**Supporting Information**

**Supplemental Table S1: Virus vectors encoding oncogenes used in the present study**

|  |  |  |
| --- | --- | --- |
| Gene | Vector | Drug for selection (concentration μg/mL)  |
| cMYC | pMX | none |
| hTERT | pCMSCVpuro | puromycin (2) |
| p53CT: c-terminal region of wild-type p53 [26] | pCX4neo | neomycin (500) |
| CDK4 | pCX4bsr | blasticidin S (5) |
| RasV12 | pBABEpuro | puromycin (2) |
| PI3CA mutant: PIK3CAH1047R [26] | pCX4bleo | bleocin (20) |
| Human papilloma virus type 16, E6/E7 | pZip-NeoSV(X)1 | neomycin (500) |

**Supplemental Table S2: Primer sets for RT-PCR to detect transduced genes in PTY and NPCPR cells**

|  |  |  |  |
| --- | --- | --- | --- |
| Primer name | Sequence | Annealing temperature (oC) | Band size (bpa) |
| GAPDH sense | GTCTTCACCACCATGGAGAAGGC | 55 | 500 |
| GAPDH anti-sense | CATGCCAGTGAGCTTCCCGTTCA |  |  |
| hTERT sense | CGTGGTTTCTGTGTGGTGTC | 60 | 200 |
| hTERT anti-sense | CCTTGTCGCCTGAGGAGTAG |  |  |
| p53CT; recognized mutant p53 sense | GTACCCATACGATGTTCCAGA | 55 | 270 |
| p53CT; recognized mutant p53 anti-sense | TTATGGCGGGAGGTAGACTG |  |  |
| CDK4 sense | GCTTTTGAGCATCCCAATGT | 55 | 533 |
| CDK4 anti-sense | ACATCTCGAGGCCAGTCATC |  |  |
| RASV12 sense | GGAAGCAGGTGGTCATTGAT | 60 | 370 |
| RASV12 anti-sense | ATCTCACGCACCAACGTGTA |  |  |
| PI3CA mutant sense | GCTATCGGCATGCCAGTGTG | 60 | 591 |
| PI3CA mutant anti-sense | TGGCGTAGCTGTGGAGATGC |  |  |
| exogenous human cMYC sense | AGAGAAGCTGGCCTCCTACC | 60 | 600 |
| exogenous human cMYC anti-sense | TCGGTTGTTGCTGATCTGTC |  |  |

a bp: base pair

The conditions of RT-PCR were as follows: previously warming the machine up at 94 oC for the initial 2 min followed by 40 cycles consisting of denaturation for 30 s at 96 oC, annealing for 30 s at 60 oC for NPC and at variable temperatures for PTY and NPCPR shown in Table S2, and extension for 30 s at 68 oC. A 4-min extension at 68 oC was added after the final cycle.

