Supplementary Information:

Whole-genome and exome sequencing of bladder cancer identifies frequent alterations in genes involved in sister chromatid cohesion and segregation

Guangwu Guo[*], Xiaojuan Sun[*], Chao Chen[*], Song Wu[*], Peide Huang[*], Zesong Li[*], Michael Dean[*], Yi Huang, Wenlong Jia, Quan Zhou, Aifa Tang, Zuoquan Yang, Xianxin Li, Pengfei Song, Xiaokun Zhao, Rui Ye, Shiqiang Zhang, Zhao Lin, Mingfu Qi, Shengqing Wan, Liangfu Xie, Fan Fan, Michael L Nickerson, Xiangjun Zou, Xueda Hu, Li Xing, Zhaojie Lv, Hongbin Mei, Shengjie Gao, Chaozhao Liang, Zhibo Gao, Jingxiao Lu, Yuan Yu, Chunxiao Liu, Lin Li, Xiaodong Fang, Zhimao Jiang, Jie Yang, Cailing Li, Xin Zhao, Jing Chen, Fang Zhang, Yongqi Lai, Zheguang Lin, Fangjian Zhou, Hao Chen, Hsiao Chang Chan, Shirley Tsang, Dan Theodorescu, Yingrui Li, Xiuqing Zhang, Jian Wang, Huanming Yang, Yaoting Gui, Jun Wang, &Zhiming Cai

* These authors contributed equally to this work.

Correspondence should be addressed to Z.C. (caizhiming2000@163.com), Jun Wang (wangj@genomics.org.cn), or Y.G. (guiyaoting@hotmail.com).

Supplementary Note

Novel significantly mutated genes in TCC

In our study we detected 13 novel significantly mutated genes that have not been reported in TCC (**Fig. 1**). These genes included *STAG2*, *ERCC2*, *SYNE2*, *ELF3*, *ESPL1*, *CSMD3*, *TRAK1*, *PDZD2*, *TRRAP*, *PIK3R4*, *KALRN*, *ATM* and *FAT4*.

To our knowledge, mutations in the well-known cancer gene *ATM* were not reported in bladder cancer previously, and it harbored mutations in 5% of the tumors in this study. Additionally, several of these mutated genes detected in present study are not well-established cancer genes, but corroborating evidences from recent studies points to their potential roles in cancer. *STAG2* and *ESPL1*, two genes involved in sister chromatid cohesion and segregation, were fully discussed in main text. *ERCC2*, encoding a component of the core-TFIIH basal transcription factor, is a major player in the nucleotide excision repair pathway and is also involved in transcription initiation and in the control of the cell cycle and apoptosis[1]. Defects in this gene can result in cancer-prone syndrome xeroderma pigmentosum complementation group D[2] and polymorphisms in *ERCC2* were reported to be associated with risk of head and neck cancer[3]. In our study, we detected somatic mutations in *ERCC2* in seven (7%) TCCs and as expected, the mutation rates in *ERCC2*-mutated tumors were significantly higher than *ERCC2*-wild-type tumors (**Supplementary Figure 8**; P=0.003). *FAT4*, belonging to the E-cadherin family, demonstrated tumor-suppressor activity in gastric adenocarcinoma[4] and were found mutated in 5% of tumors in our cohort. *TRRAP* (mutated in 5% of the tumors) functions as part of a multiprotein coactivator complex possessing histone acetyltranferase activity and was identified as candidate oncogene in melanoma[5].

In addition to well-known and candidate cancer genes, our study also revealed several genes with poorly characterized functional roles in cancer but sufficient mutational evidence to warrant experiment investigation. The protein encoded by *SYNE2* is structural nuclear envelope protein that tethers nuclei to the cytoskeleton and aids in the maintenance of the structural integrity of the nucleus[6]. Somatic mutations in *SYNE2* were

reported in genomic analyses of ovarian carcinoma[7]. Mutations in *SYNE1*, a paralog of *SYNE2* and also a nuclear envelope protein, were detected in our previous bladder cancer genome study[8]. Here, *SYNE1* and *SYNE2* were altered by 15 somatic no-silent mutations and both qualified as a significantly mutated gene (**Fig. 1**). Alterations included 7 nonsynonymous and 1 bp insertion in *SYNE1*, and 6 missense changes and a C>T causing a Q3171* in *SYNE2*. EFL3 is transcriptional activator that binds and transactivates ETS sequences, and may play a critical regulator of epithelial cell differentiation[9]. Six mutations, including three frame-shift indels and one splice site change, were detected in *EFL3*, suggesting that *EFL3* might function as a tumor suppressor. *CSMD3*, a significantly mutated gene in ovarian carcinoma[7], was frequently mutated with six mutations (6%). *PIK3R4*, a subunit of the PI3K complex, was altered in five tumors (5%).

Frequent amplification of *DHFR* in TCC

In our study, we detected a frequently amplified region containing *DHFR* gene in 5q (a frequent loss in our dataset) in 14 (14%) tumors (**Supplementary Figure 16**). Further fluorescence in situ hybridization (FISH) and Real time quantitative PCR experiments confirmed the *DHFR* amplification in our cohort (**Supplementary Figure 17**). In addition, a moderately strong correlation coefficient (R^2=0.60, P = 0.018) was observed between changes in copy number and in gene expression level for *DHFR*. Five tumors with *DHFR* amplification had matched normal RNA-Seq data and we found expression levels of *DHFR* were up-regulated in all of them. *DHFR,* encoding dihydrofolate reductase*,* has a critical role in regulating the amount of tetrahydrofolate, which is essential for *de novo* purine and thymidylate synthesis[10]. Hence *DHFR* has a critical role in cell growth and proliferation, and *DHFR* is the target of many anticancer agents including methotrexate[11] and pemetrexed[12]. Methotrexate is also a component of the neoadjuvant MVAC (methotrexate, vinblastine, Adriamycin, and cisplatin) chemotherapy before radical cystectomy, which was used for treatment of muscle-invasive bladder cancer with pathologic stage T3, T4, or node-positive tumors to eradicate micrometastases, downstage tumor, reduce implantation of circulating tumor cells during surgery, and ultimately improve survival[13]. Previous studies showed *DHFR* amplification

is a frequent mechanism of methotrexate resistance[14]. Certainly, frequent amplification of *DHFR* in TCC suggests its utility as a biomarker for contraindicating the use of methotrexate for TCC.

Supplementary References

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11. Schweitzer, B.I., Dicker, A.P. & Bertino, J.R. Dihydrofolate reductase as a therapeutic target. *FASEB J* **4**, 2441-52 (1990).
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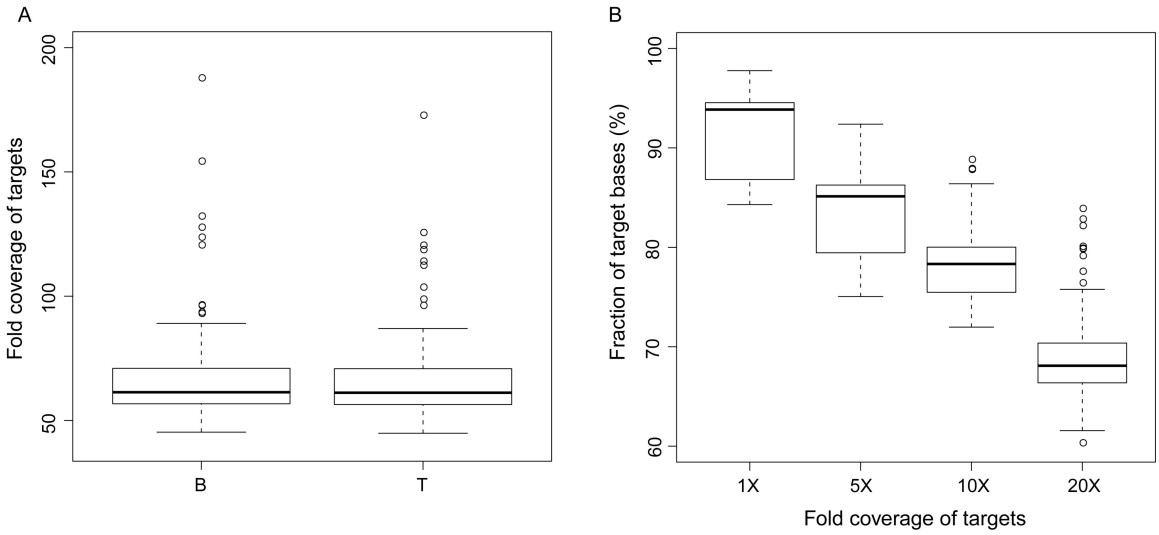
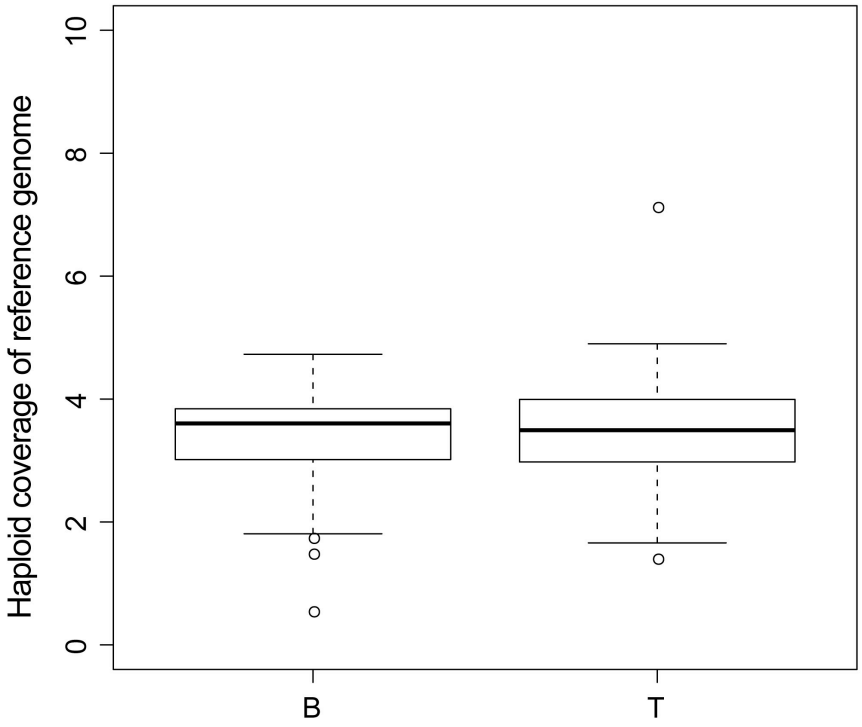
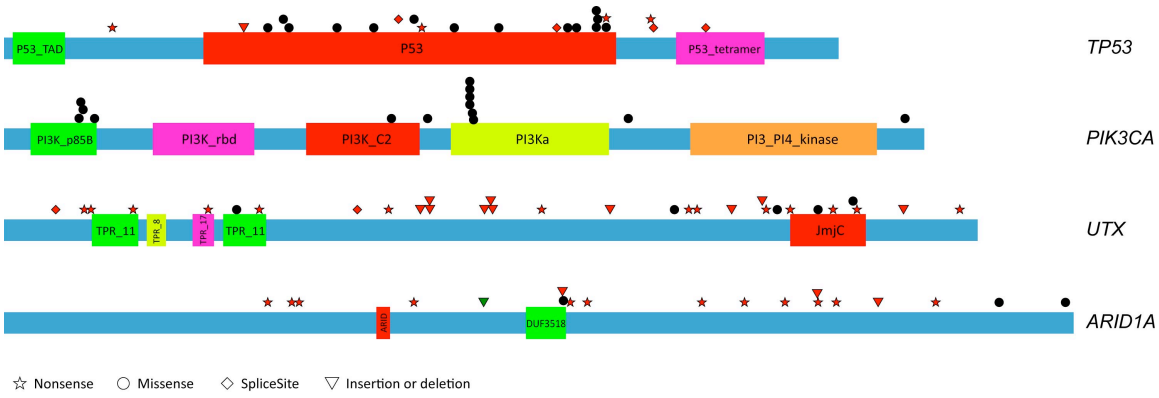
Supplementary Figures



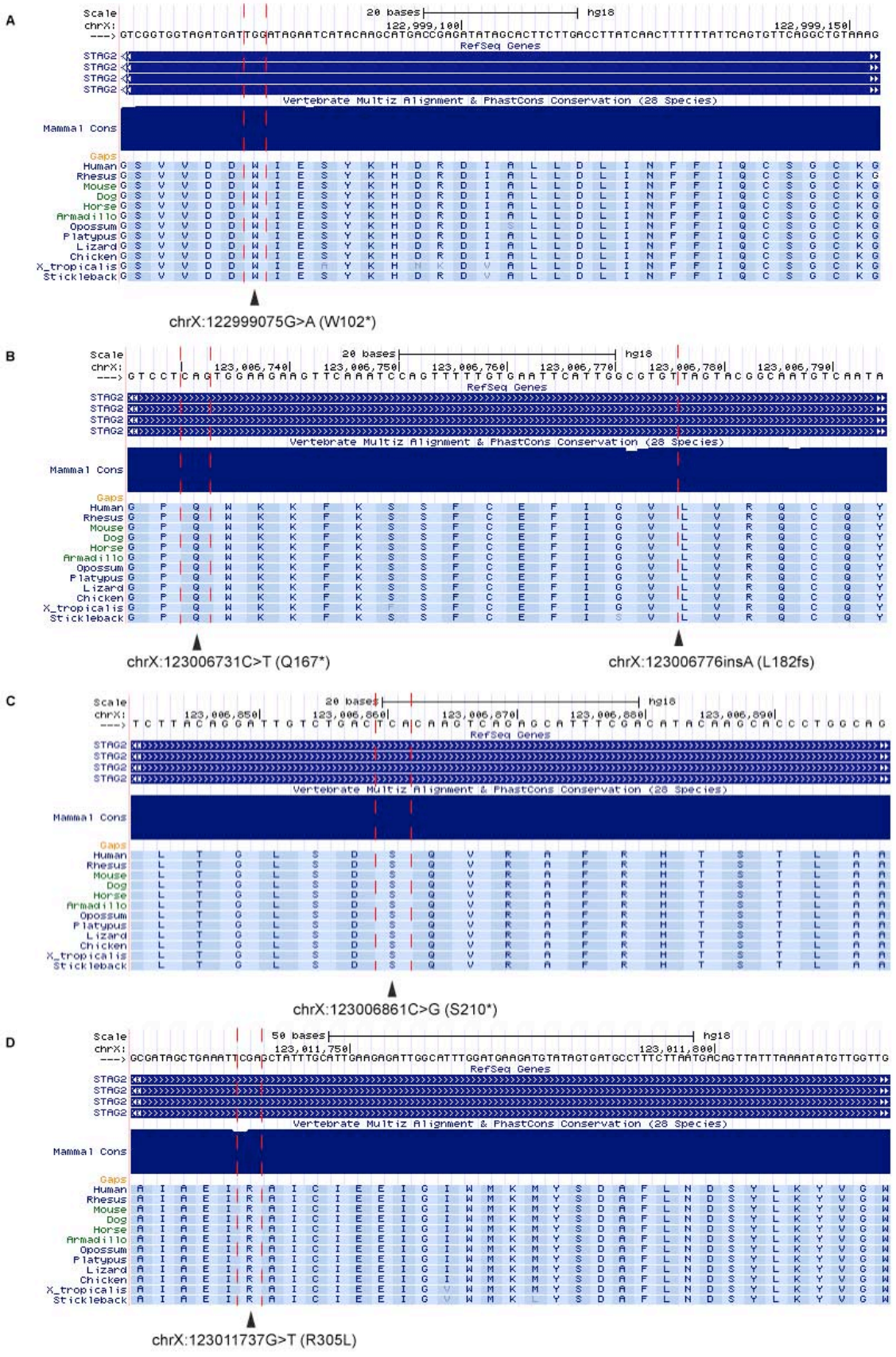
Supplementary Figure 1. Fold coverage of targeted regions for the peripheral blood (B) and tumor (T) samples from 99 TCC patients analyzed by WES. (a) The box plot depicts the distribution of mean coverage of all tumor and blood samples sequenced. Lines in the two central boxes show the medians, and lines outside the two central boxes show the first and the third quartiles of the mean depths. (**b**) The box plot depicts the distribution of fraction of targeted bases covered by at least 1×, 5×, 10 × and 20 × across the 99 pairs of samples. Lines in the inner four boxes show the medians, and lines outside the four boxes show the first and the third quartiles.



