

Supplementary Information

Profiling cisplatin resistance in head and neck cancer: a critical role of the VRAC ion channel for chemoresistance

Svenja Siemer¹, Torsten Fauth², Paul Scholz², Yara Al-Zamel¹, Aya Khamis¹, Désirée Gül¹, Laura

Freudelsperger¹, Barbara Wollenberg³, Sven Becker^{1,4}, Roland H. Stauber^{1,*}, and Jan Hagemann¹

¹ Department of Otorhinolaryngology Head and Neck Surgery; Molecular and Cellular Oncology; University Medical Center, Mainz, Germany; svenja.siemer@uni-mainz.de (S.S); yalzamel@students.uni-mainz.de (Y.A.); ayakhamis@uni-mainz.de (A.K.); desiree.guel@unimedizin-mainz.de (D.G.); laura.freudelsperger@unimedizin-mainz.de (L.F.); rstauber@uni-mainz.de (R.S.); jan.hagemann@unimedizin-mainz.de (J.H.)

² BRAIN AG, Zwingenberg, Germany; ps@brain-biotech.de (P.S.); tf@brain-biotech.de (T.F.)

³ Department of Otorhinolaryngology Head and Neck Surgery, University Hospital Klinikum rechts der Isar, Munich, Germany; Barbara.wollenberg@tum.de (B.W.)

⁴ Department of Otorhinolaryngology, University Medical Center Tuebingen, Tuebingen, Germany; sven.becker@med.uni-tuebingen.de (S.B.)

*Correspondence: rstauber@uni-mainz.de, Tel.: +49-0-6131177002

Received: date; Accepted: date; Published: date

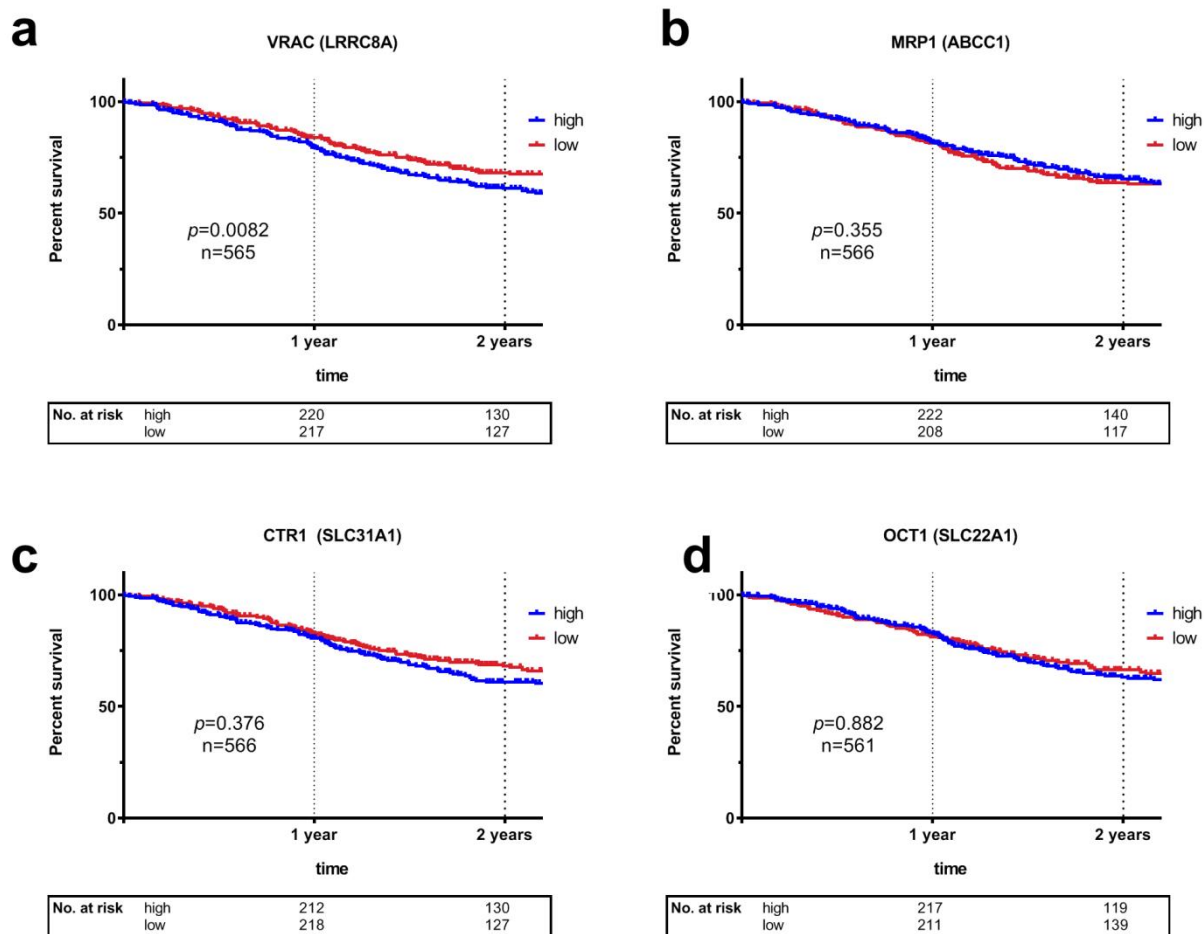


Fig. S1: Overall survival of HNSCC patients correlating with potential cisplatin resistance candidates. Overall survival of HNSCC patients depending on (a) VRAC (LRRC8A), (b) MRP1 (ABCC1), (c) CTR1 (SLC31A1), and (d) OCT1 (SLC22A1) expression levels shown by Kaplan Meier plots.

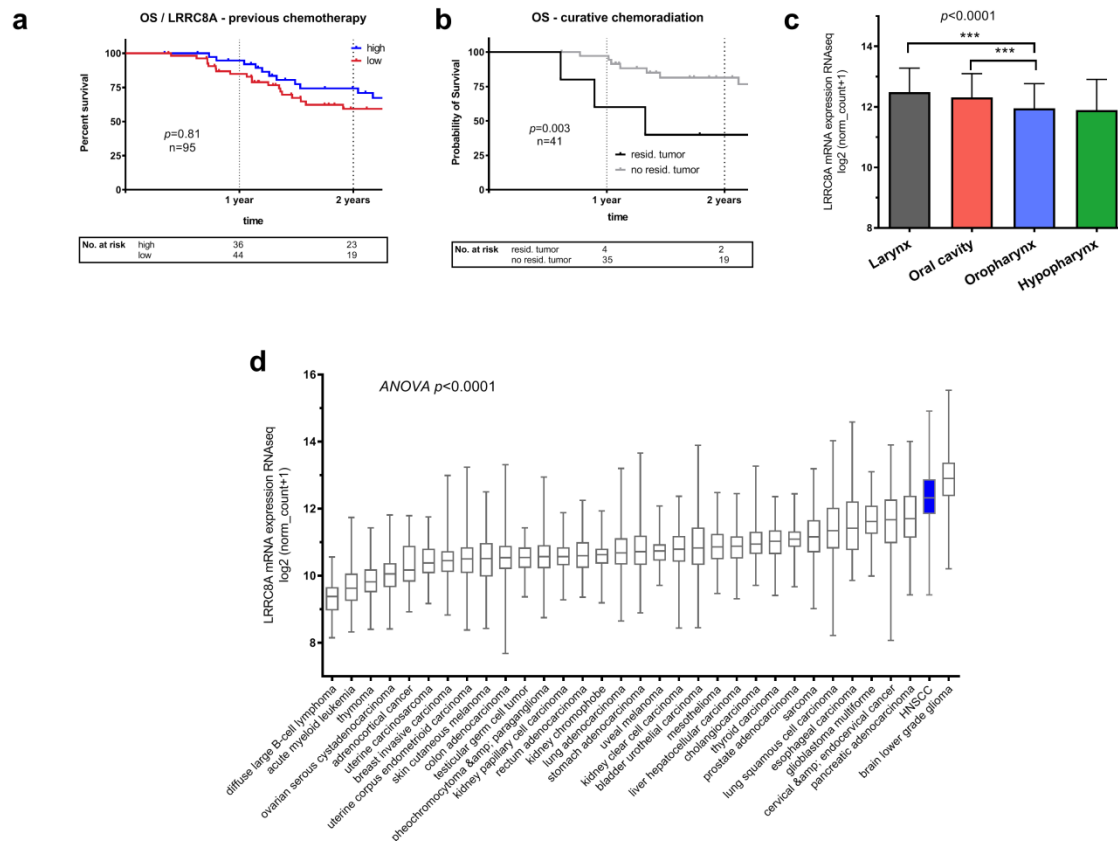


Fig. S2: Significance of VRAC's expression for clinical data depends on case stratification. (a) Overall survival of HNSCC patients, which received previous chemotherapy, depending on LRRC8A expression levels. **(b)** Overall survival of HNSCC patients, which showed or did not show residual tumors after curative chemoradiation. **(c)** Expression levels of LRRC8A across different types of cancers. HNSCC cancers show comparatively high levels of LRRC8A and are marked. **(d)** LRRC8A levels of HNSCC cancers are significantly different depending on localization.

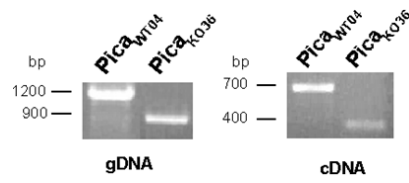


Fig. S3: Genetic Analysis of LRRC8A-Knockout clone Pica_{KO36}. Knockout was confirmed on gDNA and cDNA level. For primers and expected band sizes, see Supplementary Table S2 and S3.

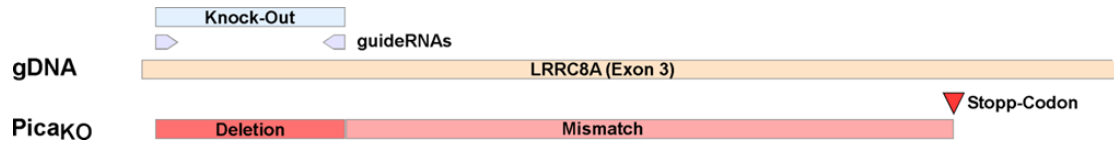


Fig. S4: Next-generation sequencing confirms LRRC8A-knockout in clone Pica_{KO}. Visualization of the gDNA sequencing result of the knockout clone Pica_{KO}. For primer sequences refer to Supplementary Table S2.