**Supplemental Table S3: List of the predicted peptides according to the results of LC-MS/MS**

|  |  |  |
| --- | --- | --- |
| **PTY** | **Sequence** | **P** |
| Down syndrome cell adhesion molecule-like protein 1 | D.GEWGEMQNITTTRER.V | 0.00006 |
| Terminal uridylyltransferase 4, isoform | R.M\*DDFQLKGIVEEKFVK.W | 0.00006 |
| Inactive serine/threonine-protein kinase TEX14 isoform | Q.LM\*AVCLSQDLEKTR.L | 0.001 |
| Prickle-like protein 2 | E.EEEEEGGMSTQQC#R.T | 0.0009 |
| Synphilin-1 isoform (Sph1) | Q.NNNNNYQAANQLK.T | 0.0007 |
| HSP-90 beta | K.ADLINNLGTIAK.S | 0.0001 |
| HSP-90 beta | R.ELISNASDALDK.I | 0.0008 |
| Semaphorin-4A | N.CSVYESC#VDC#VLAR.D | 0.00001 |
| 78kDa glucose-regulated protein, GRP78 | R.TWNDPSVQQDIK.F | 0.000006 |
| 78kDa glucose-regulated protein, GRP78 | K.TKPYIQVDIGGGQTK.T | 0.00003 |
| 78kDa glucose-regulated protein, GRP78 | K.NQLTSNPENTVFDAK.R | 0.0001 |
| 78kDa glucose-regulated protein, GRP78 | K.SQIFSTASDNQPTVTIK.V | 0.0002 |
| Heat shock 70kDa protein 9 (HSPA9), GRP75 | K.SDIGVILVGGM\*TR.M | 0.000008 |
| polypeptide N-acetylgalactosaminyltransferase 12 (GLT12) | R.PGFFGMLQNQGLKDYCF.D | 0.000008 |
| Gamma-glutamyltransferase 7 (GGT7) | K.DPFSAAAAEC#SCRQDGLTVIVTACLTFA.T | 0.0002 |
| Mediator of RNA polymerase II transcription subunit | K.VEFVNLVLLFCE.F | 0.0006 |
| Glucose transporter type 4 insulin-responsive (GLUT-4) | L.VNNVLAVLGGSLMGLANAAASYEMLILGR.F | 0.0003 |
| Membrane-spanning 4-domains subfamily A member 13 (MS4A13) | K.TGCTLWGIFKLGREVSR.I | 0.0003 |
| Tumor necrosis factor alpha-induced protein 8 (TNFAIP8) | L.YNPFGNFKPHLQK.L | 0.0004 |
|  |  |  |
| **Fibroblast cell line** | **Sequence** | **P** |
| Glucosidase II subunit alpha | K.DPAEGDGAQPEETPR.D | 0.0001 |
| Glucosidase II subunit alpha | K.M\*MDYLQGSGETPQTDVR.W | 0.000005 |
| Glucosidase II subunit alpha | K.AEKDEPGAWEETFK.T | 0.00004 |
| Glucosidase II subunit alpha | R.DDNSVELTMAEGPYK.I | 0.0002 |
| Glucosidase II subunit alpha | R.DVHNIYGLYVH.M | 0.00009 |
| Glucosidase II subunit alpha | R.KPGINVASDWSIHLR.- | 0.00004 |
| Glucosidase II subunit alpha | K.VLLVLELQGLQK.N | 0.00002 |
| Coatomer subunit beta isoform | R.NVEELVIVLKK.E | 0.001 |
| Potential calcium-dependent-cell adhesion protein (PCDC2) | G.TVQLLVQVLDVNDNDPEFDK.S | 0.0002 |
| Alpha-actinin-1 | K.GISQEQMNEFR.A | 0.000001 |
| Transitional endoplasmic reticulum ATPase isoform | K.LAGESESNLR.K | 0.0006 |
| Transitional endoplasmic reticulum ATPase isoform | R.AHVIVMAATHRPNSIDPALR.R | 0.000004 |
| Transitional endoplasmic reticulum ATPase isoform | R.KGDIFLVR.G | 0.00009 |
| Transitional endoplasmic reticulum ATPase isoform | K.M\*TNGFSGADLTEIC#QR.A | 0.0003 |
| Transitional endoplasmic reticulum ATPase isoform | K.GVLFYGPPGC#GK.T | 0.00002 |
| Transitional endoplasmic reticulum ATPase isoform | R.LGDVISIQPC#PDVK.Y | 0.0004 |
| Transitional endoplasmic reticulum ATPase isoform | R.GILLYGPPGTGK.T | 0.00001 |
| HSP-90 beta 1, GRP94 | K.NLLHVTDTGVGM\*TR.E | 0.00000008 |
| HSP-90 beta 1, GRP94 | K.NLLHVTDTGVGMTR.E | 0.0007 |
