**Supplementary S1**

**Figure S1.** Selection of differentially expressed alternative splicing events among three PTC variants. **(A)** The selection of DEAS events between CPTC and FPTC. **(B)** DEAS events between CPTC and TCPTC. **(C)** DEAS events between FPTC and TCPTC. The red pots represent the DEAS events and the gray pots represent AS events with no significant difference. **(D)** The Venn diagram of DEAS events among three PTC variants.

**Supplementary S1**

**Figure S2.** PCA of three PTC variants was shown in the scatter plot.

**Supplementary S3**

**Figure S3.** Top 10 significant differential KEGG pathways among three clusters by GSEA analyses. **(A)** Top 10 differential KEGG pathways between Cluster0 and Cluster2. **(B)** Top 10 differential KEGG pathways between Cluster1 and Cluster2.

Supplementary S2

**Figure S4.** Kaplan-Meier curve analysis of six DEAS events for OS. **(A)** KIAA1217\_10995\_AP, **(B)** DCN\_23655\_AT, **(C)** RCAN2\_76415\_AP, **(D)** TUBB3\_38175\_ES, **(E)** NNMT\_18817\_AP, **(F)** COL14A1\_85105\_AP.

**Supplementary S3**

**Figure S5.** Kaplan-Meier survival analysis of patients within three PTC variants of OS.

**Table S1.** The splicing factors gene list collected from the SpliceAid 2.

|  |  |
| --- | --- |
| Gene list | SRSF7, CELF1, DAZAP1, ESRP1, ESRP2, CELF2, FMR1, RBFOX1, RBFOX2, HNRNPA0, HNRNPA1, HNRNPA2B1, HNRNPA3, HNRNPC, HNRNPC1, HNRNPC2, HNRNPD, HNRNPD0, HNRNPDL, PCBP1, PCBP2, HNRNPF, RBMX, HNRNPH1, HNRNPH2, HNRNPH3, PTBP1, HNRNPJ, HNRNPK, HNRNPL, HNRNPLL, HNRNPM, FUS, SYNCRIP, HNRNPU, TRA2A, TRA2B, ELAVL2, ELAVL3, ELAVL4, ELAVL1, KHSRP, MBNL1, NOVA1, NOVA2, PTBP2, SFPQ, QKI |