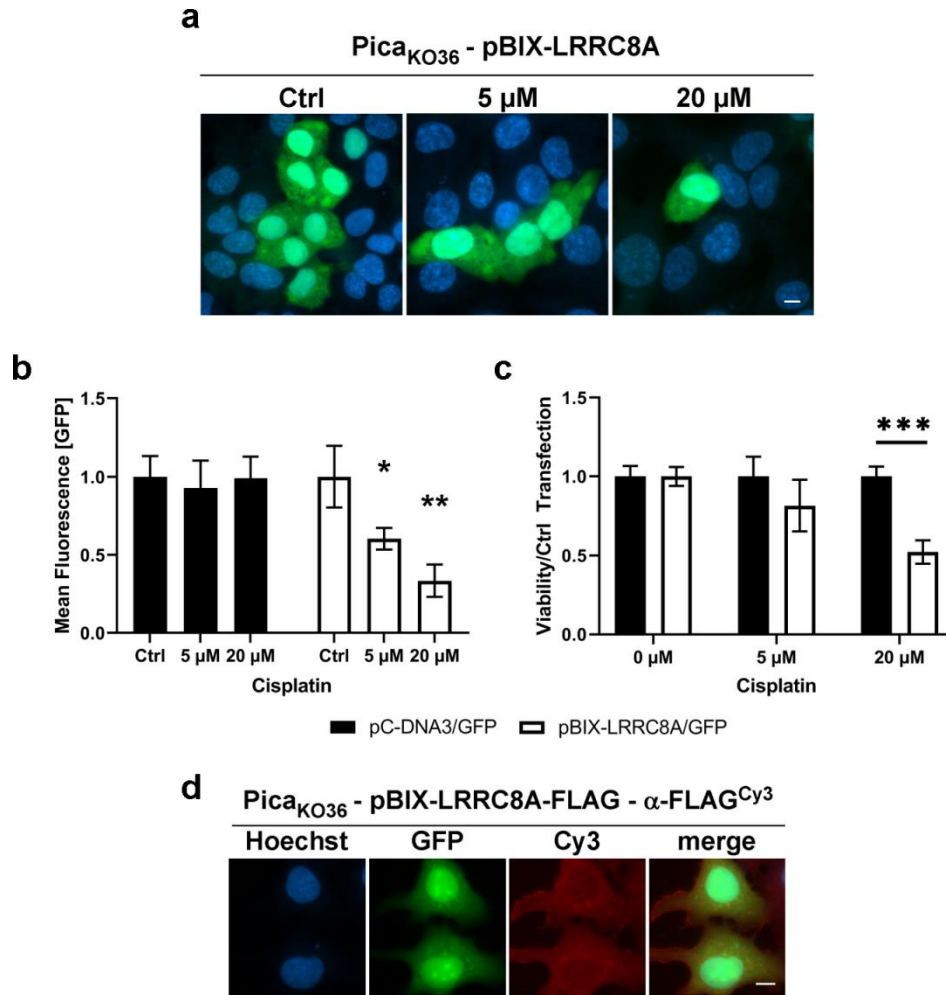


Fig. S5: Ectopic expression of LRRC8A reconstituted VRAC channel function and significantly resensitized the resistant LRRC8A-knockout cell line Pica_{KO36} to cisplatin mediated cell death. (a-b) Pica_{KO36} cells were co-transfected with pBIX-LRRC8A (1.8 μ g) together with pC3-GFP (0.2 μ g) plasmids or as control pC3-DNA3 (1.8 μ g) together with pC3-GFP (0.2 μ g) plasmids. 24 h later, cells were treated with indicated cisplatin concentrations for 48 h and the number of green cells quantified. (a) Microscopy images demonstrating that ectopic expression of LRRC8A resensitized Pica_{KO36} cells to cisplatin, leading to cell death and decrease in the number of transfected green cells. (b) Automatic high-content microscopy to quantify the number of LRRC8A/GFP expressing cells. In contrast to the control (pC-DNA3/GFP; left), LRRC8A/GFP expressing cells (right) were killed by cisplatin concentration-dependently. (c) Ectopic expression of LRRC8A reconstituted VRAC channel function and resensitized the resistant LRRC8A-knockout Pica_{KO36} cells to cisplatin mediated cell death. Viability was assessed by CellTiter-Glo[®] assay and normalized to untreated controls. (d) Pica_{KO36} cells were transfected with pBIX-LRRC8A-FLAG (1.8 μ g) together with pC3-GFP (0.2 μ g) plasmids. Expression of the FLAG-tagged LRRC8A protein at the plasma membrane/cytoplasm was confirmed by anti-FLAG-staining (red). FLAG was stained with an anti-FLAG antibody and nuclei visualized by Hoechst 33342 staining. Scale bars, 10 μ m. Statistical analyses by unpaired Student's t-test. *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.005$.

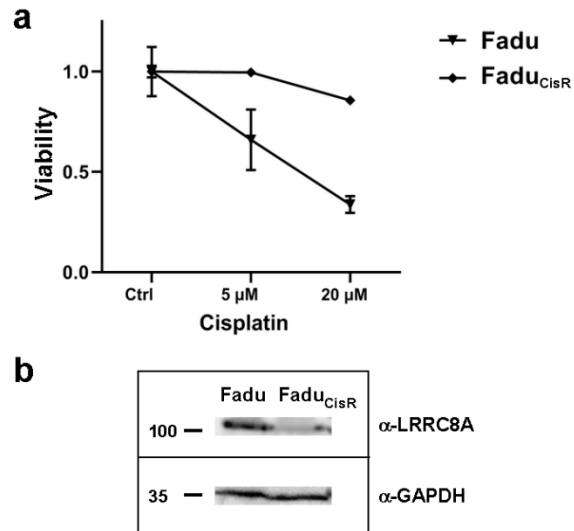


Fig. S6: Permanent cisplatin selection leads to reduced levels of LRRC8A expression in Fadu cells. (a) Fadu_{CisR} are cisplatin-resistant. Cells treated for 48h and viability normalized to untreated controls. **(b)** Immunoblot analysis reveals decreased protein levels of LRRC8A in Fadu_{CisR} cells. GAPDH served as loading control. MW (kD) is indicated.

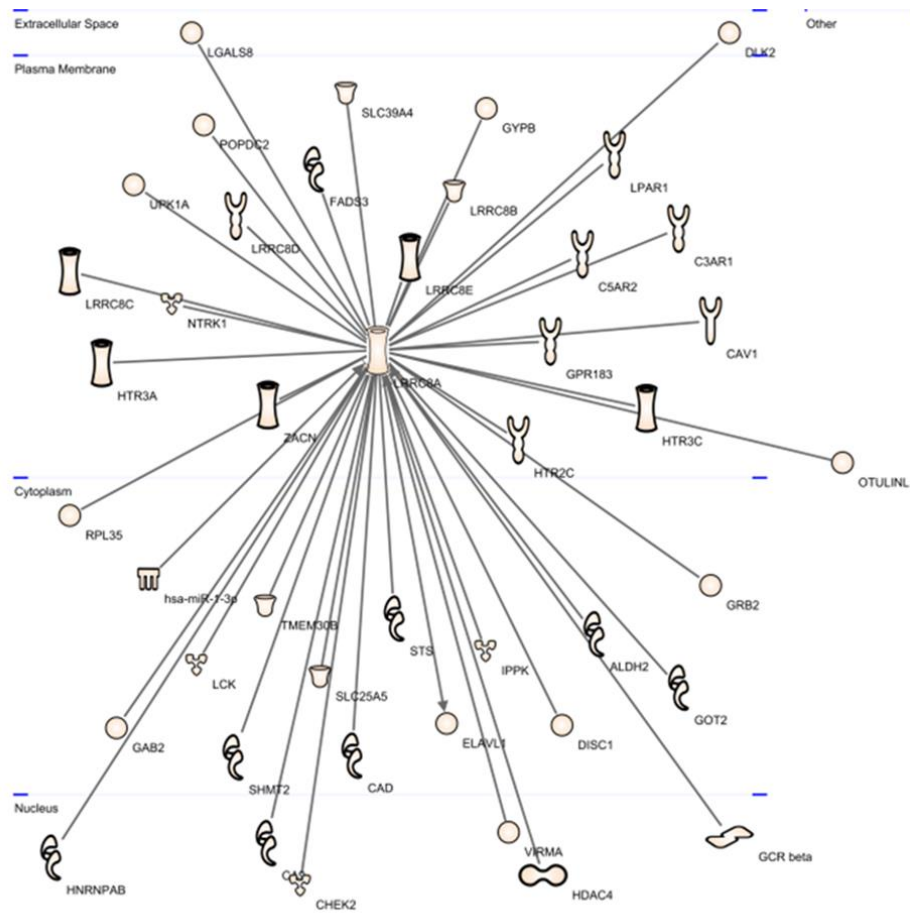


Fig. S7: Molecular network of LRRC8A interaction partners involved in cancer diseases. Ingenuity Pathway Analysis of known direct LRRC8A-interaction partners which are involved in development of cancer diseases. Cellular localization indicated.

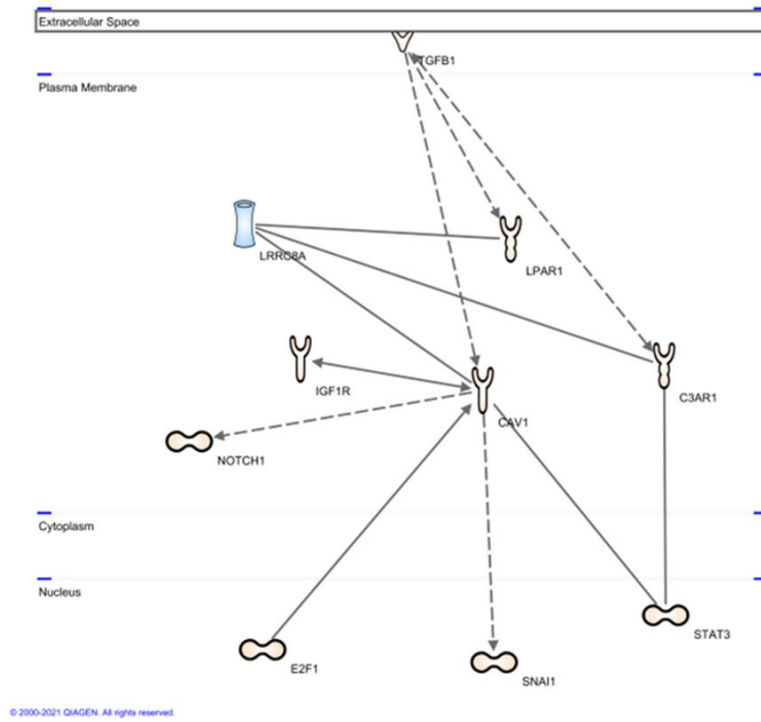


Fig. S8: Molecular network of LRRC8A interaction partners involved in cisplatin resistance. Ingenuity Pathway Analysis of known direct LRRC8A-interaction partners which are involved in development of cisplatin resistance. Cellular localization indicated.