| HSP-90 beta 1, GRP94 | K.AQAYQTGKDISTNYYASQKK.T | 0.0006 |
| HSP-90 beta 1, GRP94 | K.AQAYQTGKDISTNYYASQK.K | 0.000002 |
| HSP-90 beta 1, GRP94 | K.AQAYQTGKDISTNYYASQK.K | 0.000000005 |
| HSP-90 beta 1, GRP94 | K.DISTNYYASQK.K | 0.00008 |
| HSP-90 beta 1, GRP94 | K.DISTNYYASQKK.T | 0.000002 |
| HSP-90 beta 1, GRP94 | R.KEAESSPFVER.L | 0.0002 |
| HSP-90 beta 1, GRP94 | K.EAESSPFVER.L | 0.0006 |
| HSP-90 beta 1, GRP94 | R.GLFDEYGSKKSDYIK.L | 0.001 |
| HSP-90 beta 1, GRP94 | R.GLFDEYGSK.K | 0.0002 |
| HSP-90 beta 1, GRP94 | R.SGYLLPDTK.A | 0.0006 |
| HSP-90 beta 1, GRP94 | R.SGYLLPDTK.A | 0.0003 |
| HSP-90 beta 1, GRP94 | K.AYGDRIER.M | 0.0008 |
| HSP-90 beta 1, GRP94 | K.EGVKFDESEKTK.E | 0.0001 |
| HSP-90 beta 1, GRP94 | K.LGVIEDHSNR.T | 0.0002 |
| HSP-90 beta 1, GRP94 | K.GVVDSDDLPLNVSR.E | 0.0005 |
| HSP-90 beta 1, GRP94 | K.EFEPLLNWMK.D | 0.0005 |
| HSP-90 beta 1, GRP94 | K.FAFQAEVNR.M | 0.00007 |
| HSP-90 beta 1, GRP94 | K.GVVDSDDLPLNVSR.E | 0.000001 |
| HSP-90 beta 1, GRP94 | A.DDEVDVDGTVEEDLGK.S | 0.000008 |
| HSP-90 beta 1, GRP94 | R.EEEAIQLDGLNASQIR.E | 0.0009 |
| HSP-90 alpha | R.TLTIVDTGIGMTK.A | 0.0004 |
| HSP-90 alpha | R.APFDLFENR.K | 0.0003 |
| HSP-90 alpha | R.NPDDITNEEYGEFYK.S | 0.0002 |
| HSP-90 alpha | R.NPDDITQEEYGEFYK.S | 0.0000001 |
| HSP-90 beta | K.ADLINNLGTIAK.S | 0.0000009 |
| HSP-90 beta | K.ADLINNLGTIAK.S | 0.000004 |
| HSP-90 beta | R.ELISNASDALDKIR.Y | 0.000004 |
| HSP-90 beta | R.ELISNASDALDK.I | 0.00004 |
| HSP-90 beta | K.EQVANSAFVER.V | 0.000005 |
| HSP-90 beta | K.SIYYITGESK.E | 0.00008 |
| HSP-90 beta | R.TLTLVDTGIGM\*TK.A | 0.00001 |
| HSP-90 beta | R.GVVDSEDLPLNISR.E | 0.0006 |
| HSP-90 beta | K.LGIHEDSTNR.R | 0.0000006 |
| Amiloride-sensitive sodium channel subunit alpha isoform (SCNN1A) | M.AELIFDLLVITFLLLLR.R | 0.0005 |
| 78kDa glucose-regulated protein, GRP78 | K.SQIFSTASDNQPTVTIK.V | 0.0008 |
| Heat shock 70kDa protein 9 (HSPA9), GRP75 | R.GVVDSEDIPLNLSR.E | 0.0000003 |
| Zinc finger protein 217 isoform | Q.LKEMPSVFQNVLGSAVLSPAHK.D | 0.00009 |
| Endoplasmic reticulum resident protein 70 (ERp70) | K.GQAVDYEGSR.T | 0.0007 |
| Endoplasmic reticulum resident protein 70 (ERp70) | K.VSQGQLVVMQPEK.F | 0.000004 |
| Endoplasmic reticulum resident protein 70 (ERp70) | K.DGDDVIIIGVFK.G | 0.0001 |
| Zinc finger protein 850 | K.NHSLECLC#FRGDWEGNVQFQTLQDNQEECFKQVI | 0.0004 |
| Glucosiderse 2 subunit beta isoform | R.ESLQQM\*AEVTR.E | 0.0002 |
| Glucosiderse 3 subunit beta isoform | R.SLKDVEESIR.N | 0.0005 |
| Cytochrome p540, family 1, subfamily A, polypeptide 2 | R.LQELMAGPGHFNPYNQVVV.S | 0.0006 |
| Polypeptide N-acetylgalactosaminyltransferase 12 (SCNN1A) | R.PGFFGMLQNQGLKDYCF.D | 0.0005 |
| GDNF family receptor alpha-2 isoform | F.DMTPNYVDSSPTGIVVSPWCSCR.G | 0.0001 |
| Dynactin subunit 2 isoform (DCTN2) | A.YMWLLPTDTLGKQILPM\*LVASEMSHK.D | 0.0003 |
| Cyclic AMP-responsive element-binding protein 3-like (OASIS) | K.LLAKEGITLPTQLPL.T | 0.0006 |
| Lysosomal-associated transmembrane protein　LAMP2b | K.AYLINCVMNC#YKYINNRNVP.E | 0.001 |