Supplementary Figure 2. Haploid coverage of reference genome sequence for the peripheral blood (B) and tumor (T) samples from 99 TCC patients analyzed by whole genome sequencing.



Supplementary Figure 3. Somatic mutations in *TP53*, *PIK3CA*, *KDM6A*/*UTX* and *ARID1A*. The types and relative positions of confirmed somatic mutations are shown in the transcripts using the following symbols: red stars, nonsense mutations; bullets, missense mutations; red triangles, frame-shift indels; green triangles, in-frame indels; and diamond, mutations at splice sites. Domains and motifs in each encoded protein product are also indicated: P53_TAD, p53 transactivation domain; P53, p53 DNA-binding; P53_tetramer, p53 tetramerisation; PI3K_p85B, phosphatidylinositol 3-kinase adaptor-binding (PI3K ABD) domain; PI3K_rbd, phosphatidylinositol 3-kinase Ras-binding (PI3K RBD) domain; PI3K_C2, phosphatidylinositol 3-kinase C2 (PI3K C2) domain; PI3Ka, phosphoinositide 3-kinase, accessory (PIK) domain; PI3_PI4_kinase, phosphatidylinositol 3-/4-kinase, catalytic domain; TPR, tetratricopeptide repeat; JmjC, JmjC domain; ARID, ARID/BRIGHT DNA-binding domain; DUF3518, domain of unknown function DUF3518.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122,999,100
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RefSeq Genes
STAG2
Vertebrate Multiz Alignment & PhastCons Conservation (28 Species)
Mammal Cons
Gaps
Human
Rhesus
Mouse
Dog
Horse
Armadillo
Opossum
Platypus
Lizard
Chicken
X_tropicalis
Stickleback
chrX:122999075G>A (W102*)
B
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C
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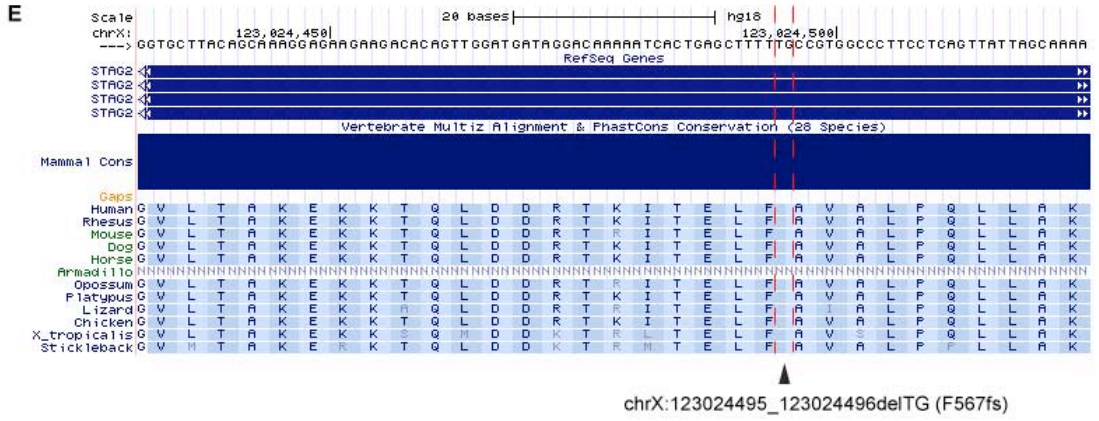
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Dog
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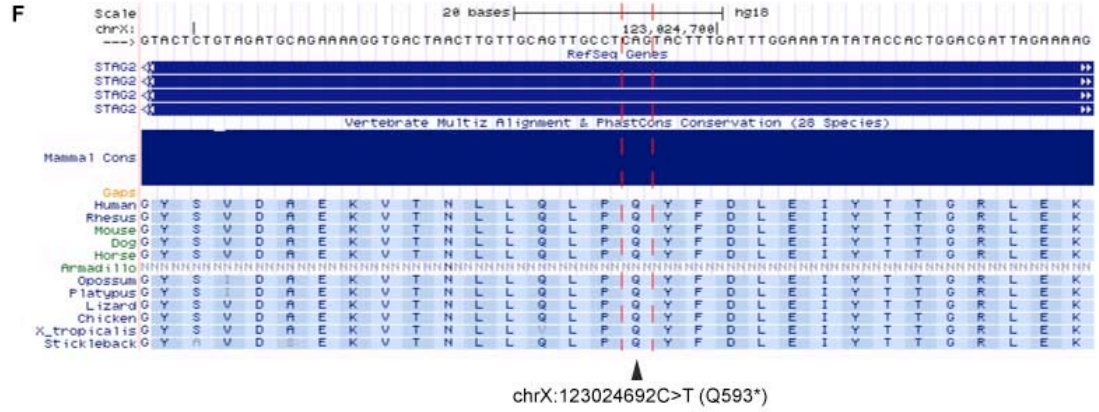
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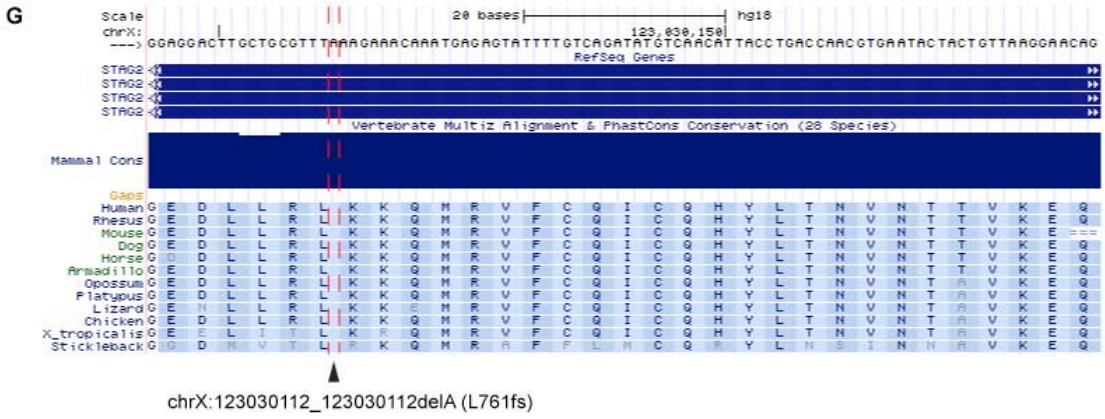
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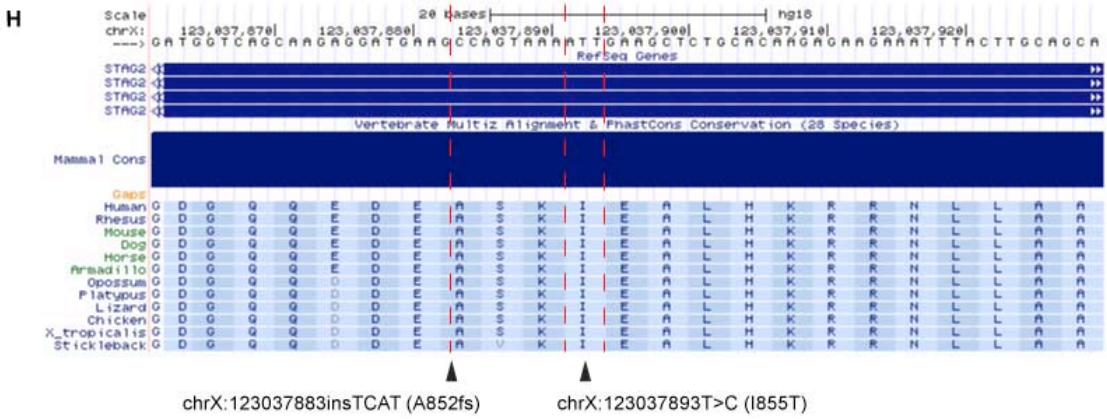
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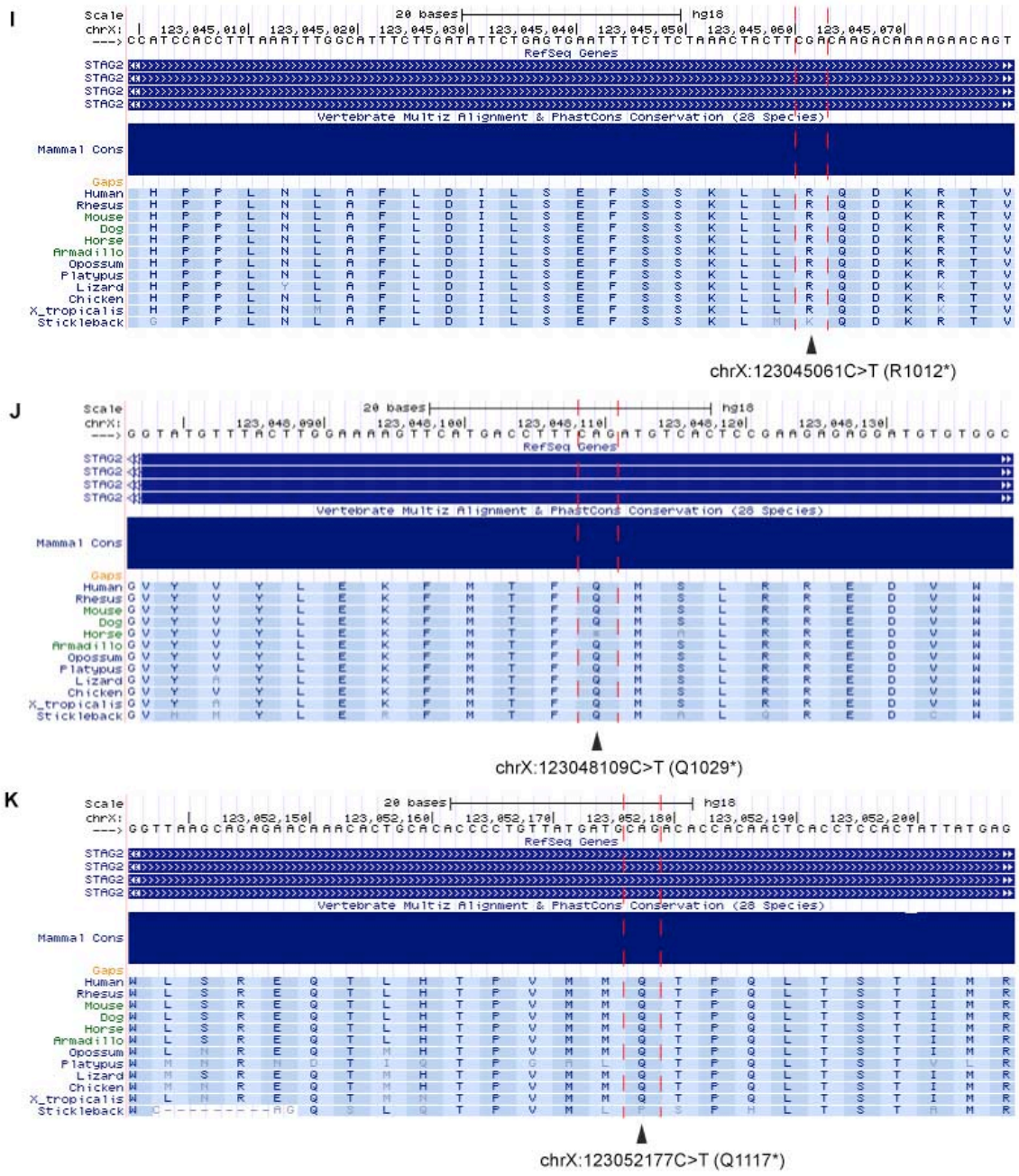
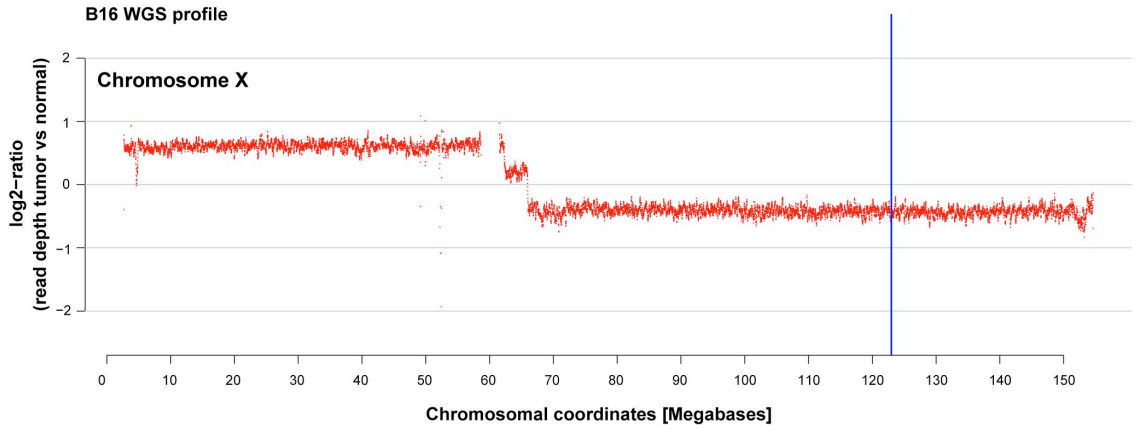