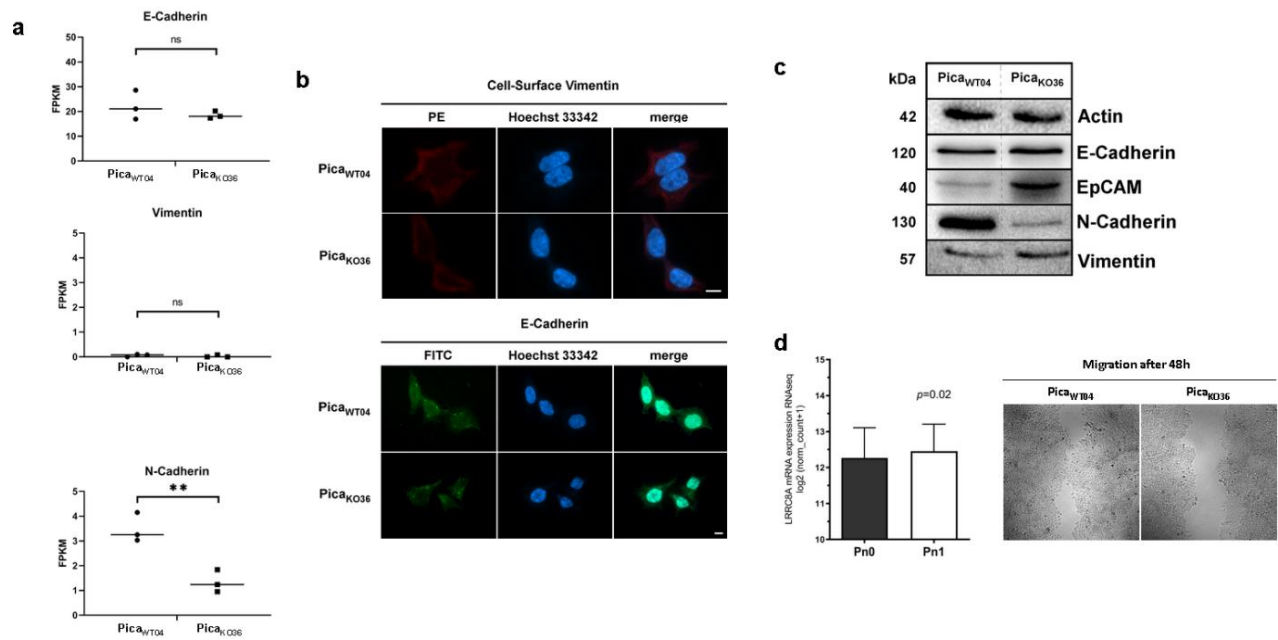


Fig. S9: VRAC expression impacts cellular phenotype and migratory potential. (a) Expression levels of EMT marker proteins in WT *versus* the VRAC-deficient KO cell line, Pica_{KO36}. RNA intensities as FPKM values are displayed. (b) Fluorescence microscopy of cell-surface vimentin (red) and E-cadherin (green) (stained with specific antibodies), nuclei stained with Hoechst (blue). Scale bar, 10 μ m. (c) Western blot to demonstrate expression levels of indicated marker proteins. Actin served as loading control. (d) (Left) High VRAC expression levels may be associated with increased perineural sheath infiltration in the TCGA HNSCC patient (n=565) cohort (p=0.02). (Right) Low VRAC expression reduces the migratory potential of Pica_{KO36} cells compared to Pica_{WT04} cells. Cells were seeded into ibidi two-well dishes and microscopy images taken 48 h after removal of the silicone barrier.

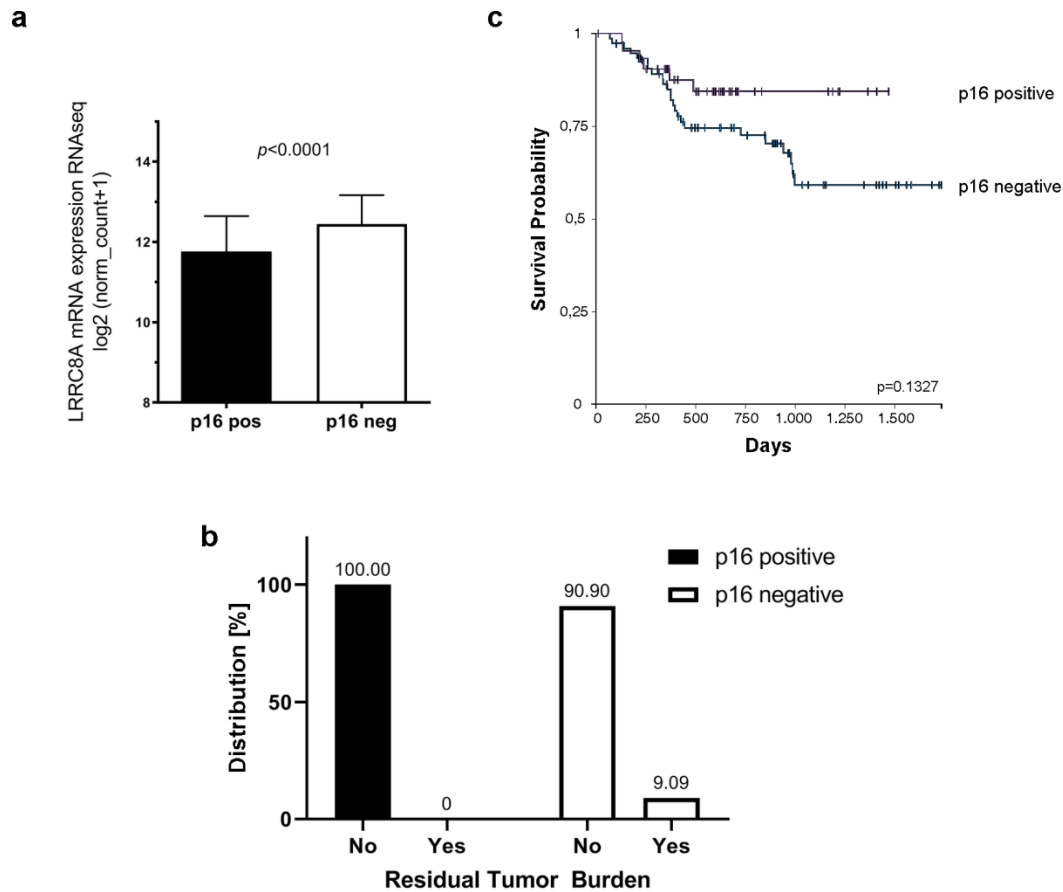


Fig. S10: Correlation of LRRC8A expression and clinical characteristics depending on the HNSCC patients' HPV status. Bioinformatic analyses were performed in the TCGA HNSCC cohort. **(a)** LRRC8A expression is significantly lower in HPV-positive (p16-positive) tumors. Bioinformatic analyses of HPV-positive *versus* -negative tumors (p16-testing as a surrogate marker for HPV-association) and LRRC8A expression were performed. **(b)** Overall survival of HNSCC patients depending on HPV status. HPV-positive patients show a better overall survival. **(c)** HPV-positive patients seem to respond better to chemoradiation. Patients with HPV-negative tumors have a higher likelihood of recurring tumor disease after treatment.

Supplemental Tables

Tab. S1: Antibodies.

| Antigen | Host | Manufacturer and Article Number | Dilution (x-fold) |
|-------------------------------------|--------|------------------------------------|-------------------|
| <u>Western Blot Analysis</u> | | | |
| Actin | rabbit | Sigma Aldrich, A2066 | 5000 |
| E-Cadherin | mouse | BD Bioscience, 610182 | 5000 |
| EpCAM/ CD326 | mouse | eBioscience; 13-9326 | 1000 |
| GAPDH | mouse | Santa Cruz, sc-47724 | 3000 |
| LRRC8A | rabbit | Novusbio; NBP2-32082 | 500 |
| N-Cadherin | mouse | BD Bioscience, 610921 | 5000 |
| Vimentin | mouse | Abnova, H00007431-M08 | 1000 |
| Rabbit (HRP coupled) | goat | Cell Signaling; 7074 | 5000 |
| Mouse (HRP coupled) | mouse | Cell Signaling; 7076 | 5000 |
| <u>Immunofluorescence</u> | | | |
| Cell-Surface Vimentin-PE | mouse | Abnova, H00007431-MP08 | 200 |
| E-cadherin | mouse | BD Bioscience, 610182 | 200 |
| EpCAM/CD326 | mouse | eBioscience; 13-9326 | 200 |
| FLAG | mouse | Sigma, F3165 | 300 |
| γ H2AX | rabbit | Bethyl; A300-081A | 2000 |
| Rabbit (Cy3 coupled) | goat | Dianova; 111-165-003 | 300 |
| Mouse (Cy3 coupled) | goat | Dianova; 115-165-062 | 300 |

Tab. S2: Primer Sequences

| Name | Sequence (5' → 3') | Application |
|------------------|------------------------|---|
| LRRC8A_fw | CTGGGATTACAGACGTGAAC | Characterization knockout clone |
| LRRC8A_rev | TGCTCGATCCGTGACTTG | Characterization knockout clone |
| LRRC8A-cDNA_fw | ATCCTTGGGGTTGAACCATGAT | Characterization knockout clone |
| sgRNA-LRRC8A_fw | GCTGCGTGTCCGCAAAGTAG | Guide sequence CRISPR/Cas9 LRRC8A knockout forward |
| sgRNA-LRRC8A_rev | CCGGCACCAGTACAACTACG | Guide sequence CRISPR/Cas9 LRRC8A knockout reverse |

Tab. S3: Expected Band Sizes Genomic Analysis

| Primer 1 | Primer 2 | Type of Analysis | Expected band size |
|-----------------|-----------------|-------------------------|---|
| LRRC8A_fw | LRRC8A_rev | PCR on gDNA | WT: 1238 bp KO: 942 bp |
| LRRC8A-cDNA_fw | LRRC8A_rev | PCR on cDNA | WT: 679 bp KO: 401 bp |

Tab. S4: RNA Sequencing Results. Only significantly differentially transcribed genes included. All values in FPKM.

