**SUPPLEMENTARY INFORMATION**

**Electroporation**

Electroporation was performed in K562 cells at 70% confluency in T25 suspension culture flasks. 20ug of CALR plasmids (CALR WT/Δ52/Ins5) are electroporated at 220V and 975µF in electroporation cuvettes (Bio-RAD, #1652088) for respective conditions. Media change was done 24hrs post electroporation and cells were harvested the 16hrs post media change for immunoblotting.

**Inhibitor treatment**

Post 24hrs transfection, cells were first washed with PBS followed by 30 mins inhibitor treatment in the incubator at 37°C and 5% $CO_2$ with or without 10µM MK-2206, 10µM GDC-0068 and 1µM GSK-2334470. Cells were pelleted down with PBS by centrifugation at 1000g for 5mins. Samples were analysed by the western blotting technique.

**RNA extraction, cDNA synthesis and qPCR**

RNA extraction was carried out by homogenization in TRIZOL reagent followed by phase separation in 0.2ml Chloroform per 1ml of TRIZOL reagent. MCTs were subjected to rest for 5mins before centrifugation at 13000 rpm for 15mins at 4 °C. Transferred the aqueous layer in fresh tube for RNA precipitation by 0.5ml isopropanol. Finally, after centrifugation, the pellet was washed with 70% ethanol and dried, then resuspended in nuclease-free water and quantified for further use. cDNA synthesis was done according to the manufacturer's protocol (BioBharti). Thereafter, qPCR was carried out by various gene specific primers**. (Table 2. Supplementary list of primers)**

**Table 1. List of Antibodies**

| S.No. | Antibody | Secondary Antibody | Dilution | Source | Identifiers |
|---|---|---|---|---|---|
| **1.** | p-mTOR (S2448) | Rabbit | 1:1000 | CST | 2971S |
| **2.** | p-mTOR (S2481) | Rabbit | 1:1000 | CST | 2974S |
| **3.** | mTOR | Rabbit | 1:1000 | CST | 2983S |
| **4.** | p-AKT (T308) | Rabbit | 1:1000 | CST | 4056S |
| **5.** | p-AKT (S473) | Rabbit | 1:1000 | CST | 4060S |
| **6.** | AKT | Mouse | 1:1000 | CST | 2920S |
| **7.** | p-P70 S6K (T421/S424) | Rabbit | 1:1000 | CST | 9204S |
| **8.** | P70 S6K | Rabbit | 1:1000 | CST | 2708S |
| **9.** | p-4EBP1 | Rabbit | 1:1000 | CST | 9451S |

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|---|---|---|---|---|---|
| **10.** | 4EBP1 | Rabbit | 1:1000 | CST | 9644S |
| **11.** | HA | Mouse | 1:1000 | CST | 2367S |
| **12.** | p-NDRG1 (T346) | Rabbit | 1:1000 | CST | 5482T |
| **13.** | NDRG1 | Rabbit | 1:1000 | CST | 5196S |
| **14.** | RICTOR (53A2) | Rabbit | 1:1000 | CST | 2114T |
| **15.** | p-FOXO1 (S256) | Rabbit | 1:1000 | CST | 9461T |
| **16.** | FOXO1 | Rabbit | 1:1000 | CST | 2880 |
| **17.** | β-Actin | Mouse | 1:1000 | CST | 3700S |
| **18.** | mCherry | Mouse | 1:1000 | Abclonal | AE002 |
| **19.** | Anti-Mouse IgG HRP linked | | 1:5000 | CST | 7076S |
| **20.** | Anti Rabbit IgG HRP linked | | 1:10000 | Invitrogen (Thermo Fisher Scientific) | G21234 |
| **21.** | p-Erk1/2 (Y202/Y204) | Rabbit | 1:2000 | CST | 4370S |
| **22.** | Erk 2 | Rabbit | 1:2000 | BioBharti | BB-AB0135 |
| **23.** | c-JUN | Rabbit | 1:1000 | Abcam | 7964 |
| **24.** | m-SIN1 | Rabbit | 1:1000 | CST | 12860S |