Supplementary Figure 4. Alignment of STAG2 amino acid sequences from different species. Mutations in *STAG2* detected in 99 tumors and consequence amino acids changes are shown.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(read depth tumor vs normal)
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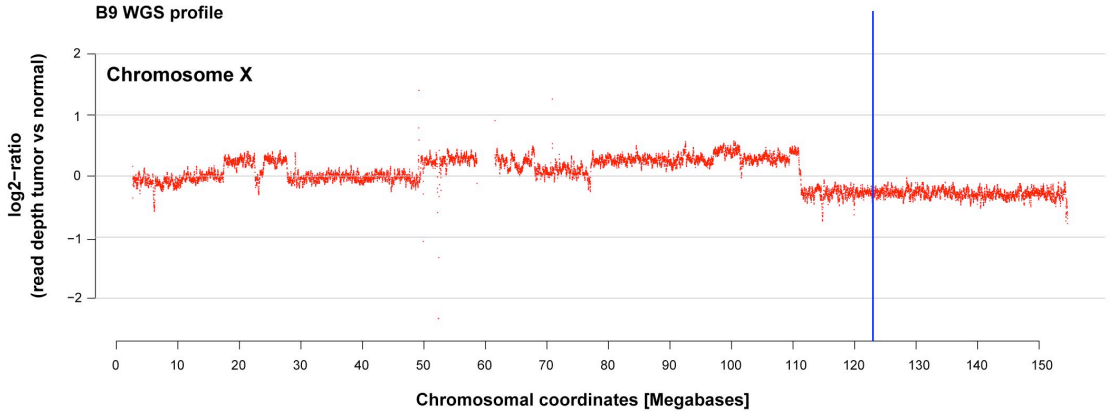
Chromosomal coordinates [Megabases]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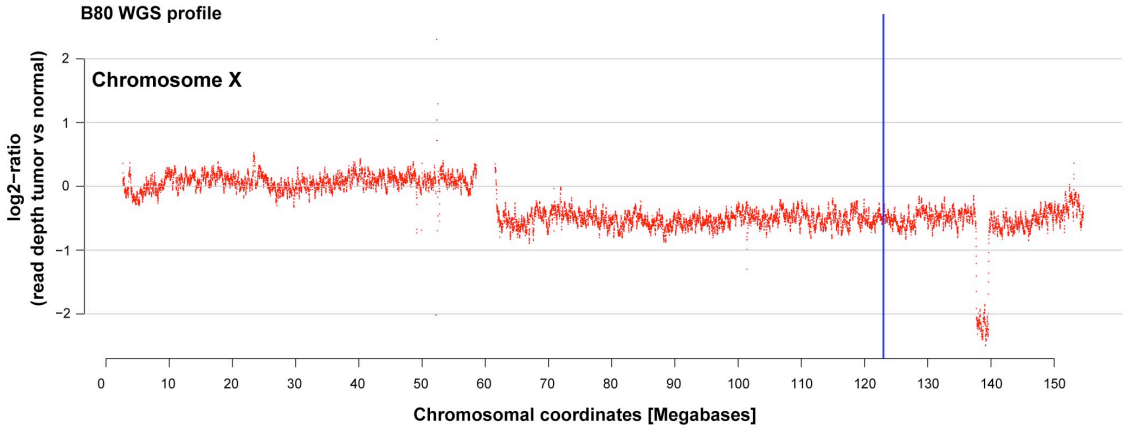
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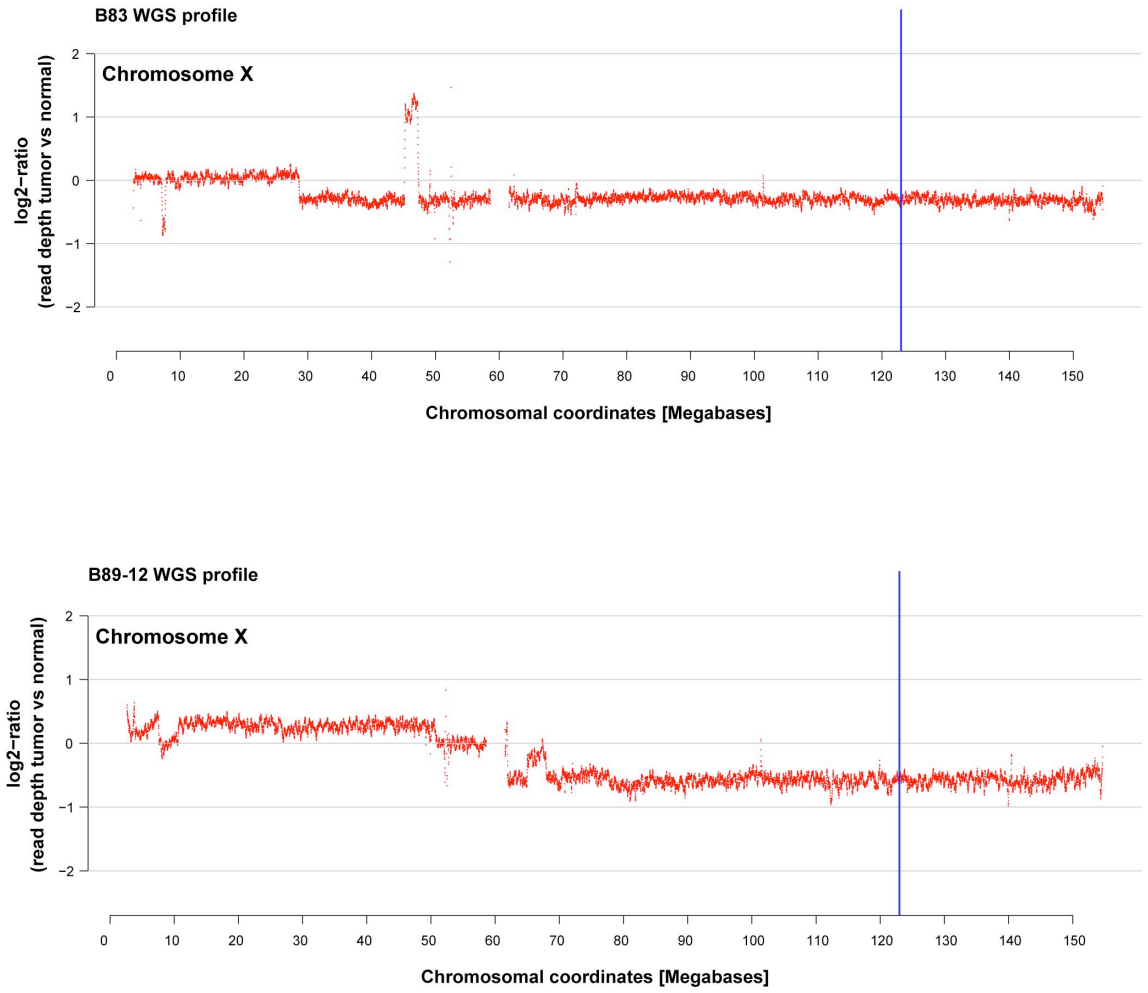
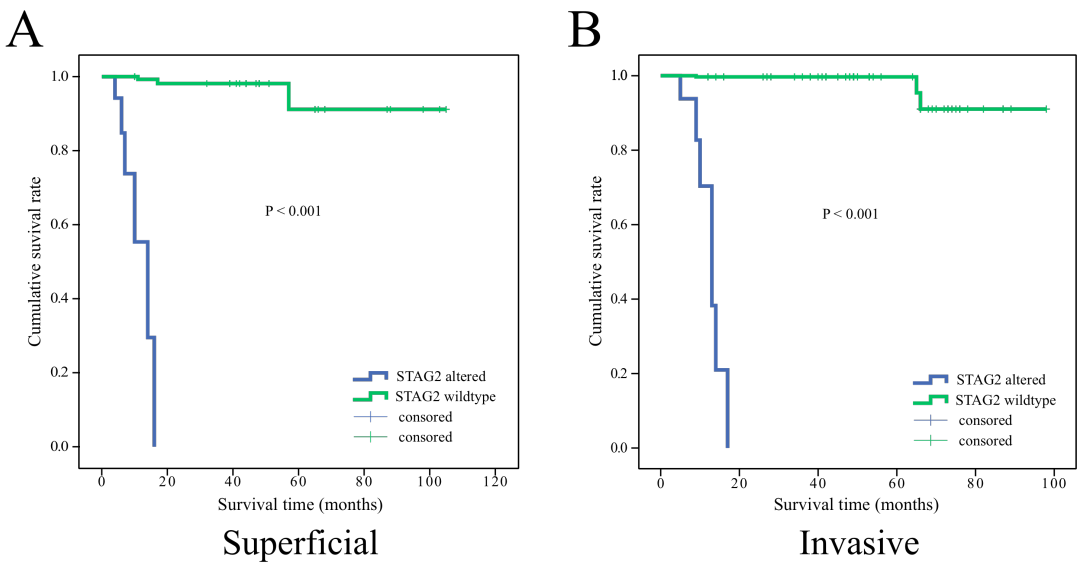
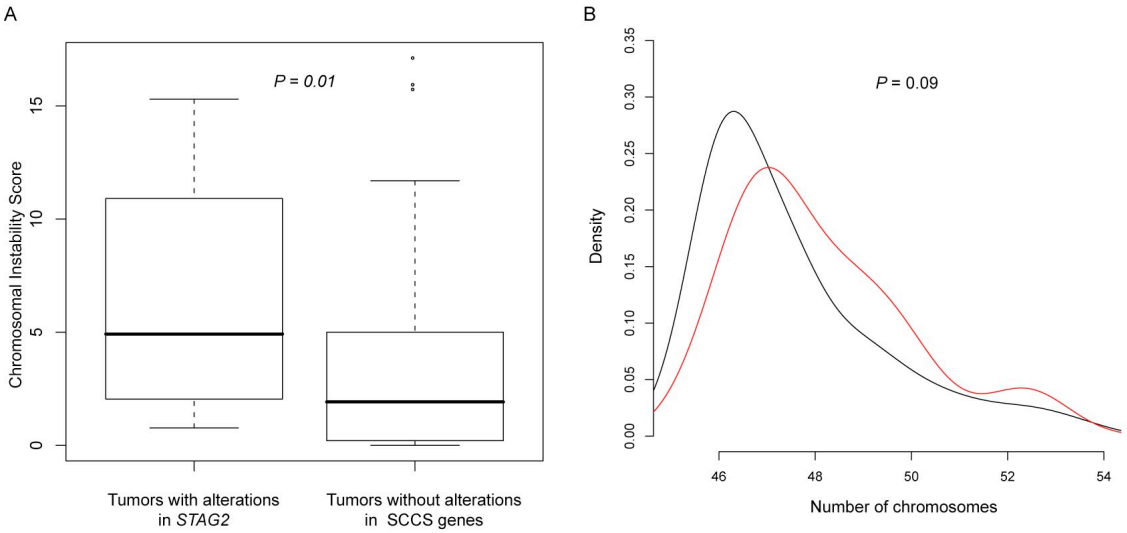


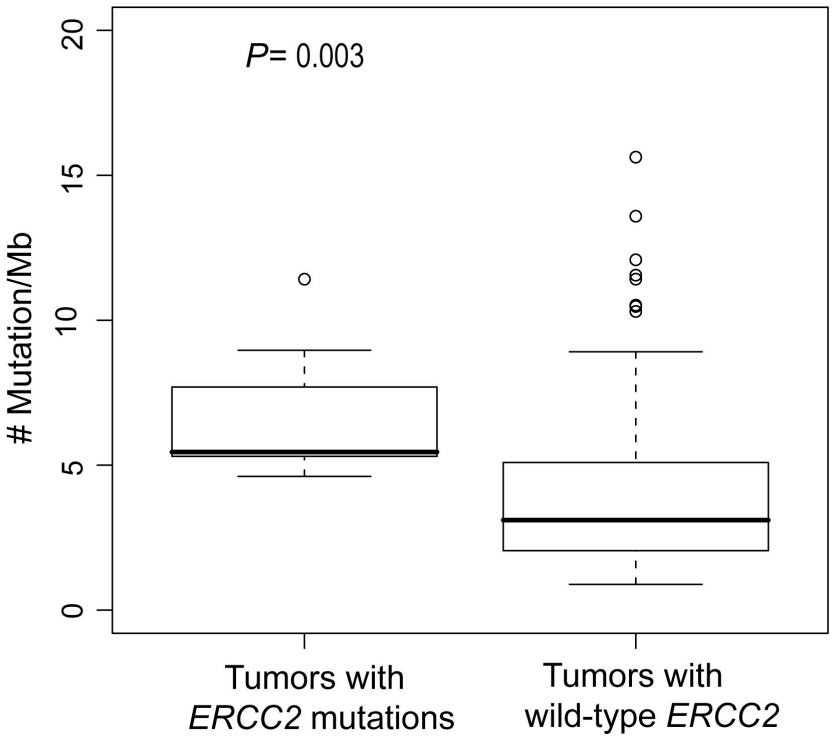
Supplementary Figure 5. Genomic deletions of *STAG2* in five of the 99 tumors. Chromosome X copy number plots as estimated by read depth of tumors *vs.* blood samples. The blue lines indicated the location of *STAG2* on chromosome X.



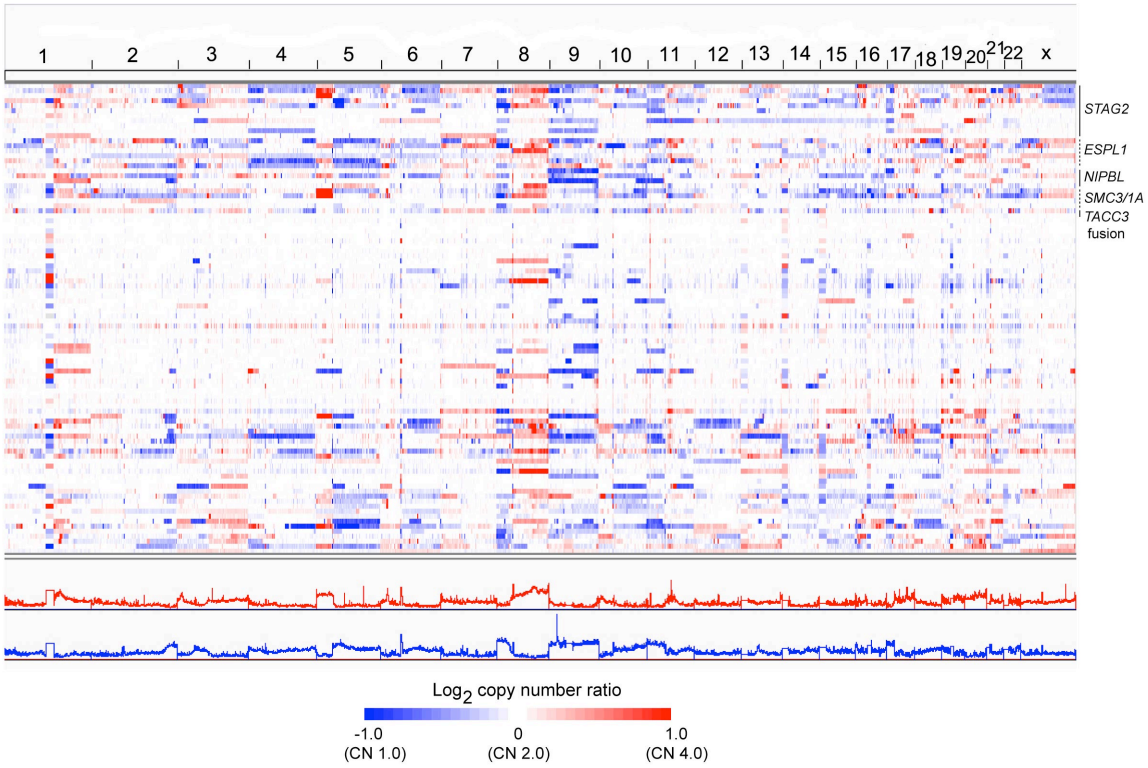
Supplementary Figure 6. Kaplan-Meier survival analysis of TCC patients with superficial (a) and invasive disease (b). In both subtypes of TCC, the survival rate for individuals with *STAG2* alterations is significantly lower (log-rank test, $P<0.001$) than that for patients with wild-type *STAG2* tumors.



