, PEG10, SCNN1A, SLC15A2, RNF113A, BANK1, TOX, ACOT13, LYZ, RUSF1, HNRNP2, PRSS8, DPP3, PKDCC, SMAGP, GDA, MAL2, GUCD1, GULP1, FUT6, MBNL1, AC124319.1, ARSL, BCAS4, HYI, MGST1, HPN, FOLR1, HMGCS2, SSPN, LINC02503, ACADVL, TMEM106A,

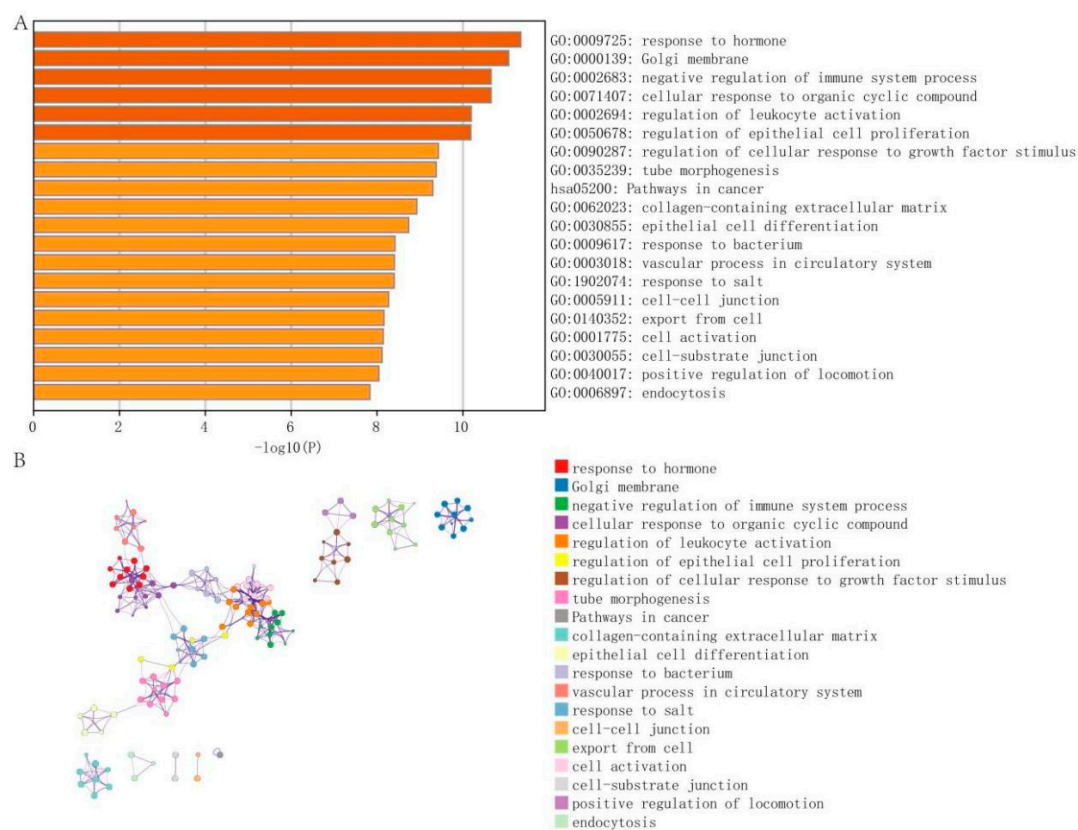
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<b>Downregulated (403)</b>	CPE, CACNA2D4, LY6D, LAMA4, LRCH1, CST1, CYSRT1, CST4, S100A1, PDLIM4, PDLIM7, KCNJ12, S100A13, AC138230.1, UTRN, SLC20A1, CSGALNACT1, CHST6, HTRA1, TRNP1, ITGB3, CYP27C1, JCAD, GNG4, ITGA5, NET1, EVPL, MRPS6, GPER1, AC010198.2, GRK6, ITGA6, SLC5A3, ADGRG6, SPRED3, AC018629.1, LFNG, LTBP2, HRAS, ITGB4, HDAC11, TYRO3, FABP5, TESC, PACSIN3, PDE4B, CDCP1, ZBTB1, PPTC7, S100A16, UNC13A, AL161431.1, RGS10, SATB2, ATOX1, BMERB1, AP1S1, CDC25B, NT5E, DUSP5-DT, RAB31, NT5DC3, MASTL, FMNL1, SCG2, IGFBP1, GAS2L1, LGALS1, PRSS3, RNU5F-1, COL6A2, ACOT7, SUFU, ETV4, AXL, CCNG1, PNPLA3, BASP1, MOB3A, ARL14, DCLK1, PPP5C, NOS1, CAV1, SLC44A3-AS1, UBE2E2, NDE1, GPAT3, CAPG, TIAM1, SMOX, CPVL, CD320, CEP19, COL6A1, POLRMT, SPRYD7, SLC30A1, ADIRF, ROBO1, PCID2, SULF2, OSBPL11, ADAM8, ITPRID2, SH2D2A, AC010624.5, IL27RA, HSD17B1, ZFYVE19, SEC14L2, GRAMD1B, MORC4, TNNT1, NPW, GAREM1, CDYL2, EFN2, MT-TT, ONECUT3, ZNF524, DDB2, MMP28, LINC02595, CDKN2AIP, EMP3, KANK2, GAL3ST1, PLOD3, PLEKHG5, CAPRIN2, ERFF1, A4GALT, S100A2, HPGD, ASIC1, COL17A1, FAM210A, TOB1, VCAN, STMN2, FBN1, CADM1, DLGAP4, CSGALNACT2, NOSTRIN, KCNC4, ID2, PCCA-DT, RUNX3, TCF7L2, STC1, SOD3, MXRA7, PRR7, BCL9L, LRRC8E, RORA, LINC01239, RRAS, PPP1R3C, BCL2L1, ADAM12, PIP5K1C, TCN1, NUP62CL, ZNF581, DRG1, TGFB1, SSTR5-AS1, FJX1, KIAA1549, SLC35F2, AP2S1, PLAT, EHD2, ANKRD18B, LRRC28, MCM8, AL035252.5, SDR16C5, ABO, BIRC7, TBC1D4, CFAP251, AHNK2, DUSP6, SLBP, INTS2, CFD, TPK1, FBXO44, CTNNA1, SOCS6, PALM2AKAP2, NNMT, CSKMT, BAIAP2L2, RAB27B, HMGA2, PAQR5, TNFRSF18, HBEGF, TMCO3, MT-TS2, JAG1, TNFRSF10D, JOSD2, FOXC2, C10orf88, YBEY, MDFI, SEMA3A, SERPINB8, FAM89B, XRCC3, NUDT18, AFAP1, NAB1, ZNF219, PLEKHG2, AHR, ADAM19, LIAS, LYNX1, TOP1MT, PAEP, CDH19, STXBP1, CCDC102A, RRP9, AL035530.2, NES, HSD17B2, TMEM209, CARD10, TCEA2, FUT11, NOSIP, TRIM7, RPL29, EREG, MAPKBP1, PPAN, BICDL1, ZNRF3, CHEK1, ITCH, ELK4, GCAT, RAP1GAP2, CEP131, SENP3, EHBP1L1, FAM83A,