**Table 2. List of Primers**

| S.No. | Primers | Sequence (5'-3') |
|---|---|---|
| **1.** | c-JUN P1 Forward seq | GGGAAACAACAACCACCCCT |
| **2.** | c-JUN P1 Reverse seq | GACTGTCTAGTGACGGTGGC |
| **3.** | c-JUN P2 Forward seq | CGGAGCATTACCTCATCCCG |
| **4.** | c-JUN P2 Reverse seq | CAGCCCGAGCTCAACACTTA |
| **5.** | c-JUN ED1 Forward seq | CAAGTCCTTCCCACTCGTGC |
| **6.** | c-JUN ED1 Reverse seq | GACAAGTTGCGACGGAGAGA |
| **7.** | c-JUN ED2 Forward seq | GACTTCTCAGTGGGCTGTCC |
| **8.** | c-JUN ED2 Reverse seq | TATACTCCTCCTCCCCCAGC |
| **9.** | c-JUN ED3 Forward seq | GGAACTCTGGGAGGGTCGAA |
| **10.** | c-JUN ED3 Reverse seq | GCCCAGAAAGTTGTGTTTGTGT |
| **11.** | qHu cJUN FP | GTGCCGAAAAAGGAAGCTGG |
| **12.** | qHu cJUN RP | CTGCGTTAGCATGAGTTGGC |
| **13.** | qHu FOXO1 FP | AGGGTTAGTGAGCAGGTTACAC |
| **14.** | qHu FOXO1 RP | TGCTGCCAAGTCTGACGAAA |
| **15.** | CALR WT Fw pcDNA (FP) | GAAGGGTACCATGCTGCTATCCGTG |
| **16.** | CALR WT Rv pcDNA (RP) | GAAGGCGGCCGCCTACAGCTCGTCCTT |
| **17.** | pcDNA CALR WT-15 RP | GAAGGCGGCCGCCTACTCCTTGTCCTCCTCA |
| **18.** | pcDNA CALR WT-30 RP | GAAGGCGGCCGCCTAATCCTCCTTGTC |
| **19.** | pcDNA CALR WT-45 RP | GAAGGCGGCCGCCTATTCTTCCTCCTCCTT |
| **20.** | pcDNA CALR WT-Exon 9 RP | GAAGGCGGCCGCCTTTGTTACGCCCCA |

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|---|---|---|
| **21.** | β-Actin mouse F | CTGGCTCCTAGCACCATGAA |
| **22.** | β-Actin mouse R | AGCTCAGTAACAGTCCGCCTA |

**Table 3. List of plasmid DNA**

| S.No. | Plasmids | Source | Identifiers |
|---|---|---|---|
| **23.** | pcDNA 3.1-HA-CALR WT | This study | |
| **24.** | pcDNA 3.1-HA-CALR Δ52 | This study | |
| **25.** | pcDNA 3.1-HA-CALR Ins5 | This study | |
| **26.** | pMSCV-IRES-GFP-HA CALR WT | This study | |
| **27.** | pMSCV-IRES-GFP-HA CALR Δ52 | This study | |
| **28.** | pMSCV-IRES-GFP-HA CALR Ins5 | This study | |
| **29.** | pMSCV-IRES-mCherry-HA CALR WT | This study | |
| **30.** | pMSCV-IRES- mCherry - HA CALR Δ52 | This study | |
| **31.** | pMSCV-IRES- mCherry - HA CALR Ins5 | This study | |
| **32.** | pRK5-FLAG-RICTOR | Gift from Prof. David Pearce and Enzo Takagi, UCSF, USA | N/A |
| **33.** | pcDNA-mSin1(1.1)-HA | Addgene | Plasmid #73388 |
| **34.** | pcDNA 3.1-V5-c-JUN | Gift from Prof. Richard Cerione and Kathy S. Rojas, Cornell, USA | N/A |

**Table 4. List of Commercial Kits and Reagents**

| S.No. | Kits and Reagents | Source | Identifiers |
|---|---|---|---|
| **1.** | ATP Determination Kit | Promega | G924A |
| **2.** | Pierce BCA Protein Estimation kit | Thermo Fisher Scientific | 23225 |
| **3.** | Qiagen Miniprep plasmid isolation kit | Qiagen | 27106 |
| **4.** | Qiagen Maxiprep plasmid isolation kit | Qiagen | 12163 |
| **5.** | 2-NBDG | Thermo Fisher Scientific | N13195 |
| **6.** | cDNA synthesis kit | BioBharti | BB-E0043 (10000 U) |
| **7.** | Pierce Protein A/G beads | Thermo Fisher Scientific | 20421 |
| **8.** | Supersignal west femto chemiluminescent substrate | Thermo Fisher Scientific | 34095 |

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|---|---|---|---|
| **9.** | Supersignal west pico plus chemiluminescent substrate | Thermo Fisher Scientific | 34580 |
| **10.** | Inhibitor MK-2206 | MedChem | HY-10358 |
| **11.** | Inhibitor GDC-0068 | MedChem | HY-15186 |
| **12.** | Inhibitor GSK-2334470 | MedChem | HY-14981 |
| **13.** | Lipofectamine | Thermo Fisher Scientific | 11668019 |