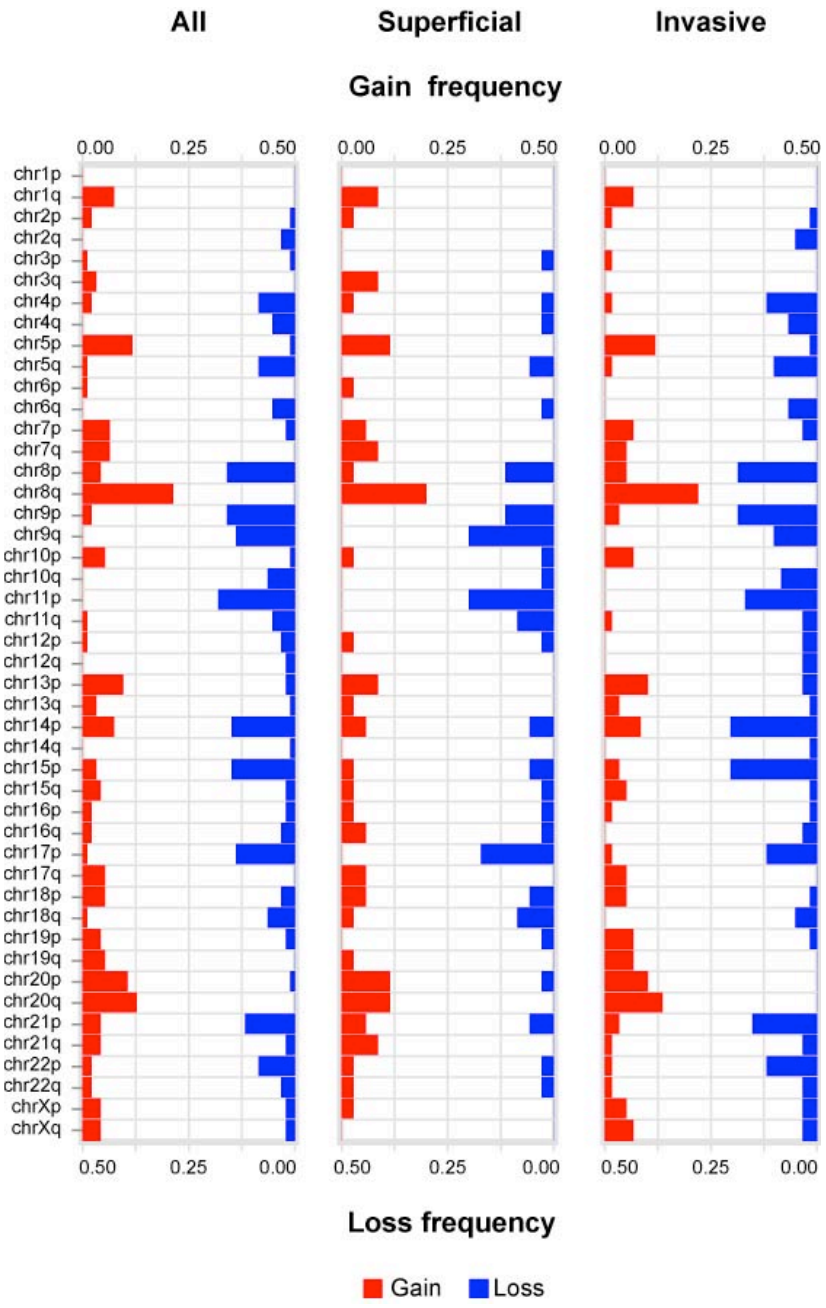
Supplementary Figure 7. *STAG2* alterations were significantly associated with aneuploidy in TCC. (a) The aneuploidy in tumor was estimated by chromosome instability (CIN) score. The CINs were evaluated basing on the copy number of chromosome arms and were calculated with formula $CIN = 100\left(\sum_{i=1}^{n}|C_i - 2|L_i / 2\sum_{i=1}^{n}L_i\right)$ where C is the copy number value of chromosome arms, L is the length of the chromosome arms and n is the number of chromosome arms. Tumors with alterations in *STAG2* show significantly more aneuploidy than tumors with wild-type SCCS genes. (**b**) Kernel density estimation of chromosome counts in tumors with *STAG2* alterations (red line) and in tumors with wild-type SCCS genes (black line). The *P* values in (**a**) and (**b**) were determined by Wilcoxon test.



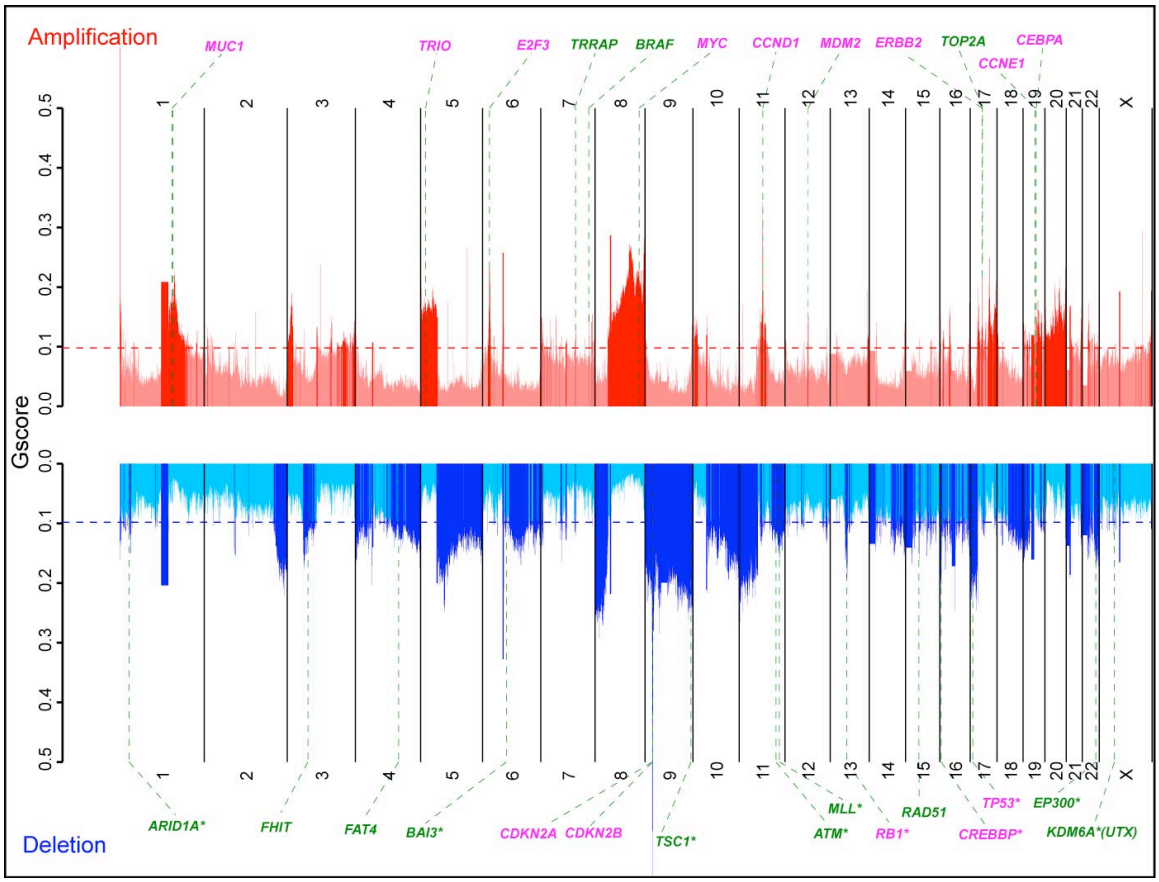
Supplementary Figure 8. The mutation rates in *ERCC2*-mutated tumors are significantly higher than *ERCC2*-wild-type tumors. *ERCC2* is a gene involved in transcription-coupled nucleotide excision repair.



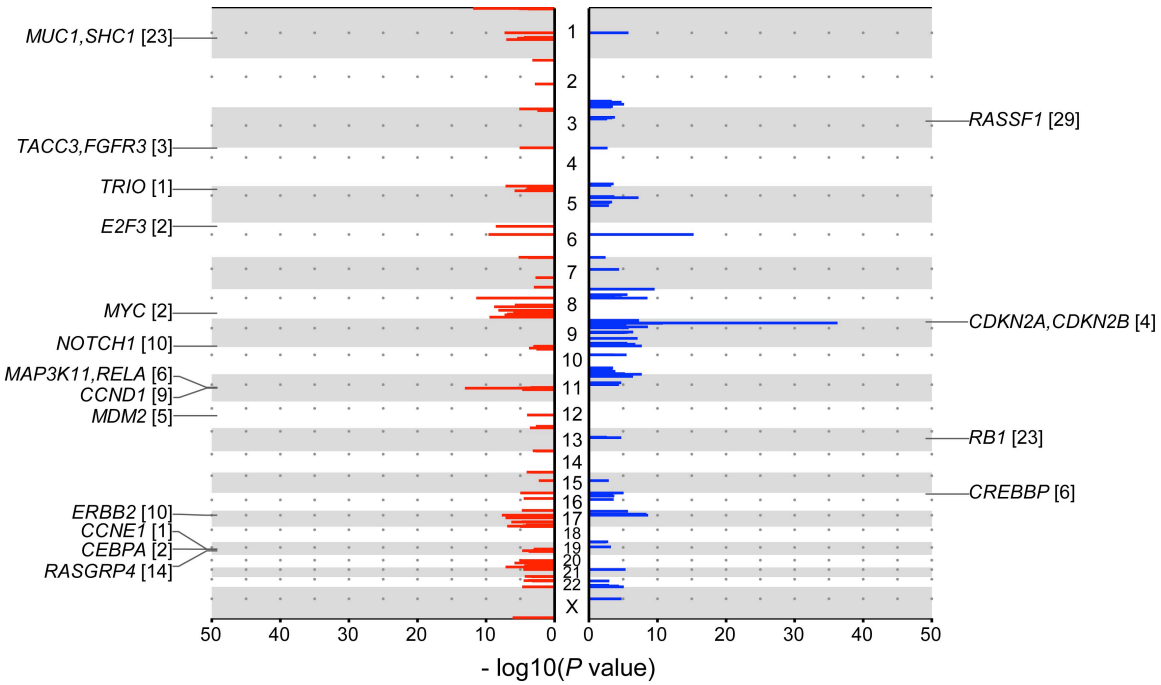
Supplementary Figure 9. Copy number alteration profiles of 99 bladder tumors rendered by Integrative Genomics Viewer (IGV). The tracks in the upper panel are tumor samples and the lower panels represent the amplification (red line) and deletion (blue line) G-score profiles across the tumor genomes. The lines and dotted lines in the right panel indicate the tumor samples with alteration in genes involved in sister chromatid cohesion and segregation.



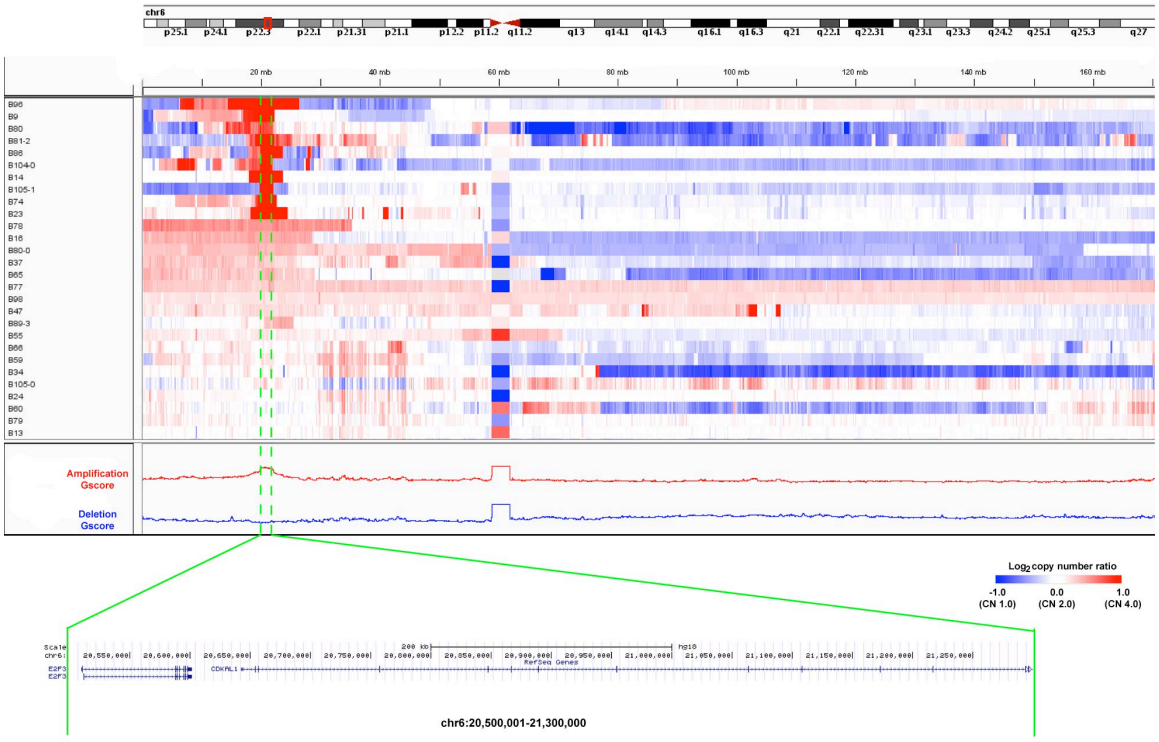
Supplementary Figure 10. Frequency of broad cytogenetic events across 99 TCCs and in the different subgroups of TCC. Each chromosomal arm region in each tumor sample is classified as copy gain (≥2.5) or loss (≤1.5) if >60% of the region consists of CNA segments.