| Sample/ Gene | Pica ^{WT04} | | | Pica ^{KO36} | | |
|-----------------|----------------------|--------|-------|----------------------|--------|--------|
| | 1 | 2 | 3 | 1 | 2 | 3 |
| HES4 | 29.67 | 21.93 | 16.09 | 18.35 | 8.06 | 10.49 |
| ISG15 | 105.64 | 122.38 | 47.75 | 31.34 | 48.54 | 43.34 |
| B3GALT6 | 14.05 | 13.78 | 14.26 | 13.86 | 9.25 | 8.90 |
| MFAP2 | 9.06 | 7.11 | 5.10 | 1.14 | 1.13 | 1.61 |
| CAMK2N1 | 6.20 | 3.33 | 3.05 | 6.99 | 6.78 | 8.55 |
| HSPG2 | 6.40 | 1.19 | 1.04 | 2.61 | 0.66 | 0.44 |
| MARCKSL1 | 47.98 | 43.49 | 39.08 | 25.97 | 20.44 | 23.27 |
| NCDN | 16.13 | 11.13 | 11.62 | 13.85 | 7.08 | 8.17 |
| ZC3H12A | 8.92 | 2.05 | 2.31 | 2.03 | 1.37 | 0.99 |
| SLC6A9 | 19.36 | 9.16 | 10.27 | 8.19 | 7.38 | 5.35 |
| PLK3 | 5.60 | 2.79 | 2.62 | 2.46 | 1.27 | 2.02 |
| ZSWIM5 | 1.16 | 1.02 | 1.03 | 2.32 | 1.75 | 2.10 |
| TSPAN1 | 62.20 | 69.79 | 66.52 | 95.10 | 134.61 | 108.92 |
| CDKN2C | 6.89 | 6.45 | 7.46 | 14.15 | 11.82 | 11.65 |
| GADD45A | 44.31 | 30.52 | 31.23 | 12.87 | 18.01 | 15.49 |
| IFI44 | 5.09 | 10.45 | 2.63 | 0.50 | 1.49 | 1.32 |
| ADGRL2 | 2.38 | 1.92 | 1.32 | 0.75 | 0.80 | 0.74 |
| DDAH1 | 5.69 | 6.41 | 7.27 | 8.61 | 10.72 | 8.56 |
| CNN3 | 24.76 | 30.79 | 25.42 | 12.31 | 20.99 | 18.46 |
| F3 | 42.61 | 29.60 | 23.65 | 8.45 | 14.01 | 11.40 |
| SORT1 | 7.33 | 9.82 | 10.40 | 6.47 | 6.00 | 4.93 |
| PBXIP1 | 5.78 | 4.72 | 3.77 | 9.23 | 5.75 | 8.80 |
| KIRREL | 7.89 | 4.08 | 2.60 | 4.71 | 2.31 | 2.40 |
| PVRL4 | 3.82 | 3.90 | 2.56 | 1.99 | 1.54 | 2.03 |
| CEP350 | 2.83 | 3.16 | 2.35 | 4.37 | 3.30 | 3.39 |
| GLUL | 30.36 | 27.45 | 27.54 | 52.96 | 54.92 | 40.56 |
| LAMC2 | 27.45 | 15.13 | 11.67 | 8.41 | 9.98 | 8.48 |
| FAM129A | 4.11 | 0.51 | 0.35 | 0.16 | 0.73 | 0.24 |
| KIF21B | 3.81 | 1.05 | 1.11 | 1.22 | 0.85 | 0.57 |
| CD55 | 28.80 | 40.58 | 38.29 | 14.70 | 27.44 | 18.33 |
| ATF3 | 2.90 | 2.22 | 1.62 | 0.22 | 1.05 | 1.22 |
| CENPF | 15.25 | 19.93 | 15.73 | 24.19 | 20.19 | 17.45 |
| TGFB2 | 1.12 | 1.51 | 0.66 | 2.57 | 1.55 | 1.12 |
| TFB2M | 13.07 | 15.84 | 15.89 | 19.68 | 21.50 | 21.59 |
| SCCPDH | 2.64 | 3.74 | 4.03 | 0.81 | 1.48 | 1.98 |
| KLHL29 | 3.55 | 1.76 | 1.07 | 1.69 | 0.87 | 1.04 |
| LBH | 33.14 | 43.63 | 62.06 | 32.22 | 20.38 | 18.81 |
| CDC42EP3 | 2.78 | 2.34 | 2.17 | 1.46 | 1.20 | 1.41 |
| EPAS1 | 21.85 | 26.41 | 16.08 | 17.89 | 14.03 | 12.25 |
| BCL11A | 1.89 | 2.43 | 1.25 | 0.56 | 0.44 | 0.69 |

| Sample/ Gene | Pica _{WT04} | | | Pica _{KO36} | | |
|-----------------|----------------------|--------|--------|----------------------|--------|--------|
| | 1 | 2 | 3 | 1 | 2 | 3 |
| PELI1 | 4.46 | 3.32 | 2.85 | 6.51 | 5.82 | 6.33 |
| TGFA | 9.12 | 6.81 | 5.24 | 2.84 | 4.64 | 4.28 |
| ADD2 | 17.85 | 12.67 | 12.31 | 10.91 | 8.89 | 7.23 |
| CYP26B1 | 7.34 | 4.54 | 3.39 | 2.42 | 1.67 | 1.72 |
| SLC4A5 | 3.12 | 4.04 | 4.74 | 1.82 | 2.70 | 2.54 |
| MTHFD2 | 248.90 | 253.55 | 291.77 | 144.23 | 206.93 | 168.14 |
| HK2 | 15.38 | 11.52 | 13.45 | 4.43 | 4.64 | 3.93 |
| CAPG | 19.23 | 18.13 | 17.14 | 7.41 | 12.02 | 13.40 |
| CHST10 | 2.64 | 4.14 | 4.23 | 1.30 | 1.33 | 1.70 |
| MALL | 5.25 | 4.24 | 7.47 | 2.06 | 3.31 | 3.32 |
| SLC20A1 | 17.82 | 18.42 | 13.67 | 10.78 | 11.61 | 9.97 |
| IL1B | 19.31 | 3.61 | 3.09 | 1.03 | 1.45 | 1.43 |
| IL1A | 9.58 | 1.09 | 0.57 | 0.30 | 0.52 | 0.62 |
| STEAP3 | 11.38 | 9.46 | 10.29 | 8.08 | 7.42 | 5.42 |
| ARHGEF4 | 6.11 | 4.39 | 4.91 | 4.49 | 2.84 | 2.43 |
| FMNL2 | 5.76 | 7.10 | 4.66 | 3.13 | 3.96 | 3.04 |
| SERPINE2 | 6.47 | 5.20 | 3.11 | 0.58 | 1.52 | 0.65 |
| SLC4A7 | 4.83 | 4.64 | 3.96 | 2.94 | 2.87 | 1.49 |
| SEMA3B | 6.24 | 4.70 | 4.88 | 2.72 | 3.40 | 2.96 |
| IFRD2 | 83.96 | 65.23 | 72.86 | 62.07 | 58.14 | 45.28 |
| FSTL1 | 0.94 | 1.55 | 1.22 | 2.42 | 2.15 | 3.10 |
| GOLGB1 | 4.53 | 5.66 | 4.39 | 8.16 | 5.99 | 5.60 |
| AMOTL2 | 21.83 | 13.68 | 13.53 | 33.09 | 19.97 | 22.75 |
| PCOLCE2 | 4.86 | 9.50 | 8.11 | 3.35 | 4.88 | 3.52 |
| TM4SF1 | 23.03 | 30.37 | 20.34 | 8.06 | 11.41 | 8.11 |
| GPR87 | 16.03 | 21.34 | 22.06 | 24.11 | 28.29 | 36.47 |
| LAMP3 | 2.46 | 1.67 | 1.20 | 0.59 | 0.60 | 0.41 |
| SOX2 | 9.39 | 7.02 | 5.67 | 1.19 | 0.31 | 0.57 |
| ST6GAL1 | 1.70 | 1.61 | 1.07 | 0.42 | 0.63 | 0.37 |
| CLDN1 | 19.57 | 10.60 | 6.60 | 6.96 | 7.49 | 5.92 |
| CPLX1 | 2.67 | 2.31 | 2.53 | 15.33 | 6.71 | 5.78 |
| FGFR3 | 157.17 | 96.55 | 89.51 | 398.23 | 164.80 | 192.87 |
| MXD4 | 7.82 | 6.07 | 5.94 | 14.43 | 7.92 | 10.37 |
| SEL1L3 | 7.77 | 5.24 | 4.33 | 2.20 | 3.08 | 2.31 |
| CXCL8 | 59.91 | 29.51 | 35.02 | 3.14 | 5.78 | 4.55 |
| CXCL1 | 29.21 | 4.44 | 4.05 | 0.92 | 1.21 | 1.42 |
| CCNG2 | 1.81 | 2.62 | 1.54 | 3.32 | 3.28 | 4.42 |
| CENPE | 2.16 | 5.04 | 4.14 | 4.67 | 4.82 | 4.70 |
| TET2 | 1.52 | 1.49 | 1.31 | 2.37 | 1.82 | 1.95 |
| LEF1 | 1.90 | 1.88 | 1.35 | 0.58 | 0.90 | 0.85 |
| PRSS12 | 1.86 | 1.96 | 1.74 | 0.66 | 1.02 | 0.39 |
| SLC7A11 | 10.58 | 8.74 | 10.94 | 6.47 | 5.22 | 4.52 |