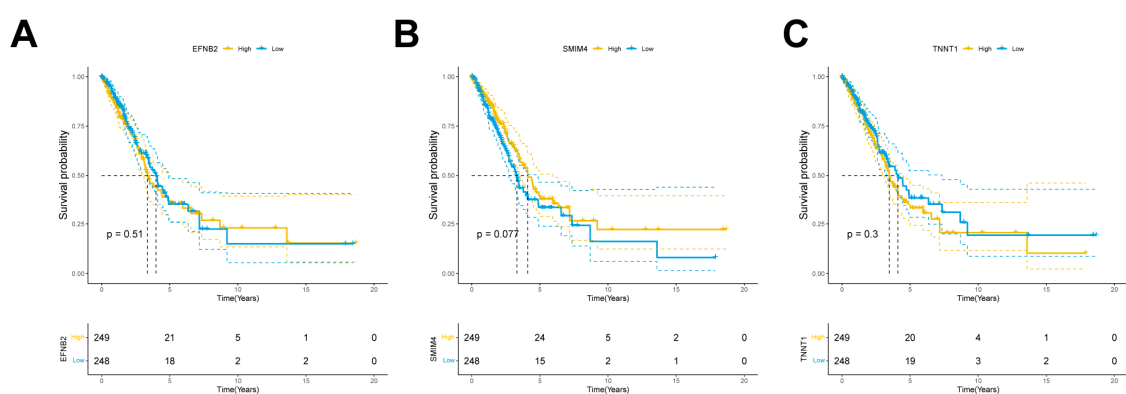
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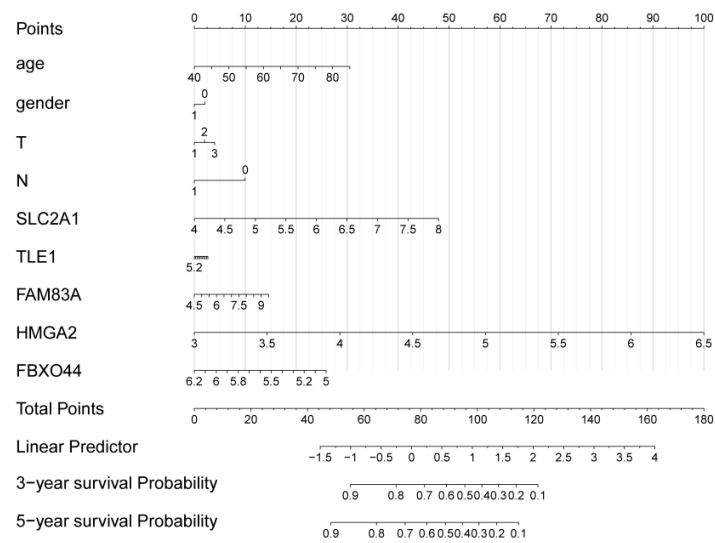
**Figure S1.** Functional enrichment of DEGs by metascape enrichment analysis.