**Table S2.** The DEAS events among three PTC variants.

|  |  |
| --- | --- |
|  | DEAS events |
| CPTC vs FPTC | NEDD4L\_45649\_AP, PTPN4\_55141\_AP, CRLF2\_88358\_AT, TNIP1\_74126\_AP, OXCT1\_71882\_AP, ACSL6\_73248\_AT, KIAA1217\_10994\_AP, LTBR\_19846\_AP, KLK10\_51263\_AP, LYNX1\_85361\_AP, RCAN2\_76415\_AP, TUBB3\_38167\_AP, PPARG\_63413\_AP, ARHGAP24\_69814\_AP, CTNNBIP1\_578\_AP, LYNX1\_85366\_AT, PADI4\_851\_AT, EPHA4\_57746\_AP, TNFRSF13B\_39449\_AT, ZNF575\_50203\_AP, TRAK1\_64266\_AP, RGS12\_68637\_AP, SAA2\_14580\_AT, LMF1\_33029\_AP, BID\_61002\_AP, HYAL3\_64984\_AP, TRIM46\_7953\_AT, MACROD2\_58714\_AP, ZNF331\_51724\_AP, DYSF\_53937\_ES, NAV1\_9387\_AP, ACSS2\_59036\_AP, NAV2\_14696\_AP, SERPINB5\_45716\_AT, SSPN\_20842\_AP, LRRC2\_64456\_AP, TUBB3\_38166\_AP, ELMO1\_79266\_AP, CD44\_15130\_ES, SHROOM4\_89139\_AP, NNMT\_18817\_AP, PLXNC1\_23721\_AP, SLA\_85217\_ES, AKT2\_49869\_AP, MAP2K6\_43187\_AP, COL14A1\_85015\_AP, DCN\_23655\_AT, TUBB3\_38175\_ES, NDE1\_34181\_AP, RAG1\_15433\_AT, RRM1\_14033\_AP, PI4K2A\_12728\_AP, SMTN\_61810\_AP, CD44\_15111\_ES, ST6GAL1\_68067\_AP, LAMB4\_81393\_AT, KIAA1217\_10995\_AP, FAM107A\_65463\_AP, MXRA8\_142\_AP |
| CPTC vs TCPTC | NNMT\_18817\_AP, MPP7\_11093\_ES, DCN\_23655\_AT, TMEM132D\_25195\_AP, C1S\_20068\_AP, RACGAP1\_21625\_AT, TUBB3\_38175\_ES, RTN4\_53592\_ES, KIAA1217\_10995\_AP, HMGA2\_22877\_AT, SSBP4\_48427\_AP, COL14A1\_85015\_AP, P2RY6\_17682\_AP, ELN\_80044\_ES, PAK6\_29958\_AP, RCAN2\_76415\_AP, UBN1\_33869\_AP |
| FPTC vs TCPTC | NEDD4L\_45649\_AP, RCAN2\_76415\_AP, ACSL6\_73248\_AT, TNIP1\_74126\_AP, ARHGAP24\_69814\_AP, CRLF2\_88358\_AT, CTNNBIP1\_578\_AP, PPARG\_63413\_AP, OXCT1\_71882\_AP, LYNX1\_85361\_AP, LTBR\_19846\_AP, LYNX1\_85366\_AT, SAA2\_14580\_AT, RGS12\_68637\_AP, KIAA1217\_10994\_AP, TUBB3\_38167\_AP, DYSF\_53937\_ES, ZNF575\_50203\_AP, TRIM46\_7953\_AT, KLK10\_51263\_AP, HDAC9\_78886\_AP, MAST1\_47878\_AT, PTPN4\_55141\_AP, TNFRSF13B\_39449\_AT, NAV1\_9387\_AP, TTC40\_13507\_AT, SERPINB5\_45716\_AT, NAV2\_14696\_AP, MKL1\_62349\_AP, ARHGAP22\_11485\_AP, PADI4\_851\_AT, HYAL3\_64984\_AP, ZNF331\_51724\_AP, LMF1\_33029\_AP, CORIN\_69182\_AT, PSG5\_50182\_AT, ACAP1\_38921\_AP, BTBD11\_24189\_AP, TRAK1\_64266\_AP, KCNAB1\_67357\_AP, ACSL5\_13109\_AP, ASPHD1\_35984\_AT, DNASE1L1\_90575\_AP, BID\_61002\_AP, EPHA10\_1825\_AT, FGF1\_73869\_AP, TANK\_55731\_AP, MGAT1\_75022\_AP, TMEM79\_8217\_AP, RAD23B\_87147\_AP, CREM\_11230\_AP, PSG5\_50183\_AT, SSPN\_20842\_AP, GPER1\_78565\_AP, ACSS2\_59036\_AP, SULT2B1\_50773\_AP, ITGA7\_22216\_ES, TSPEAR\_60826\_AT, SMAGP\_21829\_AP, DYSF\_53934\_AP, CKMT2\_72660\_ES, ATP2C1\_66756\_AP, EGFL7\_88188\_AP, IMMP1L\_14816\_ES, DIO2\_28647\_AP, MCC\_73004\_AP, BCAR3\_3796\_AP, CCDC108\_57579\_AT, ERAP2\_72871\_AD, EPHA4\_57746\_AP, SHROOM4\_89138\_AP, ANKRD30B\_44762\_AT, EVA1A\_54148\_AP, AHCYL2\_81744\_AP, KAZN\_730\_AP, RPS6KA1\_1281\_AP, SERPINA1\_29130\_ES, LPAR5\_19900\_AP, KLK10\_51264\_AP, TACC1\_83437\_AP, EXOC7\_43568\_ES, CCND3\_76154\_AP, BLOC1S6\_30440\_ES, ERMAP\_2124\_RI, TMC6\_43757\_AT, PPFIBP1\_20893\_ES, ACOX3\_68765\_AP, DST\_76569\_ES, NPIPB6\_35703\_AP, NARF\_44391\_AP, SS18\_44966\_ES, TMEM45B\_19457\_AP, C12orf73\_24074\_ES, CKMT1B\_30276\_AP, MEIS1\_53805\_AP, CACNB3\_21480\_ES, PIK3R1\_72294\_AP, RPS6KA3\_88669\_AP, SCNN1A\_19842\_ES, RARG\_21980\_AP, MCC\_73006\_AP, NCS1\_87899\_AP, TRIM16L\_39631\_AP, RTKN2\_11871\_AT, RAET1G\_78131\_AT, CBX5\_22139\_AP, CD44\_15127\_ES, NEDD4L\_45651\_AP, LMO7\_26060\_AP, BIN1\_55184\_ES, KCNC3\_51170\_AP, TIPARP\_67366\_AP, SPTBN1\_53576\_AP, FMO5\_7367\_AT, DYSF\_53935\_AP, KCTD13\_35987\_AT, RAG1\_15433\_AT, TAB3\_88762\_AA, GPR116\_76428\_AP, NALCN\_26204\_AT, GPR110\_76437\_AT, LCN6\_88203\_AP, MROH6\_85424\_AP, SULT2B1\_50774\_AP, EPB41L1\_59264\_AP, FGF1\_73871\_AP, CKMT1A\_30304\_AP, CD44\_15130\_ES, ELN\_80043\_AA, FAM86B1\_82686\_ES, TMEM132D\_25195\_AP, P2RY6\_17681\_AP, CCNDBP1\_30220\_ES, ST5\_14263\_AP, C2orf73\_53572\_AT, PDK1\_55976\_AT, ERBB3\_22355\_AT, SAA2\_14577\_AT, GLS2\_22441\_AA, NFYC\_2015\_AP, SALL1\_36401\_AP, ZNF581\_52118\_AP, ANK3\_11843\_AP, LARGE\_61941\_AP, DTNA\_45092\_AP, SLC1A2\_15413\_AT, ELP3\_83202\_AP, LYNX1\_85363\_AP, KAZN\_729\_AP, TMEM43\_63521\_ES, CTCFL\_59903\_AT, NAV1\_9389\_AP, PLXNC1\_23721\_AP, ASPHD1\_35983\_AT, ITGB4\_43489\_ES, ARHGAP24\_69815\_AP, SLC14A2\_45328\_AP, RTN4\_53592\_ES, APOC2\_50375\_RI, STRA6\_31688\_AD, TMEM79\_8218\_AP, MUC20\_68183\_AP, NAV2\_14695\_AP, F8\_90666\_AP, BRD3\_88091\_AA, VPS13D\_706\_AP, RACGAP1\_21625\_AT, TUBB3\_38166\_AP, SHROOM4\_89139\_AP, SMTN\_61810\_AP, AKT2\_49869\_AP, PDE1C\_79184\_AP, LAMB4\_81393\_AT, ELN\_80045\_ES, SSBP4\_48427\_AP, NDE1\_34181\_AP, SLC14A2\_45330\_AT, MAP2K6\_43187\_AP, P2RY6\_17682\_AP, PAK6\_29958\_AP, MPP7\_11093\_ES, ELN\_80044\_ES, ARHGEF10L\_857\_AP, ELMO1\_79266\_AP, HMGA2\_22877\_AT, LRRC2\_64456\_AP, FAM107A\_65463\_AP, SLA\_85217\_ES, GAREML\_52882\_AP, ST6GAL1\_68067\_AP, C1S\_20068\_AP, PI4K2A\_12728\_AP, RRM1\_14033\_AP, COL14A1\_85015\_AP, TUBB3\_38175\_ES, DCN\_23655\_AT, KIAA1217\_10995\_AP, NNMT\_18817\_AP, MXRA8\_142\_AP |