| Sample/ Gene | Pica _{WT04} | | | Pica _{KO36} | | |
|-----------------|----------------------|-------|-------|----------------------|-------|-------|
| | 1 | 2 | 3 | 1 | 2 | 3 |
| ELF2 | 4.49 | 5.22 | 6.11 | 8.15 | 6.81 | 8.92 |
| ARHGAP10 | 5.27 | 3.21 | 4.22 | 4.54 | 6.72 | 6.89 |
| DDX60 | 2.48 | 2.91 | 0.93 | 0.94 | 1.32 | 1.07 |
| LPCAT1 | 20.19 | 14.32 | 12.90 | 12.42 | 11.36 | 7.66 |
| IRX4 | 15.46 | 14.51 | 10.67 | 9.89 | 6.47 | 6.62 |
| MYO10 | 7.44 | 4.02 | 4.05 | 3.72 | 3.53 | 2.62 |
| RAI14 | 4.83 | 4.63 | 5.01 | 2.60 | 3.23 | 2.57 |
| OSMR | 8.31 | 7.42 | 2.89 | 2.72 | 4.53 | 2.98 |
| FST | 25.89 | 23.51 | 28.36 | 7.82 | 6.63 | 5.77 |
| POLR3G | 7.37 | 6.78 | 7.54 | 3.40 | 5.13 | 4.05 |
| PGGT1B | 1.47 | 2.34 | 2.30 | 3.21 | 4.50 | 3.22 |
| FBN2 | 8.36 | 6.28 | 4.41 | 2.54 | 2.58 | 1.68 |
| HBEGF | 3.47 | 0.97 | 1.18 | 0.56 | 0.44 | 0.75 |
| FAT2 | 2.49 | 1.56 | 0.80 | 5.23 | 2.24 | 1.88 |
| GABRP | 2.46 | 0.93 | 0.63 | 2.90 | 2.26 | 3.14 |
| DUSP1 | 4.06 | 3.56 | 3.82 | 1.37 | 1.33 | 1.90 |
| STC2 | 39.26 | 24.86 | 27.83 | 14.73 | 16.88 | 10.89 |
| DBN1 | 6.35 | 5.11 | 3.53 | 0.54 | 0.69 | 0.35 |
| N4BP3 | 5.40 | 2.74 | 2.04 | 9.60 | 4.58 | 4.25 |
| GFPT2 | 5.75 | 7.17 | 4.72 | 0.66 | 1.48 | 0.72 |
| FOXQ1 | 2.51 | 2.66 | 2.40 | 2.17 | 0.96 | 1.33 |
| TUBB2A | 7.91 | 5.38 | 5.25 | 2.51 | 3.22 | 1.59 |
| NEDD9 | 3.75 | 3.15 | 2.71 | 10.46 | 5.78 | 6.45 |
| TRIM38 | 4.26 | 4.68 | 3.29 | 5.09 | 5.51 | 6.73 |
| HLA-B | 46.70 | 15.07 | 4.35 | 1.98 | 4.08 | 2.91 |
| TAP2 | 39.60 | 21.83 | 20.42 | 19.39 | 19.10 | 10.36 |
| CDKN1A | 9.79 | 4.39 | 1.72 | 1.24 | 1.48 | 1.77 |
| PEX6 | 6.00 | 4.70 | 3.20 | 10.99 | 6.01 | 6.84 |
| VEGFA | 38.05 | 22.48 | 23.10 | 17.58 | 14.24 | 15.91 |
| ADGRF1 | 11.31 | 4.71 | 7.58 | 13.76 | 13.11 | 13.56 |
| KCNQ5 | 2.29 | 2.21 | 1.52 | 1.19 | 1.36 | 0.71 |
| ZNF292 | 1.65 | 1.72 | 1.42 | 2.26 | 1.88 | 2.25 |
| FYN | 4.09 | 2.67 | 2.11 | 0.85 | 1.63 | 1.29 |
| GJA1 | 17.89 | 20.47 | 17.66 | 11.51 | 13.33 | 8.93 |
| TNFAIP3 | 8.24 | 0.49 | 0.38 | 0.14 | 0.17 | 0.07 |
| UTRN | 1.05 | 0.85 | 0.48 | 2.07 | 1.49 | 1.55 |
| SASH1 | 3.26 | 2.57 | 1.59 | 6.83 | 3.14 | 4.25 |
| UST | 2.93 | 1.96 | 1.90 | 0.96 | 1.04 | 1.00 |
| AKAP12 | 9.88 | 5.70 | 6.05 | 0.62 | 1.14 | 0.73 |
| SOD2 | 50.82 | 16.38 | 15.49 | 17.15 | 12.31 | 13.37 |
| DFNA5 | 5.28 | 4.24 | 3.88 | 0.77 | 2.98 | 2.20 |
| CPVL | 7.01 | 10.04 | 8.28 | 2.15 | 4.79 | 2.38 |

| Sample/ Gene | Pica _{WT04} | | | Pica _{KO36} | | |
|-----------------|----------------------|-------|-------|----------------------|-------|--------|
| | 1 | 2 | 3 | 1 | 2 | 3 |
| GARS | 84.19 | 83.88 | 98.65 | 47.46 | 72.19 | 55.49 |
| STK17A | 17.21 | 17.44 | 16.55 | 9.04 | 13.75 | 10.90 |
| IGFBP3 | 1.60 | 1.54 | 0.95 | 5.96 | 3.12 | 5.08 |
| COBL | 4.81 | 4.18 | 4.04 | 2.54 | 3.11 | 2.19 |
| GRB10 | 28.14 | 28.94 | 25.20 | 17.91 | 19.99 | 15.31 |
| ASL | 16.04 | 14.12 | 15.93 | 11.53 | 11.55 | 8.29 |
| SBDSP1 | 13.16 | 11.98 | 13.91 | 6.83 | 8.44 | 6.83 |
| SEMA3E | 1.19 | 1.26 | 1.33 | 2.12 | 2.04 | 2.48 |
| SEMA3C | 20.01 | 12.59 | 6.01 | 4.74 | 4.95 | 3.71 |
| AKAP9 | 2.21 | 5.08 | 4.51 | 6.17 | 5.09 | 5.40 |
| CDK6 | 5.10 | 3.69 | 2.89 | 1.83 | 1.94 | 1.49 |
| NAMPT | 20.53 | 21.47 | 20.45 | 10.43 | 16.47 | 12.68 |
| IFRD1 | 14.80 | 14.14 | 14.21 | 6.01 | 8.49 | 7.03 |
| MET | 21.10 | 14.64 | 12.64 | 10.64 | 10.22 | 8.99 |
| ZNF467 | 2.53 | 2.80 | 1.18 | 1.38 | 1.21 | 0.65 |
| LRRCC61 | 23.12 | 18.04 | 18.31 | 13.49 | 11.38 | 9.19 |
| NEIL2 | 11.41 | 12.44 | 13.56 | 4.66 | 9.77 | 5.76 |
| STC1 | 1.68 | 2.88 | 0.76 | 0.71 | 0.83 | 0.46 |
| LOXL2 | 34.44 | 12.48 | 13.57 | 10.95 | 12.49 | 14.01 |
| NRG1 | 3.41 | 1.54 | 2.24 | 0.22 | 0.38 | 0.29 |
| PCMTD1 | 5.65 | 7.21 | 6.33 | 8.10 | 7.29 | 9.50 |
| PLAG1 | 2.36 | 2.25 | 2.09 | 3.73 | 2.65 | 3.46 |
| LRRCC1 | 3.67 | 4.78 | 5.33 | 5.08 | 7.65 | 6.82 |
| CA2 | 6.30 | 3.26 | 3.13 | 0.65 | 2.14 | 0.50 |
| DECR1 | 21.78 | 36.82 | 35.42 | 30.50 | 51.62 | 48.78 |
| DPY19L4 | 8.20 | 9.83 | 7.73 | 11.51 | 11.63 | 10.56 |
| NIPAL2 | 3.18 | 3.39 | 2.19 | 6.32 | 4.31 | 5.53 |
| TRIB1 | 13.75 | 15.19 | 10.30 | 10.10 | 10.24 | 5.93 |
| ST3GAL1 | 13.91 | 6.12 | 7.32 | 3.45 | 5.02 | 4.76 |
| NDRG1 | 44.21 | 37.42 | 29.92 | 56.36 | 45.18 | 102.16 |
| MROH6 | 2.11 | 1.75 | 1.24 | 5.24 | 2.62 | 2.72 |
| FBXL6 | 7.65 | 7.35 | 7.75 | 4.84 | 4.71 | 4.29 |
| BOP1 | 54.27 | 36.41 | 38.65 | 48.92 | 32.90 | 29.14 |
| MFSD3 | 34.70 | 21.96 | 23.34 | 25.94 | 14.34 | 12.72 |
| PLIN2 | 17.62 | 18.77 | 17.42 | 8.79 | 12.86 | 12.87 |
| AQP3 | 40.20 | 27.44 | 24.67 | 5.36 | 9.76 | 5.16 |
| ANXA2P2 | 24.13 | 27.76 | 27.29 | 15.17 | 19.75 | 18.10 |
| CA9 | 4.82 | 3.81 | 3.45 | 7.09 | 4.11 | 16.26 |
| FAM201A | 1.81 | 1.88 | 2.63 | 5.91 | 3.54 | 4.65 |
| SMC5 | 7.43 | 9.46 | 8.48 | 11.36 | 10.85 | 10.54 |
| VPS13A | 3.62 | 3.44 | 3.04 | 5.74 | 3.75 | 3.19 |
| TLE1 | 6.58 | 4.08 | 3.07 | 2.88 | 2.64 | 2.81 |

| Sample/ Gene | Pica _{WT04} | | | Pica _{KO36} | | |
|-----------------|----------------------|--------|--------|----------------------|--------|--------|
| | 1 | 2 | 3 | 1 | 2 | 3 |
| PSAT1 | 151.10 | 129.31 | 151.39 | 81.96 | 99.05 | 68.50 |
| C9orf64 | 1.81 | 1.09 | 1.69 | 2.67 | 3.34 | 3.37 |
| FGD3 | 1.78 | 1.06 | 0.99 | 3.35 | 2.77 | 3.08 |
| CORO2A | 11.18 | 7.03 | 6.10 | 4.61 | 5.20 | 4.86 |
| COL27A1 | 5.95 | 3.98 | 3.36 | 4.60 | 2.39 | 1.96 |
| CNTRL | 2.83 | 3.42 | 2.23 | 4.46 | 3.92 | 4.20 |
| PTGS1 | 4.62 | 3.60 | 1.73 | 3.67 | 5.93 | 6.52 |
| LCN2 | 110.70 | 11.99 | 10.03 | 7.72 | 8.08 | 10.12 |
| LRRC8A | 29.36 | 19.88 | 21.06 | 17.63 | 12.20 | 15.18 |
| NCS1 | 19.17 | 14.77 | 16.14 | 11.77 | 9.86 | 9.34 |
| ASS1 | 155.64 | 68.36 | 75.94 | 32.34 | 41.29 | 34.96 |
| FIBCD1 | 5.65 | 3.60 | 3.68 | 12.95 | 5.02 | 6.52 |
| EGFL7 | 51.12 | 25.84 | 26.93 | 17.11 | 13.81 | 13.25 |
| CLIC3 | 2.21 | 0.94 | 1.61 | 9.71 | 6.79 | 10.54 |
| UAP1L1 | 3.06 | 4.10 | 3.18 | 3.01 | 1.54 | 1.83 |
| ABCA2 | 10.33 | 7.15 | 7.29 | 23.06 | 9.26 | 10.21 |
| IL15RA | 8.40 | 4.09 | 4.24 | 2.86 | 2.14 | 2.40 |
| FAM107B | 9.17 | 8.35 | 6.70 | 3.32 | 5.54 | 2.93 |
| RASGEF1A | 6.06 | 7.23 | 5.34 | 3.30 | 3.87 | 3.13 |
| ANXA8 | 8.43 | 9.52 | 7.34 | 5.33 | 7.00 | 6.70 |
| ANXA8 | 14.49 | 10.45 | 10.12 | 9.90 | 10.16 | 9.25 |
| DKK1 | 35.27 | 45.29 | 49.22 | 27.76 | 34.47 | 21.74 |
| FUT11 | 1.04 | 0.80 | 0.44 | 3.72 | 1.82 | 1.52 |
| SNCG | 70.02 | 70.73 | 83.01 | 106.16 | 106.00 | 111.32 |
| ADIRF | 46.81 | 49.66 | 62.62 | 73.08 | 91.17 | 92.25 |
| IFIT2 | 6.65 | 7.82 | 3.18 | 1.77 | 4.00 | 2.94 |
| IFIT3 | 7.94 | 7.93 | 2.98 | 1.13 | 3.27 | 1.94 |
| KIF20B | 6.30 | 13.34 | 13.03 | 12.36 | 14.63 | 14.05 |
| IFIT1 | 5.16 | 5.67 | 1.74 | 1.21 | 3.39 | 1.72 |
| HHEX | 8.38 | 11.09 | 9.62 | 6.28 | 4.98 | 5.53 |
| ZNF518A | 2.60 | 3.84 | 3.98 | 4.64 | 4.02 | 4.16 |
| ANKRD2 | 33.87 | 16.60 | 29.29 | 54.55 | 47.18 | 45.59 |
| NFKB2 | 29.57 | 14.65 | 11.17 | 11.90 | 9.86 | 8.91 |
| COL17A1 | 3.45 | 1.39 | 0.77 | 0.48 | 0.39 | 0.76 |
| FGFR2 | 7.85 | 5.60 | 5.52 | 14.67 | 9.93 | 11.30 |
| TNNI2 | 14.34 | 26.79 | 31.36 | 50.47 | 48.68 | 59.77 |
| TNNT3 | 4.55 | 14.50 | 13.79 | 16.73 | 16.82 | 29.14 |
| PHLDA2 | 78.33 | 69.44 | 77.02 | 75.30 | 46.53 | 49.32 |
| PRRG4 | 6.96 | 10.22 | 10.50 | 11.07 | 11.93 | 12.40 |
| ABTB2 | 4.31 | 2.38 | 1.46 | 1.92 | 1.23 | 1.13 |
| CD44 | 10.03 | 9.09 | 5.31 | 0.52 | 1.67 | 1.05 |
| MAPK8IP1 | 3.19 | 4.01 | 2.90 | 2.43 | 1.97 | 1.70 |