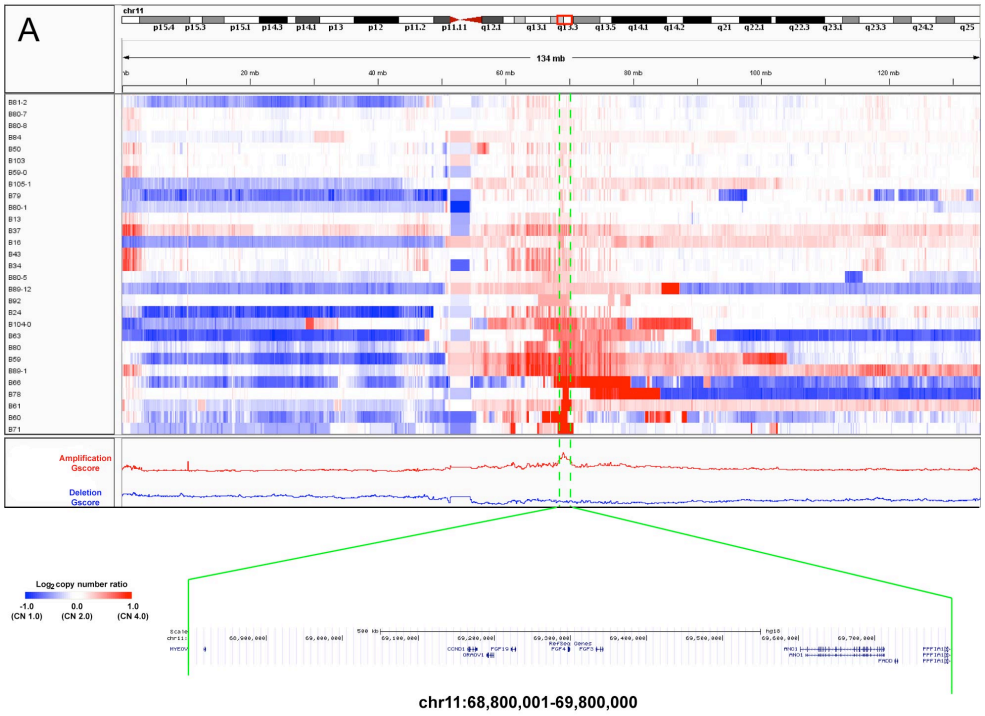
Supplementary Figure 11. Chromosomal overviews of amplification and deletion peaks with locations of putative cancer driver genes. The genes in pink indicate focal copy number alterations and * shows the genes with truncating mutations. The horizontal dotted red and blue lines indicate the G-Score value of 0.098, corresponding to $P<0.001$ level of significance.

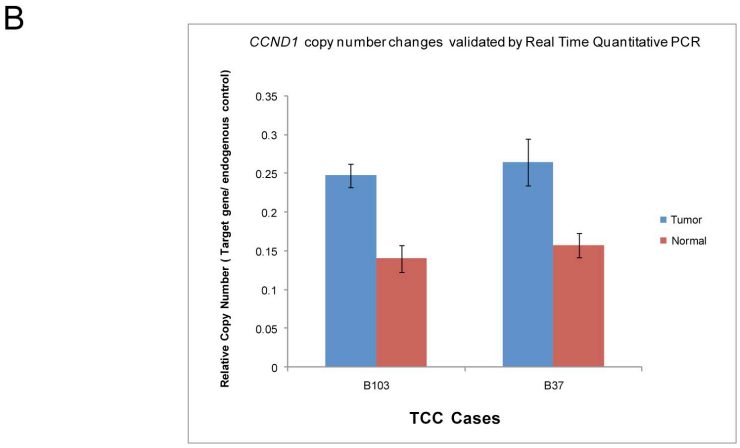


Supplementary Figure 12. GISTIC significant, recurrent focal amplifications (red) and deletions (blue) are plotted along the genome. Chromosomes are indicated in a vertical column between amplified (left) or deleted (right) regions. Genes of interest are indicated and the number of genes mapping to each region of amplifications or deletions are included in brackets.

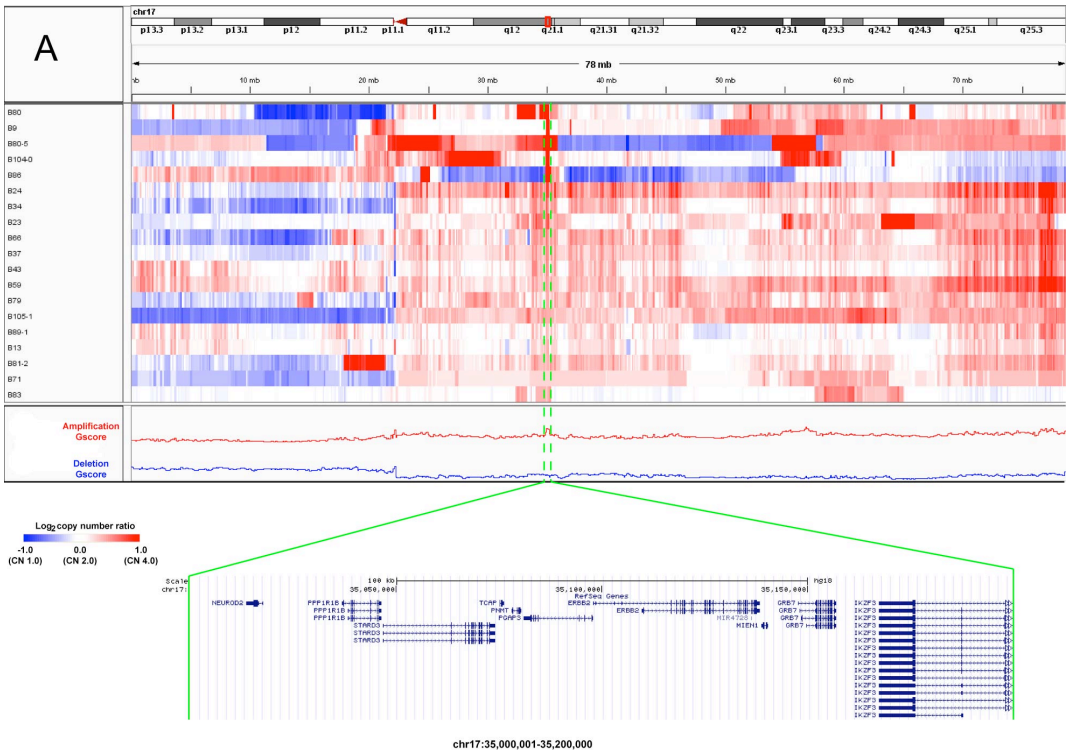


Supplementary Figure 13. A significant region of focal amplification in chromosome 6 encompassing E*2F3* in TCCs. G-Score values from GISTIC analysis are shown below the copy number profiles. Output is rendered by the Integrative Genomics Viewer (IGV). RefSeq genes mapping to the amplification region are shown below the IGV output.

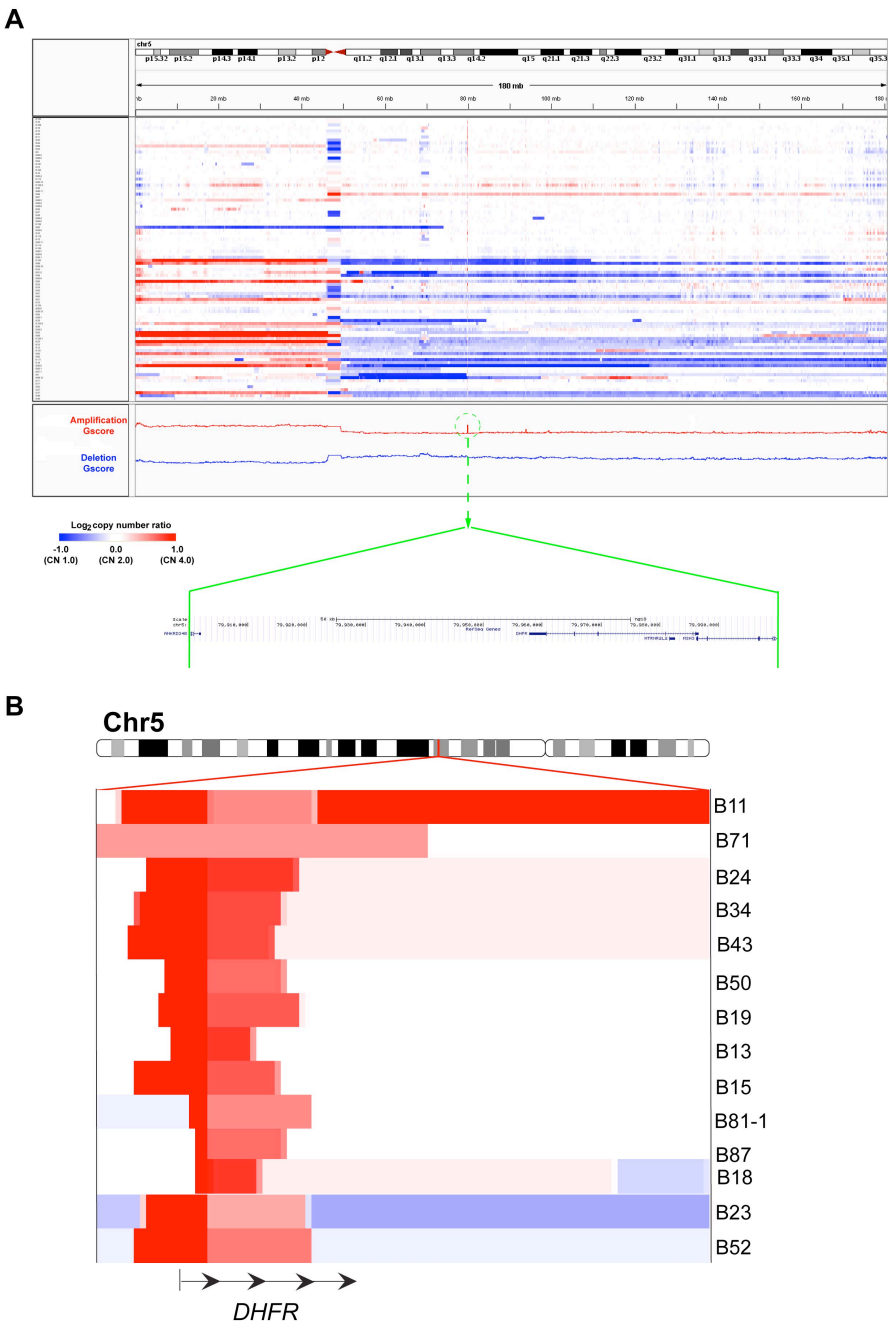




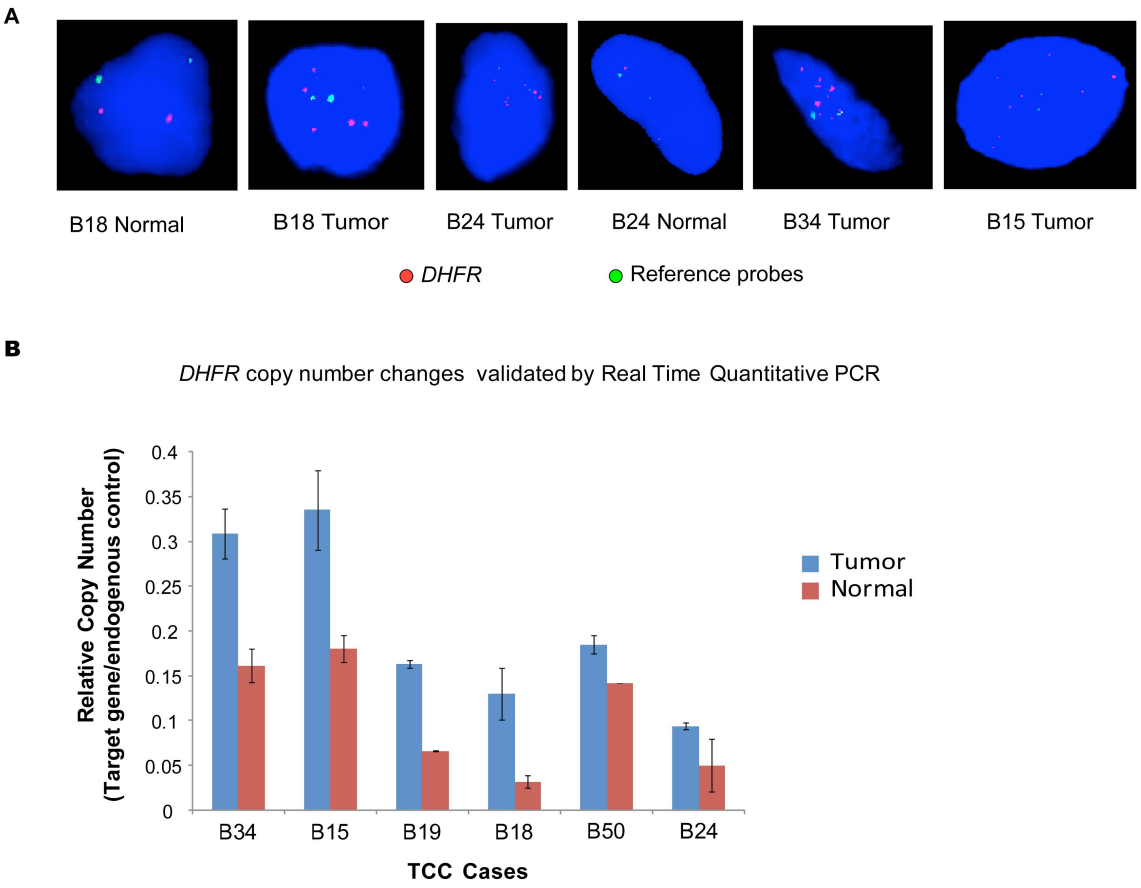
Supplementary Figure 14. A significant region of focal amplification in chromosome 11 encompassing *CCND1* in TCCs. (a) G-Score values from GISTIC analysis are shown below the copy number profiles. Output is rendered by the IGV. RefSeq genes mapping to the amplification region are shown below the IGV output. (**b)** Representative examples of validation of recurrent *CCND1* amplification in TCC samples of B103 and B37 by Real time Quantitative PCR.