**Supplemental figure S1: Soft agar colony forming assay of PTY cells and NPCPR cells**

To assess tumorigenicity *in vitro*, soft-agar colony forming assay were performed. Oncogene transduced cells (2 × 104 cells) were plated in 60-mm culture dishes in 3 mL of DMEM containing 10% FBS and 0.36% agar on a layer of 5 mL of the same medium containing 0.7% agar. Three weeks after plating, colonies were counted and photographs of the colonies were taken. (A, B) Stereoscopic microscopic image of the soft agar colony forming assay of PTY cells. Arrows indicate colonies in the wells. (A) Cells introduced with hTERT, p53CT, CDK4 and HRASv12 genes. (B) Cells introduced with hTERT, p53CT, CDK4, HRASV12, PI3CA mutant and cMYC genes. (C) Expression of transduced genes in PTY and NPCPR cells. PT-PCR was performed to confirm the expression of the transduced-oncogenes. Total RNA was isolated using TRIZOL® Reagent (Life Technologies). First-strand cDNA was made from total RNA with SuperScript™ III Reverse Transcriptase (Life Technologies ). RT-PCR was performed with AmpliTaq Gold (Life Technologies #4398813) according to the manufacturer’s instructions. Primer sets are indicated in Supplemental Table S2. p53CT gene contains the HA sequence as a tag, which was amplified with the primers to exclude wild type p53 genes. The primers for monkey cMYC were designed to recognize a monkey specific sequence. The other primers were designed according to the sequence of transduced genes. (D) Number of colonies in the soft agar colony forming assay of PTY cells. (E) Colonies of NPCPR cells in the soft-agar colony forming assay (arrows).

**Supplemental figure S2: SDS-PAGE of the lysates of PTY cells and immortalized fibroblasts**

 PTY cells and immortalized fibroblasts transduced with p53CT, CDK4 and hTERT genes were lysed in 1% Triton X-100 containing lysis buffer. Cell lysates were immunologically precipitated by IgG fraction in the plasma of monkey #1 in Fig.4. After electrophoresis, the polyacrylamide gel was stained with Coomassie Brilliant Blue (CBB) to visualize proteins. Arrows at lanes 1 and 3 show common bands in the samples of PTY cells and immortalized fibroblasts. Antigens of interest in the gel bands (arrows) were cut into pieces. The gel pieces were extracted and digested into peptides and then analyzed by a liquid chromatography system, Paradigm MG4 (AMR Inc.), linked with a tandem mass spectrometer, Finigan LCQ Advantage MAX (Thermo Electron Corp.). All MS/MS spectra were identified using Xcalibur Bioworks ((v.3.2), Thermo Electron Corp.). LC-MS/MS analysis was performed at the Center of Research Laboratory at Shiga University of Medical Science. The analysis showed that the bands indicated by upper and lower arrows in lanes l and 3 were GRP94 and GRP78, respectively.

**Supplemental figure S3: Co-existence of GRPs and monkey IgG on the surface of immortalized cells**

The expressions of GRPs on various immortalized cells was analyzed by flow cytometry and immunofluorescence staining: PTY (A, E, I, M), NPCPR (B, F, J, N), fibroblasts immortalized by transduction of p53CT, CDK4 and hTERT genes (C, G, K, O), and fibroblasts immortalized by transduction of E6/E7 and hTERT genes (D, H, L, P). (A-H) Dot plots of the flow cytometry analysis. Gray dots indicate cells stained with an isotype control antibody and plasma of monkeys without transplantation. Red dots indicated cells stained with anti-GRPs and plasma of monkeys rejecting tumors. (I-P) The cells were cultured in 2-well glass slide chambers for 2-3 days. Then the cells were fixed in 4% paraformaldehyde and were permeabilized with 0.5% saponin in PBS containing 0.1% BSA. After incubation with anti-GRP94, anti-GRP78 and inactivated-monkey plasma, FITC-conjugated goat polyclonal anti-mouse IgG, CY3-conjugated goat anti-mouse IgG and TR-conjugated goat polyclonal anti-rat IgG were used as secondary antibodies. The cells were double-stained by monkey plasma (green) and anti-GRP94 (I-L) or anti-GRP78 (M-P) (red). The merged yellow color indicates co-existing anti-GRP and monkey IgG.

**Supplemental figure 4: IgG against GRP94 in plasma is autoantibody.**

(A) CBB staining of polyacrylamide gel after electrophoresis of the control ladder marker and recombinant GRP94 and recombinant GRP78. GRP94 and GRP78 proteins were applied into each well simultaneously. (B) Western blot analysis against GRP94 and GRP78 proteins with plasma of normal monkeys (a) - (e) without transplantation and monkey with transplantation, which were same as monkey #1 in Fig 4. Plasma of the individual normal healthy monkeys (a) - (e) and plasma of a monkey rejecting PTY cells before and after tumor rejection were used as primary antibodies. Anti-monkey IgG HRP was used as a secondary antibody. (C, D) Ig (including IgG and IgM) specific for GRP94 (C) and GRP78 (D) was detected using ELISA. No significant difference was detected among samples.