| Sample/ Gene | Pica _{WT04} | | | Pica _{KO36} | | |
|-----------------|----------------------|--------|--------|----------------------|--------|--------|
| | 1 | 2 | 3 | 1 | 2 | 3 |
| MDK | 87.65 | 64.27 | 63.76 | 23.62 | 26.53 | 28.82 |
| FAM111B | 2.52 | 3.41 | 4.00 | 4.55 | 5.28 | 4.65 |
| FAM111A | 2.62 | 2.00 | 1.05 | 3.08 | 2.52 | 4.03 |
| TMEM132A | 47.44 | 17.75 | 16.39 | 33.05 | 12.75 | 12.85 |
| RAB3IL1 | 8.46 | 3.96 | 4.03 | 1.92 | 1.55 | 1.45 |
| WDR74 | 40.34 | 41.87 | 42.57 | 64.94 | 69.55 | 69.15 |
| ATL3 | 1.93 | 2.76 | 2.79 | 0.73 | 1.35 | 1.51 |
| DNAJC4 | 5.09 | 3.47 | 4.63 | 9.18 | 6.41 | 9.11 |
| MAP4K2 | 4.45 | 2.89 | 2.25 | 2.77 | 2.12 | 0.92 |
| NEAT1 | 51.86 | 45.62 | 32.75 | 26.55 | 24.16 | 21.64 |
| SYT12 | 33.93 | 41.11 | 39.22 | 65.63 | 60.73 | 50.43 |
| CDK2AP2 | 100.72 | 73.96 | 78.53 | 173.58 | 117.96 | 133.20 |
| PITPNM1 | 52.14 | 30.29 | 25.58 | 91.01 | 42.09 | 43.79 |
| ALDH3B2 | 3.08 | 2.95 | 3.43 | 8.42 | 6.80 | 6.96 |
| CHKA | 23.65 | 28.42 | 30.75 | 51.80 | 39.92 | 44.67 |
| GAL | 128.45 | 144.54 | 183.41 | 58.71 | 73.74 | 45.05 |
| FAM181B | 1.08 | 0.86 | 1.48 | 4.74 | 2.83 | 3.11 |
| CTSC | 41.89 | 39.20 | 34.39 | 18.05 | 25.87 | 19.70 |
| CEP295 | 1.27 | 1.70 | 1.21 | 1.97 | 2.00 | 1.91 |
| NPAT | 2.33 | 2.51 | 3.23 | 3.88 | 3.57 | 3.15 |
| ETS1 | 9.84 | 3.87 | 1.90 | 0.76 | 1.30 | 0.73 |
| CCND2 | 41.60 | 33.42 | 29.01 | 72.87 | 61.02 | 66.07 |
| EMP1 | 4.29 | 5.10 | 5.54 | 1.74 | 3.40 | 1.86 |
| ARHGDIB | 43.20 | 28.03 | 34.38 | 43.43 | 57.04 | 58.04 |
| FGD4 | 1.81 | 2.15 | 2.02 | 3.34 | 2.64 | 2.39 |
| PRICKLE1 | 5.72 | 5.59 | 5.21 | 3.54 | 3.87 | 2.66 |
| RAPGEF3 | 12.63 | 6.29 | 7.52 | 25.24 | 12.78 | 11.67 |
| WNT10B | 7.28 | 5.20 | 5.36 | 1.71 | 2.24 | 1.45 |
| DDN | 6.97 | 6.14 | 6.89 | 6.17 | 3.38 | 3.23 |
| IGFBP6 | 19.91 | 16.90 | 12.21 | 6.02 | 9.68 | 6.22 |
| INHBE | 10.64 | 4.48 | 5.16 | 1.06 | 1.16 | 0.97 |
| AGAP2 | 0.56 | 0.45 | 0.44 | 3.98 | 2.21 | 3.00 |
| FRS2 | 2.45 | 2.85 | 3.17 | 3.77 | 3.55 | 3.57 |
| PHLDA1 | 21.03 | 12.33 | 9.75 | 4.03 | 6.90 | 4.01 |
| CHST11 | 2.67 | 0.84 | 1.05 | 0.72 | 0.53 | 0.38 |
| MTERF2 | 3.14 | 2.95 | 3.36 | 4.19 | 5.38 | 6.45 |
| TXNRD1 | 173.22 | 129.01 | 176.78 | 101.03 | 100.02 | 87.57 |
| FAM109A | 7.45 | 4.28 | 3.85 | 16.00 | 8.58 | 5.63 |
| OAS1 | 4.53 | 1.69 | 0.18 | 0.64 | 0.54 | 0.67 |
| OASL | 8.70 | 17.64 | 5.43 | 1.09 | 4.00 | 3.45 |
| HCAR2 | 9.55 | 7.43 | 4.00 | 12.93 | 10.93 | 8.86 |
| MMP17 | 10.12 | 3.89 | 3.19 | 4.55 | 2.13 | 2.67 |

| Sample/ Gene | Pica _{WT04} | | | Pica _{KO36} | | |
|-----------------|----------------------|--------|--------|----------------------|--------|--------|
| | 1 | 2 | 3 | 1 | 2 | 3 |
| PSPC1 | 39.38 | 38.36 | 48.45 | 16.10 | 27.81 | 22.75 |
| UBAC2 | 26.87 | 31.97 | 28.37 | 16.94 | 19.88 | 22.05 |
| COL4A1 | 3.49 | 2.33 | 1.19 | 1.62 | 1.07 | 0.52 |
| COL4A2 | 15.60 | 10.99 | 5.15 | 10.20 | 6.67 | 3.76 |
| MMP14 | 22.91 | 12.27 | 8.86 | 26.18 | 20.59 | 20.90 |
| CDH24 | 5.86 | 2.57 | 3.49 | 3.28 | 1.94 | 1.70 |
| PCK2 | 29.12 | 19.38 | 20.64 | 12.61 | 15.14 | 8.60 |
| IRF9 | 15.69 | 12.67 | 3.94 | 2.73 | 3.24 | 5.24 |
| EGLN3 | 4.85 | 4.77 | 3.25 | 8.34 | 6.87 | 11.60 |
| NFKBIA | 126.77 | 38.23 | 36.22 | 38.34 | 33.72 | 39.35 |
| DLGAP5 | 15.59 | 23.89 | 20.50 | 21.76 | 29.10 | 25.72 |
| TRIP11 | 7.38 | 11.19 | 10.39 | 14.20 | 11.04 | 11.25 |
| OTUB2 | 22.18 | 14.31 | 13.67 | 6.87 | 11.09 | 6.74 |
| PPP4R4 | 5.91 | 3.12 | 2.35 | 1.08 | 1.99 | 1.60 |
| IFI27 | 16.20 | 17.67 | 2.45 | 4.46 | 1.56 | 4.02 |
| WARS | 42.21 | 39.69 | 38.24 | 21.48 | 28.39 | 22.40 |
| CHAC1 | 19.49 | 10.89 | 12.60 | 6.77 | 5.13 | 3.80 |
| TPM1 | 25.82 | 21.85 | 18.88 | 33.52 | 34.93 | 29.14 |
| STRA6 | 2.89 | 1.44 | 1.74 | 1.02 | 0.50 | 0.41 |
| HOMER2 | 17.28 | 17.14 | 19.03 | 6.39 | 7.00 | 6.41 |
| PDE8A | 18.28 | 10.34 | 9.78 | 7.47 | 8.22 | 9.66 |
| HAPLN3 | 7.57 | 4.66 | 2.57 | 3.05 | 2.07 | 2.44 |
| ISG20 | 4.11 | 3.33 | 2.11 | 0.46 | 1.26 | 1.55 |
| SLCO3A1 | 4.36 | 1.45 | 0.76 | 0.77 | 0.62 | 0.79 |
| SYNM | 1.85 | 1.98 | 1.73 | 1.15 | 1.05 | 0.63 |
| HAGHL | 12.50 | 9.18 | 8.52 | 8.33 | 4.48 | 5.51 |
| KREMEN2 | 8.65 | 1.26 | 2.12 | 1.99 | 1.31 | 1.25 |
| PKD1P1 | 15.04 | 6.79 | 6.59 | 17.58 | 6.18 | 5.63 |
| SMG1P2 | 3.86 | 3.59 | 3.43 | 4.16 | 3.90 | 3.01 |
| SLX1B | 36.77 | 35.52 | 25.17 | 37.33 | 19.60 | 19.05 |
| SMG1P2 | 0.00 | 0.91 | 1.88 | 0.00 | 1.08 | 1.64 |
| GPT2 | 44.74 | 28.88 | 32.59 | 25.76 | 23.17 | 16.17 |
| IRX3 | 8.95 | 4.80 | 4.43 | 5.34 | 3.12 | 3.37 |
| LPCAT2 | 3.04 | 3.48 | 3.11 | 1.56 | 1.63 | 1.72 |
| MT1X | 29.54 | 60.69 | 36.74 | 14.21 | 13.90 | 24.63 |
| MT2A | 498.77 | 467.30 | 304.90 | 239.70 | 251.49 | 339.58 |
| KIFC3 | 29.47 | 25.72 | 24.93 | 50.28 | 37.86 | 38.69 |
| CDH5 | 10.93 | 7.53 | 7.14 | 22.57 | 15.58 | 9.42 |
| ST3GAL2 | 4.87 | 3.62 | 2.26 | 2.32 | 2.19 | 1.44 |
| ATP2C2 | 3.26 | 1.62 | 1.94 | 1.06 | 0.69 | 0.71 |
| TUBB3 | 12.75 | 9.90 | 8.27 | 7.54 | 4.57 | 6.56 |
| GGT6 | 7.74 | 6.08 | 5.58 | 14.94 | 8.11 | 12.20 |

