Supplement 2: The pathways in which the top ten mutated genes are involved

| Pathway | TP53 | RB1 | RICTOR | ROS1 | NTRK1 | PTEN | KEAP1 | MCL1 | APC | Total |
|---|------|-----|--------|------|-------|------|-------|------|-----|-------|
| Pathways in cancer | + | + | | | + | + | + | | + | 6 |
| Hepatocellular carcinoma | + | + | | | | + | + | | + | 5 |
| PI3K-Akt signaling pathway | + | | | | + | + | | + | | 4 |
| MicroRNAs in cancer | + | | | | | + | | + | + | 4 |
| Human papillomavirus infection | + | + | | | | + | | | + | 4 |
| Human T-cell leukemia virus 1 infection | + | + | | | | + | | | + | 4 |
| Breast cancer | + | + | | | | + | | | + | 4 |
| Cellular senescence | + | + | | | | + | | | | 3 |
| mTOR signaling pathway | | + | + | | | + | | | | 3 |
| Central carbon metabolism in cancer | + | | | | + | + | | | | 3 |
| Melanoma | + | + | | | | + | | | | 3 |
| Prostate cancer | + | + | | | | + | | | | 3 |
| Autophagy - animal | + | + | | | | + | | | | 3 |
| Glioma | + | + | | | | + | | | | 3 |
| Apoptosis | + | | | | + | | | + | | 3 |
| p53 signaling pathway | + | + | | | | + | | | | 3 |
| Small cell lung cancer | + | + | | | | + | | | | 3 |
| Gastric cancer | + | + | | | | | | | + | 3 |
| Metabolic pathways | | + | | | | + | | | + | 3 |
| Endometrial cancer | + | | | | | + | | | + | 3 |
| Cell cycle | + | + | | | | | | | + | 3 |
| MAPK signaling pathway | + | | | | + | | | | | 2 |
| Human cytomegalovirus infection | + | + | | | | | | | | 2 |
| Hepatitis B | + | + | | | | | | | | 2 |
| Endocrine resistance | + | + | | | | | | | | 2 |
| Chronic myeloid leukemia | + | + | | | | | | | | 2 |
| Viral carcinogenesis | + | + | | | | | | | | 2 |
| Kaposi sarcoma-associated herpesvirus | + | + | | | | | | | | 2 |
| infection | | Т | | | | | | | | |
| Non-small cell lung cancer | + | + | | | | | | | | 2 |
| JAK-STAT signaling pathway | | + | | | | | | + | | 2 |
| Pancreatic cancer | + | + | | | | | | | | 2 |
| Bladder cancer | + | + | | | | | | | | 2 |
| Hepatitis C | + | + | | | | | | | | 2 |
| Transcriptional misregulation in cancer | + | | | | + | | | | | 2 |

| Longevity regulating pathway | + | + | | | | | | 2 |
|---|---|---|---|---|---|---|---|----------|
| Biosynthesis of secondary metabolites | | + | | | + | | | 2 |
| Epstein-Barr virus infection | + | + | 1 | 1 | | | | 2 |
| Neurotrophin signaling pathway | + | | | + | | | | 2 |
| Fluid shear stress and atherosclerosis | + | | | 1 | | + | | 2 |
| Sphingolipid signaling pathway | + | | 1 | 1 | + | | | 2 |
| Huntington disease | + | + | | | | | | 2 |
| Thyroid cancer | + | | | + | | | | 2 |
| Inflammatory mediator regulation of TRP | | | | | | | | 0 |
| channels | | + | | + | | | | 2 |
| Complement and coagulation cascades | | + | + | | | | | 2 |
| Alzheimer disease | | + | | | | | + | 2 |
| Colorectal cancer | + | | | | | | + | 2 |
| Cushing syndrome | | + | | | | | + | 2 |
| Regulation of actin cytoskeleton | | + | | | | | + | 2 |
| Hippo signaling pathway | + | | | | | | + | 2 |
| Wnt signaling pathway | + | | | | | | + | 2 |
| Th17 cell differentiation | | + | | | | | + | 2 |
| Microbial metabolism in diverse | | + | | | | | + | 2 |
| Th1 and Th2 cell differentiation | | + | | | | | + | 2 |
| Quorum sensing | | + | | | | | + | 2 |
| Inflammatory bowel disease (IBD) | | + | | | | | + | 2 |
| Basal cell carcinoma | + | | | | | | + | 2 |
| Ras signaling pathway | | | | + | | | | 1 |
| EGFR tyrosine kinase inhibitor resistance | | | | | + | | | 1 |
| FoxO signaling pathway | | | | | + | | | 1 |
| Proteoglycans in cancer | + | | | | | | | 1 |
| Thyroid hormone signaling pathway | + | | | | | | | 1 |
| Focal adhesion | | | | | + | | | 1 |
| Shigellosis | + | | | | | | | 1 |
| Calcium signaling pathway | | + | | | | | | 1 |
| cAMP signaling pathway | | + | | | | | | 1 |
| Gap junction | | + | | | | | | 1 |
| Herpes simplex virus 1 infection | + | | | | | | | 1 |
| MAPK signaling pathway - fly | | | + | | | | | 1 |
| Measles | + | | | | | | | 1 |
| PD-L1 expression and PD-1 checkpoint | | | | | + | | | 1 |
| pathway in cancer | | | | | Т | | | <u> </u> |
| Parkinson disease | + | | | | | | | 1 |