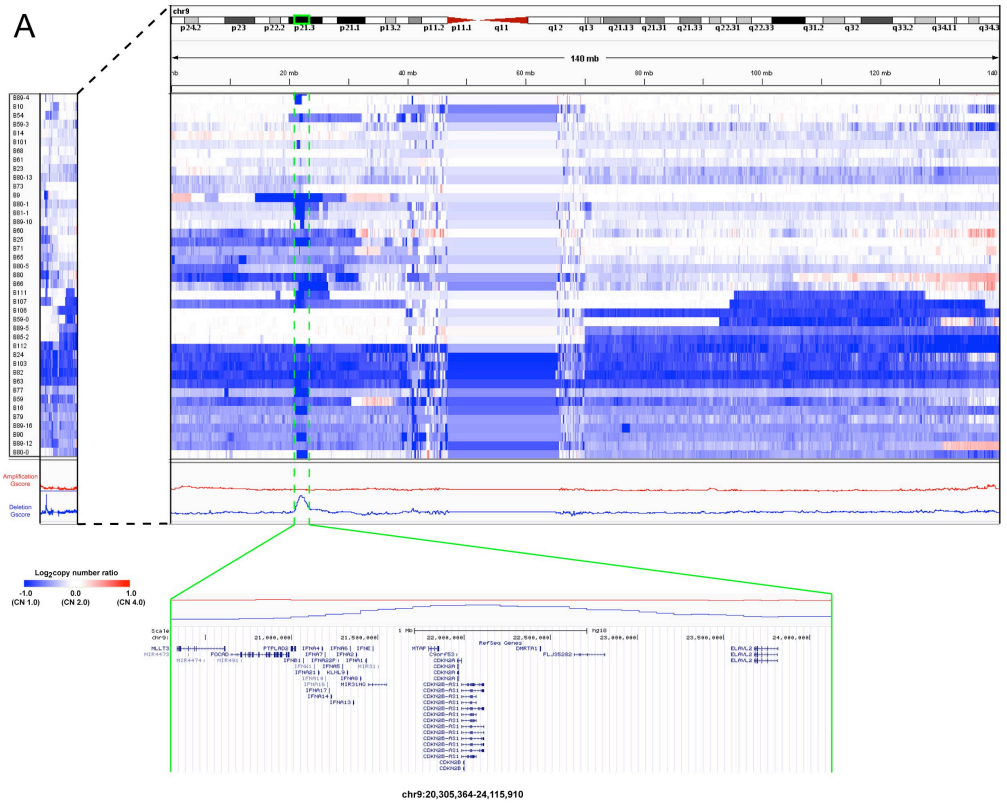
Supplementary Figure 15. A significant region of focal amplification in chromosome 17 encompassing *ERBB2* in TCCs. (a) G-Score values from GISTIC analysis are shown below the copy number profiles. Output is rendered by the IGV. RefSeq genes mapping to the amplification region are shown below the IGV output. **(b)** Representative examples of validation of recurrent *ERBB2* amplification in TCC samples of B80, B9, B80-5, B86, and B23 by Real time Quantitative PCR.



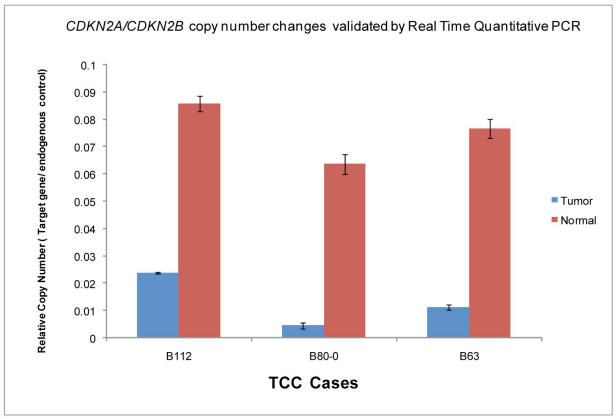
Supplementary Figure 16. (a) Frequent amplifications of a region containing *DHFR* in 5q, a frequent loss in TCCs. Output is rendered by the IGV. RefSeq genes mapping to the significant region are shown below the IGV output. **(b)** The relative position of *DHFR* locus and the TCC cases with copy number alterations in *DHFR* are shown at bottom and right of the figure, respectively.



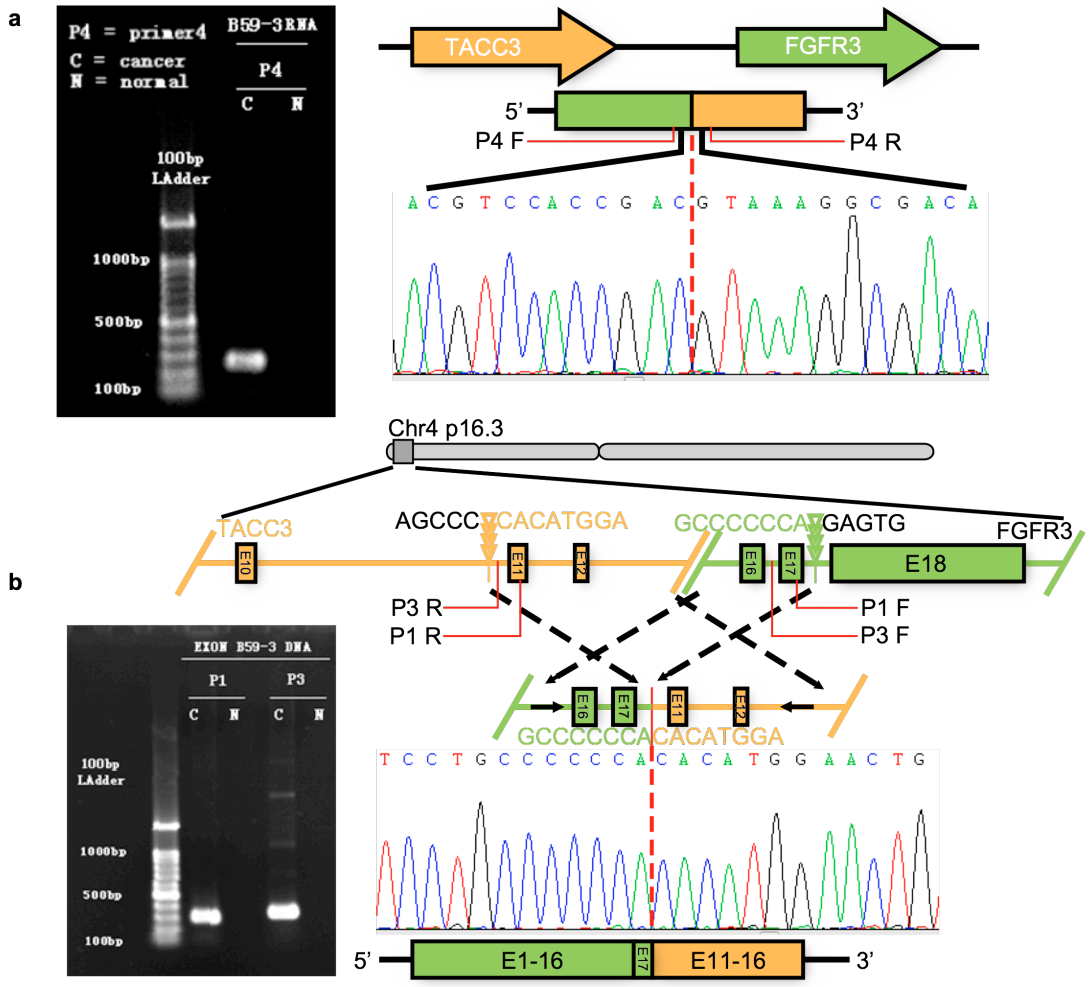
Supplementary Figure 17. Representative examples of validation of *DHFR* amplification in TCCs by Fluorescence in situ hybridization (a) and Real time quantitative PCR (b).



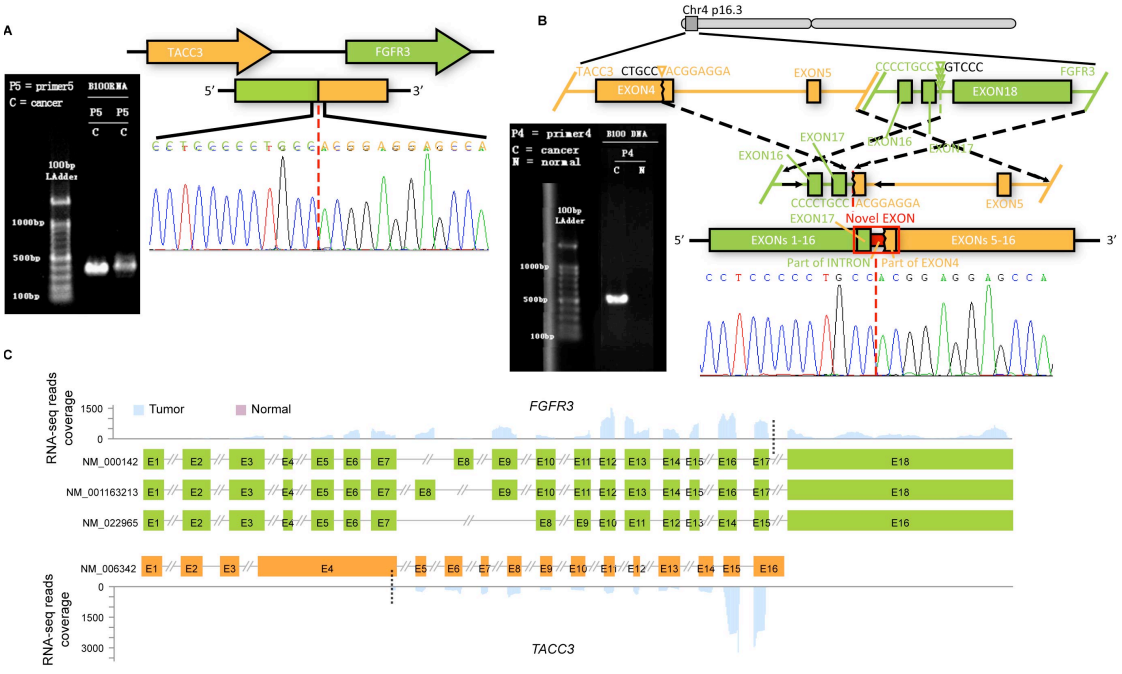
B



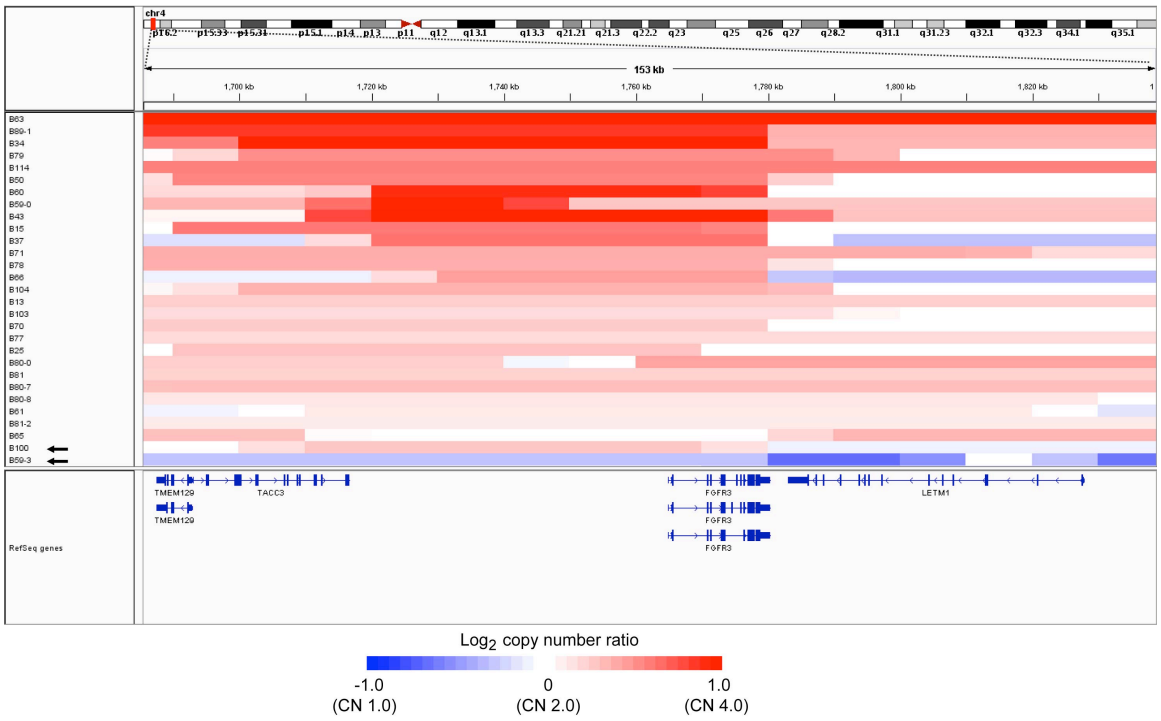
Supplementary Figure 18. A significant region of focal deletion in chromosome 9 containing *CDKN2A/B* in TCCs. (a) G-Score values from GISTIC analysis are shown below the copy number profiles. Output is rendered by the IGV. RefSeq genes mapping to the deleted region are shown below the IGV output. **(b)** Representative examples of validation of recurrent *CDKN2A/B* deletion in DNA from TCC samples of B112, B80-0, and B63 by Real time Quantitative PCR.



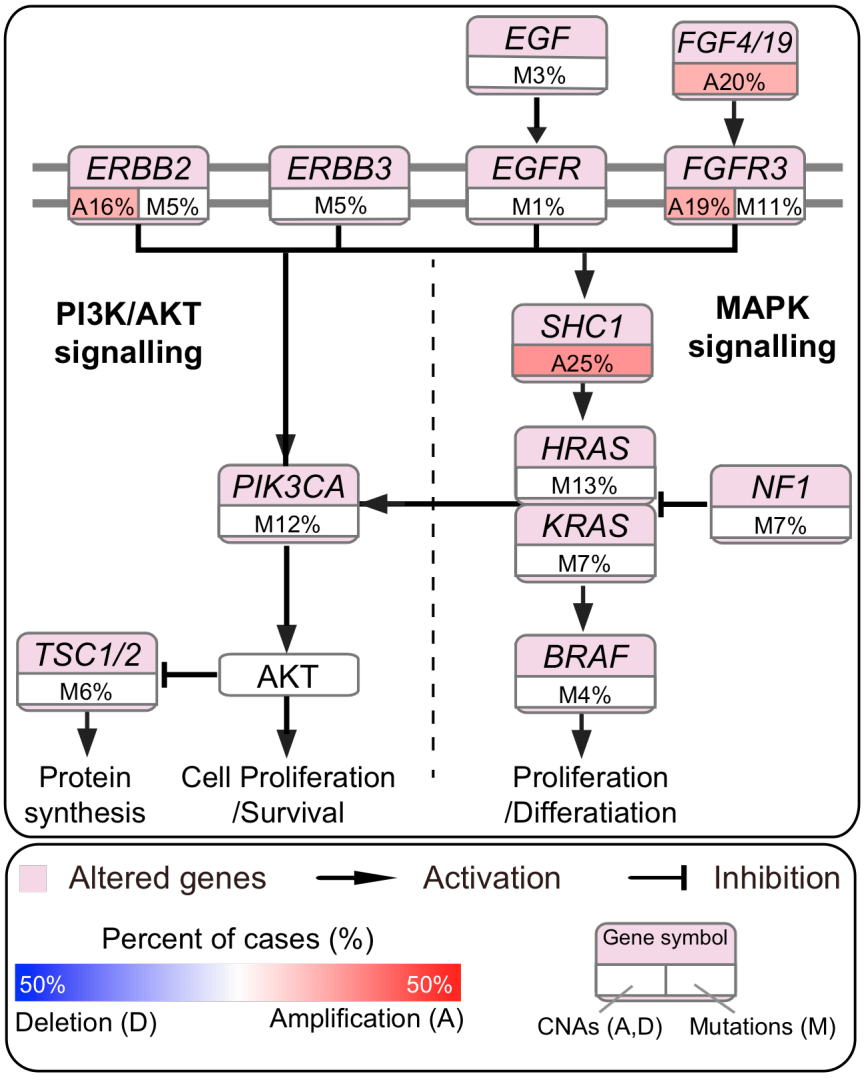
Supplementary Figure 19. *FGFR3-TACC3* fusion identified in B59-3 tumor. **(a)** Left, *FGFR3-TACC3* RT-PCR product from B59-3 tumor and normal cDNA. Right, Sanger sequencing of the RT-PCR product. **(b)** Genomic fusion of *FGFR3* intron 17 with intron 10 of *TACC3* resulting in exon 17 of *FGFR3* being spliced 5' to exon 11 of *TACC3* in the fused mRNA. Triangles indicate the genomic positions of the breakpoints. The detail information on positions and sequences of primers, P1, P3 and P4, was provided in the Supplementary Table 12.