| Sample/ Gene | Pica _{WT04} | | | Pica _{KO36} | | |
|-----------------|----------------------|-------|-------|----------------------|-------|-------|
| | 1 | 2 | 3 | 1 | 2 | 3 |
| ACADVL | 53.56 | 38.84 | 35.62 | 25.02 | 30.77 | 29.34 |
| KCTD11 | 4.22 | 2.81 | 3.47 | 9.67 | 6.94 | 6.75 |
| NEURL4 | 9.70 | 6.41 | 6.90 | 16.98 | 12.60 | 10.14 |
| CENPV | 14.51 | 11.20 | 17.95 | 7.83 | 7.89 | 8.37 |
| SLC47A2 | 13.75 | 10.75 | 8.71 | 21.66 | 19.28 | 20.63 |
| ALDH3A1 | 60.51 | 24.55 | 39.65 | 7.30 | 10.87 | 9.02 |
| CDK5R1 | 2.12 | 2.06 | 2.24 | 1.47 | 0.99 | 0.79 |
| SLFN5 | 5.47 | 1.95 | 1.09 | 1.65 | 1.11 | 1.20 |
| SLFN13 | 3.92 | 4.72 | 3.63 | 6.09 | 5.65 | 5.71 |
| SLFN11 | 3.14 | 3.55 | 2.59 | 5.37 | 5.98 | 5.74 |
| MRM1 | 13.36 | 11.99 | 11.84 | 9.44 | 8.45 | 6.42 |
| PGAP3 | 4.30 | 3.18 | 3.08 | 6.56 | 4.94 | 6.21 |
| IGFBP4 | 12.66 | 15.29 | 10.42 | 4.05 | 3.35 | 1.90 |
| TNS4 | 16.86 | 10.48 | 7.66 | 20.07 | 17.29 | 14.95 |
| NAGLU | 11.62 | 8.21 | 7.93 | 7.74 | 5.37 | 4.90 |
| VAT1 | 16.05 | 11.83 | 10.57 | 6.31 | 7.63 | 6.84 |
| HOXB9 | 3.00 | 2.25 | 2.13 | 0.61 | 0.69 | 0.42 |
| MRC2 | 4.21 | 2.51 | 1.13 | 1.47 | 0.84 | 1.04 |
| LINC00674 | 2.18 | 2.60 | 2.61 | 3.38 | 3.30 | 3.66 |
| SOX9 | 11.56 | 11.10 | 7.68 | 8.82 | 7.81 | 4.06 |
| LINC00673 | 14.48 | 12.81 | 11.15 | 6.34 | 9.37 | 6.66 |
| TRIM47 | 21.16 | 13.55 | 16.44 | 15.22 | 10.33 | 10.12 |
| CYGB | 2.77 | 0.77 | 0.78 | 4.00 | 2.47 | 2.79 |
| ST6GALNA C2 | 3.05 | 1.45 | 3.36 | 5.83 | 4.44 | 6.94 |
| TIMP2 | 4.11 | 2.60 | 1.49 | 1.13 | 1.11 | 1.80 |
| TBC1D16 | 8.92 | 4.12 | 4.80 | 4.98 | 2.65 | 2.07 |
| RAC3 | 22.76 | 16.61 | 20.07 | 14.51 | 11.81 | 12.48 |
| PYCR1 | 124.18 | 76.44 | 87.81 | 71.65 | 60.96 | 48.43 |
| METRNL | 9.59 | 8.66 | 5.57 | 2.72 | 4.16 | 2.57 |
| TWSG1 | 6.89 | 7.87 | 9.47 | 11.70 | 11.19 | 11.79 |
| ANKRD12 | 1.38 | 2.73 | 2.23 | 2.52 | 2.92 | 2.69 |
| CDH2 | 3.03 | 4.15 | 3.25 | 1.24 | 1.84 | 0.95 |
| FSTL3 | 3.61 | 2.31 | 1.52 | 1.02 | 1.02 | 1.12 |
| GAMT | 41.93 | 30.01 | 31.58 | 24.79 | 21.78 | 24.53 |
| FSD1 | 7.58 | 5.68 | 4.73 | 2.60 | 1.95 | 1.91 |
| C3 | 33.25 | 1.94 | 0.51 | 0.67 | 1.03 | 0.72 |
| ZNF358 | 5.57 | 3.38 | 2.99 | 14.26 | 9.66 | 12.05 |
| ICAM1 | 42.52 | 8.53 | 5.89 | 7.39 | 6.92 | 5.82 |
| NFIX | 6.71 | 5.62 | 4.92 | 3.63 | 2.97 | 2.68 |
| PALM3 | 0.52 | 0.70 | 0.80 | 3.97 | 2.74 | 2.54 |
| ADGRL1 | 8.82 | 4.07 | 4.40 | 4.95 | 2.58 | 3.57 |

| Sample/ Gene | Pica _{WT04} | | | Pica _{KO36} | | |
|-----------------|----------------------|-------|-------|----------------------|-------|-------|
| | 1 | 2 | 3 | 1 | 2 | 3 |
| NOTCH3 | 7.56 | 5.74 | 5.32 | 4.38 | 2.55 | 2.90 |
| GDF15 | 168.63 | 69.38 | 58.21 | 82.08 | 57.33 | 47.92 |
| PDCD2L | 28.57 | 27.41 | 29.90 | 18.59 | 21.06 | 14.58 |
| LRFN1 | 5.33 | 2.96 | 3.94 | 2.27 | 1.28 | 1.21 |
| BLVRB | 54.29 | 35.57 | 46.40 | 66.26 | 69.38 | 77.89 |
| TGFB1 | 4.50 | 3.57 | 1.82 | 0.21 | 0.30 | 0.47 |
| RELB | 9.60 | 3.64 | 2.84 | 2.99 | 1.59 | 3.07 |
| IGFL1 | 132.78 | 34.46 | 25.10 | 10.80 | 16.56 | 29.66 |
| ALDH16A1 | 13.96 | 8.15 | 7.27 | 5.27 | 5.18 | 3.41 |
| KLK6 | 49.85 | 68.33 | 81.35 | 38.01 | 47.94 | 30.67 |
| TRIB3 | 82.92 | 53.09 | 63.16 | 50.17 | 45.49 | 33.67 |
| RSPO4 | 3.07 | 1.56 | 1.72 | 0.33 | 0.27 | 0.48 |
| C20orf194 | 1.80 | 1.79 | 1.26 | 3.22 | 2.17 | 2.87 |
| JAG1 | 23.55 | 17.09 | 12.60 | 9.73 | 7.64 | 5.19 |
| GIN51 | 19.50 | 27.66 | 31.44 | 33.06 | 39.01 | 43.62 |
| ZNF337 | 7.33 | 8.21 | 7.52 | 12.15 | 12.30 | 10.98 |
| SDC4 | 64.39 | 30.84 | 28.53 | 20.91 | 26.38 | 28.44 |
| CYP24A1 | 13.22 | 7.43 | 5.12 | 1.58 | 1.25 | 2.73 |
| BMP7 | 3.21 | 1.92 | 1.73 | 0.50 | 0.33 | 0.36 |
| HELZ2 | 9.38 | 3.70 | 1.78 | 4.43 | 1.84 | 1.75 |
| ARFRP1 | 17.38 | 14.81 | 15.65 | 9.24 | 8.32 | 7.53 |
| RGS19 | 8.40 | 5.69 | 6.48 | 6.79 | 2.29 | 4.34 |
| C2CD2 | 5.69 | 5.09 | 5.12 | 14.08 | 11.38 | 12.42 |
| RIPK4 | 15.06 | 11.93 | 13.48 | 28.50 | 19.25 | 21.49 |
| ZBTB21 | 2.53 | 3.09 | 2.99 | 4.34 | 3.74 | 3.38 |
| MX1 | 4.72 | 3.54 | 1.10 | 0.49 | 1.10 | 0.96 |
| CBS | 23.60 | 18.28 | 20.64 | 13.13 | 13.93 | 10.93 |
| PDE9A | 5.07 | 3.52 | 4.31 | 1.64 | 1.03 | 0.58 |
| SLC19A1 | 39.77 | 26.57 | 27.14 | 33.95 | 19.64 | 14.03 |
| ZDHHC8 | 4.53 | 2.84 | 1.63 | 1.13 | 0.67 | 0.83 |
| MN1 | 1.10 | 1.52 | 0.82 | 3.86 | 2.18 | 2.09 |
| LIF | 43.76 | 25.94 | 34.73 | 21.84 | 17.31 | 25.74 |
| HMOX1 | 12.11 | 5.77 | 4.95 | 3.45 | 3.16 | 3.71 |
| C1QTNF6 | 22.73 | 19.58 | 15.98 | 37.97 | 27.44 | 31.72 |
| GCAT | 11.97 | 11.36 | 13.09 | 8.73 | 8.61 | 6.31 |
| APOBEC3B | 40.28 | 21.51 | 27.85 | 12.89 | 13.21 | 12.49 |
| TBL1X | 7.98 | 7.60 | 6.63 | 4.81 | 5.34 | 3.76 |
| SPIN4 | 3.19 | 3.51 | 2.85 | 7.48 | 6.81 | 6.70 |
| LINC01278 | 3.37 | 3.45 | 3.17 | 5.44 | 7.15 | 5.64 |
| AMER1 | 1.34 | 1.17 | 1.43 | 3.06 | 2.51 | 1.95 |
| ARHGEF9 | 1.34 | 1.42 | 1.20 | 3.41 | 3.34 | 3.26 |
| LAS1L | 17.27 | 20.09 | 22.58 | 31.76 | 31.58 | 28.19 |