**Table S3.** The differences of DEAS events which were differentially expressed in PTC variants in clustering groups. P values were calculated by wilcoxon test.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| DEAS events | Cluster1/Cluster0 | | Cluster2/Cluster0 | | Cluster2/Cluster1 | |
| log2FC | p value | log2FC | p value | log2FC | p value |
| TUBB3\_38175\_ES | 2.11 | 2.66E-42 | -1.43 | 1.00E-09 | -3.54 | 1.17E-21 |
| KIAA1217\_10995\_AP | 2.51 | 3.38E-54 | -0.79 | 7.46E-05 | -3.29 | 8.94E-22 |
| NNMT\_18817\_AP | 1.44 | 5.29E-11 | -2.93 | 2.84E-04 | -4.37 | 2.00E-11 |
| DCN\_23655\_AT | 1.59 | 1.87E-19 | -2.23 | 2.93E-13 | -3.83 | 6.64E-19 |
| RCAN2\_76415\_AP | -1.24 | 3.02E-10 | 2.53 | 5.50E-26 | 3.77 | 2.89E-22 |
| COL14A1\_85105\_AP | 1.12 | 4.15E-10 | -1.20 | 0.0190 | -2.32 | 1.61E-08 |

**Table S4.** Three bioactive compounds with common mode of action in the CMap analysis.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Name | Score | Description | Target | MOA |
| Orantinib | -99.79 | FGFR inhibitor | PDGFRB, AURKA, AURKB, KDR, EGFR, FGFR1, FGFR2, PDGFRA, TBK1 | FGFR inhibitor, VEGFR inhibitor, PDGFR receptor inhibitor |
| Tyrphostin-AG-1295 | -99.47 | PDGFR receptor inhibitor | FLT3, KDR, PDGFRA, PDGFRB | PDGFR receptor inhibitor |
| AG-370 | -99.47 | PDGFR receptor inhibitor | PDGFRB | PDGFR receptor inhibitor |