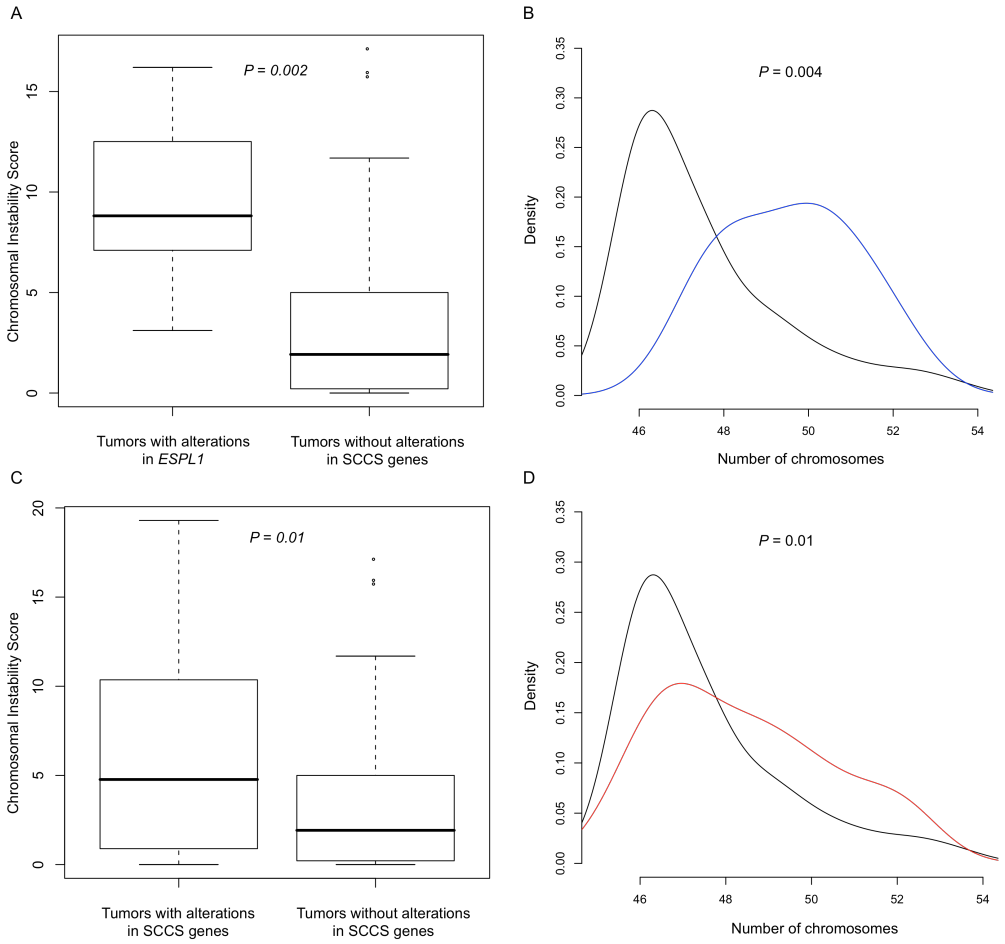
Supplementary Figure 20. *FGFR3-TACC3* fusion identified in B100 tumor. (**a)** Left, *FGFR3-TACC3* RT-PCR product from B100 tumor cDNA (normal bladder tissue is unavailable). Right, Sanger sequencing of RT-PCR product. (**b)** Genomic fusion of *FGFR3* intron 17 with exon 4 of *TACC3*. In the fused mRNA, exon 17 and fragment of intron 17 in *FGFR3*, and fragment of exon 4 in *TACC3* are merged into a novel exon. Triangles indicate the genomic positions of breakpoints. (**c)** RNA-Seq coverage analysis of *FGFR3* (top) and *TACC3* (bottom) in B100 tumor tissue. Three transcripts of *FGFR3* and one transcript of *TACC3* are shown. The black dotted lines indicate the breakpoints. E, exon(s)



Supplementary Figure 21. Copy number alterations at *TACC3/FGFR3* locus across samples rendered by the IGV. RefSeq genes mapping to this region are shown below the IGV output. TCC case IDs are shown to the left of the figure. The arrows indicate the two tumor samples harboring *FGFR3-TACC3* fusion.



Supplementary Figure 22. Genetic alterations in TCC frequently occur in genes of PI3K/AKT signaling and Ras-MAPK signaling pathways. Alterations are defined by somatic mutations, focal amplifications and deletions. Alteration frequencies are expressed as a percentage of all cases. Red denotes amplified genes and blue denotes deleted genes



Supplementary Figure 23. Tumors with alterations in *ESPL1* (a and b) and SCCS genes (c and d) show significantly more aneuploidy than tumors with wild-type SCCS genes. Chromosome instability is calculated as described in Supplementary Figure 7. Panels c and d showed the kernel density estimation of chromosome counts in tumors with *ESPL1* alterations (blue line), tumors with alterations in SCCS genes (red) and tumors with wild-type SCCS genes (black line). The *P* values were determined by Wilcoxon test.

Supplementary Tables

Supplementary Table 1. Clinical characteristics of the 99 TCC patients.

Case ID	Sex	Age (year)	TNM	Grade	Superficial/ Invasive	Primary/Relapsed	Analyzed by WES	Analyzed by WGS	Analyzed by RNA-Seq
B10	M	52	T2N0M0	2	Invasive	Primary	Yes	Yes	Yes
B100	M	25	T1N0M0	1	Superficial	Primary	Yes	Yes	Yes
B101	F	69	T1N0M0	1	Superficial	Primary	Yes	Yes	Yes
B102	M	45	T1N0M0	1	Superficial	Primary	Yes	Yes	No
B103	M	54	T1N0M0	1	Superficial	Primary	Yes	Yes	No
B104	M	52	T2N0M0	1	Invasive	Primary	Yes	Yes	No
B104-0	M	72	T1N0M0	1	Superficial	Primary	Yes	Yes	No
B105	M	62	T2NxMx	1	Invasive	Relapsed	Yes	Yes	No
B105-0	M	60	T2NxMx	1	Invasive	Primary	Yes	Yes	Yes
B105-1	M	64	T2NxMx	2	Invasive	Primary	Yes	Yes	Yes
B106	M	56	T2NxMx	1	Invasive	Primary	Yes	Yes	No
B107	M	68	T2NxMx	3	Invasive	Primary	Yes	Yes	No
B109	M	46	T1N0M0	1	Superficial	Relapsed	Yes	Yes	No
B11	M	80	T4N0M0	3	Invasive	Relapsed	Yes	Yes	No
B110	M	54	T1N0M0	1	Superficial	Primary	Yes	Yes	No
B111	M	45	T1N0M0	1	Superficial	Primary	Yes	Yes	No
B112	M	62	T3N1M0	1	Invasive	Relapsed	Yes	Yes	No
B114	M	73	T1bN0M0	1	Superficial	Primary	Yes	Yes	No
B13	M	64	T2N0M0	2	Invasive	Primary	Yes	Yes	Yes
B14	M	57	T2N0M0	2	Invasive	Primary	Yes	Yes	No
B15	M	40	T4N0M0	2	Invasive	Primary	Yes	Yes	Yes
B16	M	72	T1N0M0	3	Superficial	Primary	Yes	Yes	No
B18	M	66	T1N0M0	2	Superficial	Primary	Yes	Yes	Yes*
B19	M	69	T4NXMX	3	Invasive	Relapsed	Yes	Yes	No
B21	M	61	T2N0M0	1	Invasive	Primary	Yes	Yes	No
B22	M	79	T4N0M0	2	Invasive	Primary	Yes	Yes	Yes
B23	M	85	T1N0M0	3	Superficial	Primary	Yes	Yes	Yes*
B24	M	53	T4N0M0	1	Invasive	Primary	Yes	Yes	No
B25	M	65	T4aN0M0	3	Invasive	Relapsed	Yes	Yes	Yes*
B34	M	66	T3aN0M0	3	Invasive	Primary	Yes	Yes	Yes*
B35	M	80	T1N0M0	2	Superficial	Primary	Yes	Yes	No
B37	M	71	T4N0M0	3	Invasive	Primary	Yes	Yes	No
B41	M	69	T3bN0M0	2	Invasive	Primary	Yes	Yes	No
B43	M	43	T3aN1M0	3	Invasive	Primary	Yes	Yes	No

B45	M	82	T1bN0M0	1	Superficial	Primary	Yes	Yes	Yes*
B47	M	84	T3aN0M0	3	Invasive	Primary	Yes	Yes	No
B5	M	53	T4N0M0	2	Invasive	Primary	Yes	Yes	No
B50	M	73	T2bNXMX	2	Invasive	Primary	Yes	Yes	No
B52	M	57	T3N0M0	1	Invasive	Primary	Yes	Yes	Yes*
B54	M	49	T4N1M0	2	Invasive	Primary	Yes	Yes	Yes*
B55	M	41	T3N0M0	2	Invasive	Primary	Yes	Yes	No
B56	M	41	T1NxMx	2	Superficial	Primary	Yes	Yes	Yes*
B57	F	72	T2aNxMx	1	Invasive	Primary	Yes	Yes	Yes*
B58	M	62	T2aNxMx	1	Invasive	Primary	Yes	Yes	No
B59	F	67	T3NxMx	2	Invasive	Primary	Yes	Yes	Yes*
B59-0	M	50	T2NxMx	2	Invasive	Primary	Yes	Yes	Yes
B59-1	M	43	T1N0M0	1	Invasive	Primary	Yes	Yes	Yes
B59-3	M	65	T2N0M0	2	Invasive	Primary	Yes	Yes	No
B60	F	80	T4N0M0	3	Invasive	Primary	Yes	Yes	No
B61	F	53	T3N0M0	3	Invasive	Primary	Yes	Yes	No
B62-0	M	58	T1N0M0	1	Superficial	Primary	Yes	Yes	No
B63	M	70	T2aN0M0	3	Invasive	Primary	Yes	Yes	Yes*
B64	M	66	T1N0M0	1	Superficial	Primary	Yes	Yes	Yes*
B65	M	87	T3aN0M0	2	Invasive	Relapsed	Yes	Yes	Yes
B66	M	54	T2N0M0	2	Invasive	Primary	Yes	Yes	Yes
B66-0	F	50	TaN0M0	3	Superficial	Primary	Yes	Yes	Yes
B68	M	85	T2N0M0	2	Invasive	Primary	Yes	Yes	Yes*
B70	M	65	T2N0M0	2	Invasive	Primary	Yes	Yes	Yes
B71	M	65	T2N0M0	3	Invasive	Relapsed	Yes	Yes	Yes*
B73	M	44	T1N0M0	1	Superficial	Relapsed	Yes	Yes	Yes*
B74	M	60	T3aN0M0	3	Invasive	Primary	Yes	Yes	Yes
B77	M	75	T1N0M0	2	Superficial	Primary	Yes	Yes	Yes*
B78	M	80	TaN0M0	2	Superficial	Primary	Yes	Yes	No
B79	M	63	T3N0M0	2	Invasive	Primary	Yes	Yes	No
B80	M	76	T4aN0M0	3	Invasive	Primary	Yes	Yes	No
B80-0	M	82	T1N0M0	2	Superficial	Primary	Yes	Yes	Yes
B80-1	M	58	T2N0M0	2	Invasive	Relapsed	Yes	Yes	No
B80-11	M	28	T1N0M0	1	Superficial	Primary	Yes	Yes	Yes
B80-13	M	63	TaN0M0	1	Superficial	Primary	Yes	Yes	Yes
B80-3	M	51	T4N0M0	2	Invasive	Primary	Yes	Yes	No
B80-4	M	54	T1N0M0	1	Superficial	Primary	Yes	Yes	Yes
B80-5	M	73	TaN0M0	2	Superficial	Relapsed	Yes	Yes	No
B80-7	M	58	T3N0M0	2	Invasive	Primary	Yes	Yes	Yes
B80-8	F	63	T2N0M0	3	Invasive	Primary	Yes	Yes	Yes
B81	M	63	T2N0M0	3	Invasive	Primary	Yes	Yes	No
B81-1	M	62	T2N0M0	1	Invasive	Primary	Yes	Yes	No
B81-2	M	61	T2N0M0	2	Invasive	Primary	Yes	Yes	No
B82	M	56	T3N0M0	2	Invasive	Primary	Yes	Yes	No
B83	F	84	T3N0M0	1	Invasive	Primary	Yes	Yes	No

B84	M	64	T1N0M0	1	Superficial	Primary	Yes	Yes	No
B85-0	M	76	TaN0M0	1	Superficial	Primary	Yes	Yes	Yes
B85-2	M	74	TaN0M0	1	Superficial	Primary	Yes	Yes	No
B86	M	48	T2N0M0	1	Invasive	Primary	Yes	Yes	No
B87	M	57	T1N0M0	2	Superficial	Primary	Yes	Yes	No
B88	M	56	T3N0M0	2	Invasive	Primary	Yes	Yes	No
B89-1	M	65	T2N0M0	2	Invasive	Primary	Yes	Yes	No
B89-10	M	65	T1N0M0	1	Superficial	Primary	Yes	Yes	No
B89-11	F	38	T1N0M0	1	Superficial	Primary	Yes	Yes	No
B89-12	F	72	T2N0M0	3	Invasive	Primary	Yes	Yes	Yes
B89-16	M	68	T1N0M0	1	Superficial	Primary	Yes	Yes	No
B89-3	M	65	T3N0M0	1	Invasive	Primary	Yes	Yes	No
B89-4	M	71	T1N0M0	1	Superficial	Primary	Yes	Yes	Yes
B89-5	M	50	T1N0M0	1	Superficial	Primary	Yes	Yes	Yes
B9	M	81	T3N0M0	3	Invasive	Primary	Yes	Yes	Yes
B90	M	84	T1N0M0	1	Superficial	Primary	Yes	Yes	No
B92	M	53	T3bN1Mx	3	Invasive	Primary	Yes	Yes	No
B96	M	69	T3N0M0	2	Invasive	Relapsed	Yes	Yes	No
B98	M	63	T3N1MX	3	Invasive	Relapsed	Yes	Yes	No
B99	F	37	T1N0M0	1	Superficial	Primary	Yes	Yes	No

* 16 tumors for which their matched, morphologically normal bladder tissues were analyzed by RNA-Seq

Supplementary Table 2. Summary statistics of exome sequencing data obtained from 99 TCC tumor-blood pairs.