| Sample/ Gene | Pica _{WT04} | | | Pica _{KO36} | | |
|-----------------|----------------------|--------|--------|----------------------|---------|--------|
| | 1 | 2 | 3 | 1 | 2 | 3 |
| MSN | 59.54 | 53.39 | 49.48 | 72.23 | 92.48 | 76.62 |
| YIPF6 | 5.26 | 5.59 | 5.00 | 10.39 | 10.24 | 9.42 |
| PJA1 | 5.05 | 5.65 | 4.14 | 6.67 | 9.40 | 8.38 |
| IGBP1 | 12.97 | 14.33 | 17.46 | 26.33 | 33.88 | 37.59 |
| PDZD11 | 17.95 | 22.81 | 24.53 | 31.86 | 44.84 | 43.11 |
| KIF4A | 8.36 | 10.24 | 8.87 | 16.49 | 18.96 | 17.24 |
| FOXO4 | 2.96 | 2.55 | 2.09 | 5.99 | 5.87 | 6.68 |
| SNX12 | 20.29 | 20.10 | 21.39 | 33.39 | 38.45 | 36.27 |
| DLG3 | 8.51 | 9.68 | 9.03 | 15.59 | 17.46 | 17.36 |
| MED12 | 4.41 | 4.29 | 3.92 | 8.61 | 7.24 | 5.50 |
| ERCC6L | 4.04 | 4.84 | 5.23 | 8.15 | 8.80 | 6.82 |
| HDAC8 | 8.55 | 11.42 | 10.07 | 15.32 | 20.47 | 20.37 |
| PHKA1 | 1.97 | 2.10 | 2.24 | 4.14 | 3.88 | 2.98 |
| RLIM | 4.00 | 4.67 | 4.34 | 8.64 | 8.04 | 7.02 |
| ABCB7 | 6.26 | 6.90 | 7.12 | 9.26 | 13.81 | 11.92 |
| MAGT1 | 11.68 | 13.54 | 13.06 | 19.95 | 23.40 | 20.84 |
| RPS4X | 574.02 | 724.51 | 765.61 | 1086.02 | 1522.04 | 1524.7 |
| COX7B | 107.45 | 175.30 | 172.03 | 165.89 | 318.18 | 276.70 |
| ATRX | 3.61 | 6.57 | 5.03 | 11.83 | 10.26 | 10.67 |
| ATP7A | 0.96 | 0.91 | 0.74 | 2.76 | 1.78 | 1.69 |
| TAF9B | 4.22 | 5.79 | 4.97 | 10.51 | 12.15 | 9.81 |
| BRWD3 | 1.52 | 1.41 | 1.01 | 3.35 | 2.78 | 2.20 |
| APOOL | 1.99 | 2.00 | 2.25 | 3.93 | 4.60 | 4.37 |
| CHM | 1.41 | 1.96 | 2.01 | 3.35 | 3.68 | 3.48 |
| PGK1 | 127.22 | 138.00 | 148.60 | 206.03 | 269.12 | 295.34 |
| PCDH19 | 1.93 | 0.21 | 0.35 | 5.47 | 2.97 | 2.61 |
| SRPX2 | 2.94 | 1.25 | 0.62 | 5.43 | 4.73 | 6.69 |
| TSPAN6 | 6.78 | 6.11 | 6.39 | 10.40 | 15.96 | 11.34 |
| DIAPH2 | 2.13 | 2.87 | 2.72 | 4.21 | 5.31 | 5.08 |
| CSTF2 | 12.98 | 11.47 | 12.79 | 23.46 | 22.44 | 19.22 |
| CENPI | 1.60 | 1.33 | 1.60 | 2.87 | 3.88 | 2.87 |
| TRMT2B | 3.87 | 4.11 | 3.82 | 6.60 | 6.67 | 5.94 |
| NONO | 109.58 | 128.99 | 128.10 | 192.37 | 233.32 | 233.17 |
| TCEAL8 | 13.19 | 19.20 | 18.46 | 21.75 | 40.42 | 43.04 |
| WBP5 | 14.89 | 20.68 | 15.96 | 22.42 | 43.63 | 41.06 |
| TCEAL1 | 2.48 | 4.11 | 4.45 | 7.20 | 8.08 | 11.69 |
| NGFRAP1 | 97.12 | 105.60 | 89.54 | 142.49 | 177.40 | 180.96 |
| RPL36A | 273.09 | 435.56 | 482.76 | 444.18 | 858.75 | 971.18 |
| TCEAL4 | 18.84 | 28.77 | 25.61 | 28.78 | 50.19 | 54.13 |
| CXorf57 | 0.61 | 1.00 | 1.06 | 1.57 | 2.69 | 1.77 |
| FAM199X | 6.37 | 7.49 | 6.64 | 13.63 | 12.13 | 10.81 |
| NUP62CL | 2.17 | 2.28 | 2.11 | 4.27 | 5.84 | 4.44 |

| Sample/ Gene | Pica _{WT04} | | | Pica _{KO36} | | |
|-----------------|----------------------|--------|--------|----------------------|--------|--------|
| | 1 | 2 | 3 | 1 | 2 | 3 |
| RBM41 | 1.39 | 2.87 | 2.38 | 3.52 | 3.39 | 3.01 |
| PRPS1 | 20.57 | 22.22 | 23.84 | 33.21 | 44.52 | 36.40 |
| PSMD10 | 31.24 | 43.55 | 43.87 | 54.00 | 78.43 | 70.89 |
| NXT2 | 3.41 | 2.81 | 2.88 | 5.96 | 6.14 | 7.08 |
| ACSL4 | 5.11 | 7.61 | 7.63 | 9.79 | 13.10 | 9.71 |
| TMEM164 | 3.32 | 3.09 | 3.37 | 7.50 | 7.43 | 6.49 |
| AMMECR1 | 2.89 | 2.95 | 2.95 | 5.60 | 4.63 | 4.52 |
| ALG13 | 2.72 | 3.57 | 4.55 | 5.05 | 6.71 | 6.92 |
| MORF4L2 | 83.41 | 109.89 | 114.89 | 125.46 | 173.62 | 168.46 |
| KLHL13 | 3.04 | 4.10 | 3.58 | 7.57 | 8.06 | 7.38 |
| IL13RA1 | 9.03 | 9.31 | 8.29 | 13.84 | 21.45 | 17.58 |
| PLS3 | 35.05 | 40.61 | 36.47 | 47.87 | 68.28 | 56.76 |
| UPF3B | 22.61 | 33.22 | 35.74 | 33.88 | 49.19 | 42.22 |
| ZBTB33 | 12.12 | 14.31 | 14.13 | 19.92 | 19.78 | 18.25 |
| C1GALT1C1 | 15.94 | 19.02 | 19.67 | 21.21 | 27.74 | 27.79 |
| THOC2 | 11.81 | 16.09 | 14.32 | 17.95 | 18.47 | 18.48 |
| XIAP | 12.03 | 13.53 | 11.67 | 17.10 | 16.57 | 16.54 |
| ELF4 | 16.65 | 14.93 | 15.33 | 26.85 | 23.31 | 22.16 |
| RBMX2 | 17.96 | 22.52 | 22.78 | 25.43 | 39.56 | 36.35 |
| PHF6 | 13.64 | 19.04 | 19.45 | 27.32 | 28.41 | 24.12 |
| STAG2 | 25.99 | 31.07 | 27.00 | 40.98 | 40.04 | 37.02 |
| MBNL3 | 1.72 | 2.61 | 1.75 | 4.32 | 3.45 | 3.08 |
| SLC9A6 | 5.15 | 4.85 | 5.18 | 6.94 | 7.71 | 7.92 |
| VGLL1 | 1.62 | 0.19 | 0.81 | 5.23 | 4.33 | 6.91 |
| FHL1 | 17.96 | 14.14 | 12.45 | 7.14 | 10.59 | 8.95 |
| ATP11C | 2.37 | 3.13 | 3.20 | 5.18 | 4.67 | 4.53 |
| LDOC1 | 14.79 | 10.62 | 12.27 | 39.52 | 30.21 | 29.74 |
| IDS | 5.36 | 3.80 | 5.22 | 10.91 | 8.67 | 7.65 |
| CXorf40B | 10.28 | 9.01 | 12.87 | 16.10 | 18.17 | 17.58 |
| TMEM185A | 5.90 | 3.70 | 4.84 | 11.77 | 9.99 | 10.37 |
| FMR1 | 5.99 | 7.86 | 7.45 | 12.92 | 14.13 | 13.77 |
| CD99L2 | 1.42 | 1.54 | 1.82 | 3.30 | 2.78 | 2.75 |
| MTMR1 | 10.31 | 11.33 | 9.91 | 21.13 | 20.90 | 22.18 |
| VMA21 | 4.45 | 7.37 | 7.64 | 10.44 | 13.39 | 11.28 |
| HMGB3 | 14.58 | 19.66 | 20.85 | 29.27 | 35.76 | 35.81 |
| CETN2 | 13.64 | 27.37 | 26.37 | 29.16 | 43.59 | 46.76 |
| ZNF275 | 2.04 | 2.09 | 2.03 | 4.00 | 2.98 | 3.23 |
| NSDHL | 13.05 | 19.83 | 22.43 | 33.37 | 35.97 | 42.32 |
| MAGEA4 | 126.45 | 154.44 | 166.61 | 230.23 | 268.43 | 261.35 |
| FAM58A | 8.55 | 9.48 | 9.13 | 20.85 | 17.30 | 16.01 |
| HAUS7 | 12.30 | 10.17 | 13.25 | 27.15 | 23.75 | 22.45 |
| SLC6A8 | 1.97 | 1.94 | 1.59 | 4.62 | 2.90 | 5.77 |

| Sample/ Gene | Pica _{WT04} | | | Pica _{KO36} | | |
|-----------------|----------------------|--------|--------|----------------------|--------|--------|
| | 1 | 2 | 3 | 1 | 2 | 3 |
| ABCD1 | 4.31 | 2.81 | 3.05 | 11.57 | 6.13 | 6.66 |
| PLXNB3 | 1.25 | 0.59 | 0.61 | 3.76 | 1.80 | 1.68 |
| L1CAM | 2.18 | 1.55 | 1.63 | 10.53 | 7.21 | 4.87 |
| BCAP31 | 131.41 | 146.12 | 159.71 | 258.48 | 301.59 | 281.43 |
| NAA10 | 46.31 | 40.34 | 51.56 | 75.41 | 82.40 | 80.35 |
| SSR4 | 86.44 | 93.87 | 96.67 | 139.35 | 180.95 | 186.47 |
| TMEM187 | 4.81 | 4.17 | 4.02 | 9.15 | 8.23 | 10.11 |
| MECP2 | 10.09 | 7.92 | 8.49 | 22.05 | 19.12 | 18.42 |
| IRAK1 | 99.68 | 57.29 | 69.12 | 208.14 | 119.31 | 121.26 |
| FUNDC2 | 14.81 | 21.49 | 20.50 | 21.23 | 31.42 | 28.54 |
| BRCC3 | 9.27 | 10.16 | 9.51 | 16.04 | 16.88 | 16.49 |
| CLIC2 | 0.48 | 0.46 | 0.49 | 1.03 | 2.18 | 2.00 |