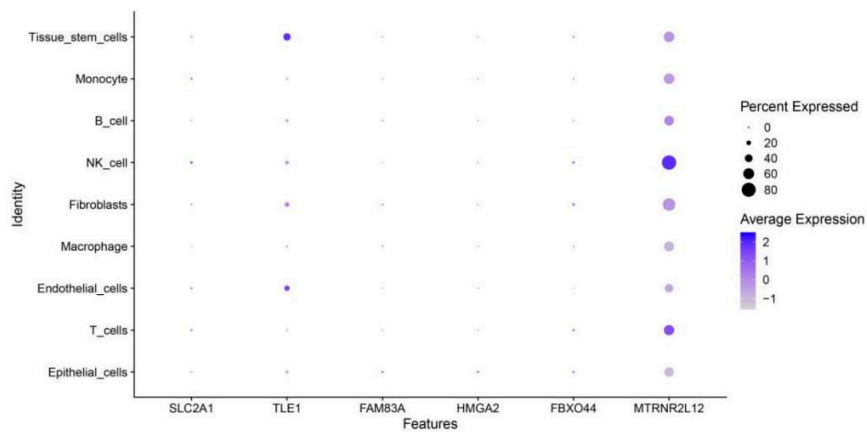
**Figure S2.** The expression levels of EFNB2, SMIM4, and TNNT1 and their association with LUAD patient prognosis.



Figure S3. SLC2A1 correlates with LUAD-related signalling molecules



**Figure S4.** Nomogram and calibration curves for prediction of prognosis of LUAD patients (GSE30219)



**Figure S5.** Distribution of key genes for drug resistance in 9 different cell types.