| Axon regeneration | | | | | + | | 1 |
|--|---|---|---|--|---|--|---|
| Platinum drug resistance | + | | | | | | 1 |
| Neuroactive ligand-receptor interaction | | + | | | | | 1 |
| Autophagy - yeast | | + | | | | | 1 |
| Two-component system | | + | | | | | 1 |
| Vascular smooth muscle contraction | | | + | | | | 1 |
| Bile secretion | | + | | | | | 1 |
| Spinocerebellar ataxia | | + | | | | | 1 |
| GnRH secretion | | + | | | | | 1 |
| Epithelial cell signaling in Helicobacter pylori | | | | | | | 1 |
| infection | | + | | | | | |
| Insulin resistance | | | | | + | | 1 |
| Cytokine-cytokine receptor interaction | | + | | | | | 1 |
| Ovarian steroidogenesis | | + | | | | | 1 |
| Inositol phosphate metabolism | | | | | + | | 1 |
| Regulation of lipolysis in adipocytes | | + | | | | | 1 |
| Carbon metabolism | | + | | | | | 1 |
| Longevity regulating pathway - worm | | | | | + | | 1 |
| cGMP-PKG signaling pathway | | + | | | | | 1 |
| Aldosterone synthesis and secretion | | + | | | | | 1 |
| Cortisol synthesis and secretion | | + | | | | | 1 |
| Amyotrophic lateral sclerosis (ALS) | + | | | | | | 1 |
| Phosphatidylinositol signaling system | | | | | + | | 1 |
| Cholesterol metabolism | | + | | | | | 1 |
| NOD-like receptor signaling pathway | + | | | | | | 1 |
| Vitamin digestion and absorption | | + | | | | | 1 |
| Mitophagy - animal | + | | | | | | 1 |
| Fat digestion and absorption | | + | | | | | 1 |
| Phagosome | | + | | | | | 1 |
| Adrenergic signaling in cardiomyocytes | | + | | | | | 1 |
| Streptomycin biosynthesis | | + | | | | | 1 |
| Renin secretion | | + | | | | | 1 |
| Salivary secretion | | + | | | | | 1 |
| Pancreatic secretion | | + | | | | | 1 |
| Dilated cardiomyopathy (DCM) | | + | | | | | 1 |
| Biosynthesis of phenylpropanoids | | | | | + | | 1 |
| Protein digestion and absorption | | + | | | | | 1 |
| Ferroptosis | + | | | | | | 1 |

| Methane metabolism | + | | | | 1 |
|---|---|--|---|--|---|
| Biosynthesis of terpenoids and steroids | | | + | | 1 |
| Nonribosomal peptide structures | + | | | | 1 |
| Bacterial secretion system | + | | | | 1 |
| Sesquiterpenoid and triterpenoid | | | + | | 1 |

Abberation: Pathway: the name of the pathway; Total: the total number of the genes involved in this pathway; +: this gene is involved in this pathway.