Case	Sample	Total reads	No. of uniquely mapping reads	% of uniquely mapping reads	No. of reads overlapping targets	% of reads overlapping targets	No. of non-duplicated reads	% of non-duplicated reads	Mean fold coverage	% of targets covered by at least 1×	% of targets covered by at least 8×
B100	Blood	45,617,985	40,496,989	88.77%	34,032,102	74.60%	34,005,589	74.54%	57.48	94.26%	81.20%
	Tumor	51,124,567	45,293,589	88.59%	39,293,178	76.86%	39,248,344	76.77%	67.71	94.62%	82.48%
B101	Blood	44,138,427	39,322,008	89.09%	31,864,931	72.19%	31,851,613	72.16%	53.70	94.29%	80.79%
	Tumor	50,410,636	44,882,254	89.03%	37,312,202	74.02%	37,292,515	73.98%	63.31	94.69%	82.19%
B102	Blood	45,263,458	40,323,145	89.09%	32,116,663	70.95%	32,105,997	70.93%	53.56	94.08%	80.59%
	Tumor	41,545,900	36,749,548	88.46%	31,268,302	75.26%	31,250,722	75.22%	53.43	94.04%	80.57%
B103	Blood	46,267,339	41,172,099	88.99%	34,283,583	74.10%	34,266,234	74.06%	57.73	94.07%	80.79%
	Tumor	43,732,676	38,926,751	89.01%	33,278,547	76.10%	33,258,709	76.05%	56.74	93.95%	80.58%
B104-0	Blood	52,154,612	46,425,313	89.01%	39,449,141	75.64%	39,422,416	75.59%	67.72	94.65%	82.24%
	Tumor	44,804,931	39,723,409	88.66%	34,524,966	77.06%	34,502,803	77.01%	59.23	93.68%	80.17%
B104	Blood	52,699,043	46,711,670	88.64%	38,563,344	73.18%	38,544,516	73.14%	65.27	94.94%	82.82%
	Tumor	42,113,127	37,346,769	88.68%	32,024,012	76.04%	32,008,020	76.00%	54.46	93.99%	80.76%
B105-0	Blood	45,063,552	39,938,424	88.63%	33,189,037	73.65%	33,161,788	73.59%	56.43	94.58%	81.69%
	Tumor	41,380,554	36,587,329	88.42%	31,661,597	76.51%	31,624,318	76.42%	54.42	93.89%	80.70%
B105-1	Blood	35,911,495	31,769,381	88.47%	27,408,490	76.32%	27,395,371	76.29%	46.94	93.48%	78.99%
	Tumor	34,820,140	30,867,364	88.65%	26,983,420	77.49%	26,970,747	77.46%	46.21	93.12%	78.28%
B105	Blood	37,500,548	33,275,151	88.73%	28,613,977	76.30%	28,602,095	76.27%	49.14	93.60%	79.42%
	Tumor	34,163,495	30,270,455	88.60%	26,458,671	77.45%	26,445,635	77.41%	45.73	93.26%	78.50%
B106	Blood	58,894,536	52,249,872	88.72%	42,879,705	72.81%	42,841,712	72.74%	72.71	95.59%	84.20%
	Tumor	43,624,709	38,572,318	88.42%	32,710,378	74.98%	32,677,187	74.91%	55.59	94.24%	81.37%
B107	Blood	70,952,075	62,915,487	88.67%	51,791,304	72.99%	51,763,063	72.95%	87.81	95.92%	85.32%
	Tumor	52,162,313	45,949,891	88.09%	39,083,100	74.93%	39,063,690	74.89%	65.97	94.48%	82.45%
B109	Blood	47,181,321	41,732,855	88.45%	35,924,422	76.14%	35,906,525	76.10%	61.90	94.50%	82.04%
	Tumor	60,487,207	53,450,846	88.37%	45,124,465	74.60%	45,105,293	74.57%	75.88	95.35%	84.40%
B10	Blood	229,631,568	148,875,857	64.83%	92,507,046	40.28%	91,205,579	39.72%	120.57	91.61%	74.18%
	Tumor	226,986,829	144,608,247	63.71%	97,098,763	42.78%	95,090,707	41.89%	125.58	89.80%	73.54%
B110	Blood	47,508,793	41,953,678	88.31%	36,366,444	76.55%	36,339,092	76.49%	62.91	94.55%	82.16%
	Tumor	44,354,130	39,120,994	88.20%	34,152,216	77.00%	34,133,498	76.96%	58.32	94.28%	81.93%
B111	Blood	61,273,322	54,419,544	88.81%	45,421,471	74.13%	45,399,250	74.09%	76.86	95.46%	84.52%
	Tumor	53,683,861	47,209,498	87.94%	41,008,656	76.39%	40,985,037	76.35%	69.62	94.74%	83.02%
B112	Blood	52,343,024	46,403,424	88.65%	37,752,261	72.12%	37,736,477	72.09%	63.24	94.97%	82.90%
	Tumor	54,983,654	48,674,405	88.53%	41,169,246	74.88%	41,148,521	74.84%	69.54	95.11%	83.68%

B114	Blood	47,420,568	41,882,314	88.32%	36,255,251	76.45%	36,238,049	76.42%	61.70	94.49%	82.21%
	Tumor	57,644,816	50,982,194	88.44%	43,853,397	76.08%	43,834,003	76.04%	73.89	94.93%	83.77%
B11	Blood	46,665,643	41,349,540	88.61%	34,647,057	74.25%	34,630,336	74.21%	58.53	94.26%	81.27%
	Tumor	46,430,687	41,021,602	88.35%	35,181,858	75.77%	35,158,843	75.72%	59.25	93.79%	80.63%
B13	Blood	46,546,564	41,375,612	88.89%	34,662,785	74.47%	34,648,336	74.44%	58.58	94.36%	81.47%
	Tumor	47,167,148	41,928,540	88.89%	35,650,339	75.58%	35,636,195	75.55%	59.95	94.02%	81.27%
B14	Blood	54,220,107	48,201,520	88.90%	40,055,782	73.88%	40,038,534	73.84%	66.96	94.66%	82.77%
	Tumor	42,665,048	37,779,980	88.55%	33,143,006	77.68%	33,127,601	77.65%	56.43	93.69%	80.73%
B15	Blood	49,014,746	43,664,246	89.08%	36,129,533	73.71%	36,108,612	73.67%	60.49	94.40%	81.86%
	Tumor	45,124,837	40,144,798	88.96%	34,666,423	76.82%	34,641,595	76.77%	58.93	94.17%	81.76%
B16	Blood	46,993,567	41,750,046	88.84%	35,204,326	74.91%	35,182,316	74.87%	59.42	94.41%	81.98%
	Tumor	56,941,058	50,260,508	88.27%	43,945,226	77.18%	43,908,471	77.11%	74.41	94.77%	83.45%
B18	Blood	100,749,288	89,541,155	88.88%	75,729,809	75.17%	75,602,936	75.04%	127.72	96.48%	87.87%
	Tumor	42,016,338	37,110,380	88.32%	34,012,790	80.95%	33,938,770	80.78%	59.53	93.56%	81.00%
B19	Blood	48,606,291	43,218,017	88.91%	36,853,459	75.82%	36,826,599	75.77%	62.36	94.38%	82.30%
	Tumor	43,549,716	38,603,105	88.64%	33,223,489	76.29%	33,201,417	76.24%	56.20	93.94%	80.98%
B21	Blood	48,690,545	42,871,015	88.05%	37,439,786	76.89%	37,385,383	76.78%	64.46	94.75%	82.89%
	Tumor	59,487,105	52,526,094	88.30%	43,220,295	72.65%	43,177,925	72.58%	71.82	94.65%	83.20%
B22	Blood	48,511,146	42,825,915	88.28%	36,358,321	74.95%	36,330,588	74.89%	61.04	94.23%	81.71%
	Tumor	46,441,414	41,048,961	88.39%	36,294,365	78.15%	36,263,535	78.08%	61.57	93.76%	81.31%
B23	Blood	66,279,539	58,629,547	88.46%	49,139,325	74.14%	49,095,720	74.07%	82.21	95.14%	84.46%
	Tumor	43,142,095	38,148,487	88.43%	33,988,425	78.78%	33,946,498	78.69%	58.29	93.47%	80.36%
B24	Blood	55,517,532	49,035,505	88.32%	41,731,649	75.17%	41,682,965	75.08%	70.21	94.67%	83.34%
	Tumor	44,227,141	38,881,680	87.91%	34,614,180	78.26%	34,557,885	78.14%	59.33	93.53%	80.61%
B25	Blood	58,633,085	51,581,352	87.97%	42,860,658	73.10%	42,809,834	73.01%	71.50	94.72%	83.20%
	Tumor	51,593,229	45,328,260	87.86%	39,423,086	76.41%	39,358,114	76.29%	66.83	94.40%	82.69%
B34	Blood	66,839,880	58,798,829	87.97%	49,245,308	73.68%	49,194,401	73.60%	82.82	95.25%	84.36%
	Tumor	55,645,505	48,291,248	86.78%	43,176,055	77.59%	43,117,951	77.49%	73.72	94.58%	83.22%
B35	Blood	43,491,937	38,228,772	87.90%	34,207,951	78.65%	34,154,882	78.53%	58.90	93.83%	81.16%
	Tumor	53,759,172	47,446,247	88.26%	41,908,383	77.96%	41,855,879	77.86%	71.33	94.47%	83.09%
B37	Blood	61,848,069	54,716,513	88.47%	45,962,891	74.32%	45,921,956	74.25%	77.27	95.22%	84.33%
	Tumor	44,818,501	39,503,157	88.14%	35,585,399	79.40%	35,530,801	79.28%	61.68	93.74%	81.22%
B41	Blood	50,957,146	45,067,578	88.44%	37,133,765	72.87%	37,109,470	72.82%	62.21	94.55%	81.94%
	Tumor	44,391,297	38,850,982	87.52%	34,420,392	77.54%	34,383,381	77.46%	59.20	94.01%	81.31%
B43	Blood	49,259,758	43,609,248	88.53%	37,812,973	76.76%	37,778,315	76.69%	63.98	93.75%	81.56%
	Tumor	42,083,008	37,115,188	88.20%	32,570,488	77.40%	32,542,273	77.33%	55.18	93.68%	80.64%
B45	Blood	58,777,387	52,025,900	88.51%	44,717,528	76.08%	44,677,411	76.01%	75.54	94.60%	83.61%
	Tumor	45,046,526	39,831,899	88.42%	34,915,185	77.51%	34,884,810	77.44%	59.31	94.06%	81.57%
B47	Blood	48,657,208	43,283,896	88.96%	36,316,088	74.64%	36,291,456	74.59%	60.86	93.92%	81.38%
				88.95%	34,360,576	75.54%	34,339,721	75.49%	57.56	93.50%	80.45%

B50	Blood	49,374,135	44,440,762	90.01%	35,776,889	72.46%	35,763,412	72.43%	59.60	85.68%	75.97%
	Tumor	41,330,797	37,130,481	89.84%	31,440,333	76.07%	31,425,674	76.03%	52.94	84.35%	74.63%
B52	Blood	68,791,077	61,872,496	89.94%	52,691,505	76.60%	52,637,692	76.52%	89.05	86.58%	78.17%
	Tumor	43,643,559	39,337,523	90.13%	34,255,807	78.49%	34,219,457	78.41%	58.20	84.30%	75.38%
B54	Blood	76,449,440	68,738,910	89.91%	57,305,436	74.96%	57,264,297	74.90%	96.47	87.58%	78.83%
	Tumor	47,223,820	42,339,739	89.66%	36,158,383	76.57%	36,132,740	76.51%	61.18	85.46%	76.67%
B55	Blood	44,824,273	40,151,167	89.57%	33,645,417	75.06%	33,614,730	74.99%	56.20	84.66%	75.56%
	Tumor	39,554,480	35,286,746	89.21%	30,774,069	77.80%	30,739,454	77.71%	52.02	84.37%	75.42%
B56	Blood	46,989,685	41,661,154	88.66%	34,748,836	73.95%	34,737,947	73.93%	58.63	94.29%	81.90%
	Tumor	46,650,304	41,357,090	88.65%	36,132,719	77.45%	36,115,906	77.42%	61.59	94.09%	81.70%
B57	Blood	64,667,175	57,809,318	89.40%	44,017,356	68.07%	44,005,616	68.05%	72.25	94.69%	82.72%
	Tumor	72,098,051	64,335,091	89.23%	51,937,822	72.04%	51,917,135	72.01%	87.01	95.41%	84.63%
B58	Blood	49,652,614	44,664,546	89.95%	33,500,946	67.47%	33,489,619	67.45%	56.62	87.48%	76.17%
	Tumor	58,125,899	52,304,209	89.98%	39,048,495	67.18%	39,033,250	67.15%	65.97	88.23%	77.06%
B59-0	Blood	167,080,953	149,547,513	89.51%	113,349,553	67.84%	113,271,393	67.79%	187.79	97.77%	90.05%
	Tumor	49,125,439	43,472,530	88.49%	37,187,412	75.70%	37,164,910	75.65%	63.52	94.62%	82.46%
B59-1	Blood	137,649,299	123,185,036	89.49%	93,517,884	67.94%	93,456,579	67.89%	154.29	97.35%	89.17%
	Tumor	44,183,802	39,259,877	88.86%	32,869,941	74.39%	32,856,148	74.36%	54.89	93.91%	81.04%
B59-3	Blood	49,031,727	43,202,843	88.11%	37,548,743	76.58%	37,527,080	76.54%	64.04	94.44%	82.46%
	Tumor	76,507,731	67,485,052	88.21%	58,015,306	75.83%	57,969,450	75.77%	98.79	95.83%	85.79%
B59	Blood	111,176,027	99,277,954	89.30%	79,247,134	71.28%	79,198,191	71.24%	132.17	96.46%	87.58%
	Tumor	49,150,881	43,690,877	88.89%	37,766,092	76.84%	37,744,592	76.79%	64.41	94.05%	81.66%
B5	Blood	48,811,053	43,382,960	88.88%	35,534,224	72.80%	35,520,497	72.77%	59.65	94.55%	82.12%
	Tumor	43,936,513	39,143,033	89.09%	32,905,219	74.89%	32,890,032	74.86%	55.62	93.32%	79.80%
B60	Blood	80,248,373	71,502,639	89.10%	56,222,354	70.06%	56,189,983	70.02%	93.55	95.79%	85.67%
	Tumor	42,814,091	38,002,718	88.76%	32,155,352	75.10%	32,138,765	75.07%	54.16	93.47%	80.11%
B61	Blood	46,303,733	41,165,887	88.90%	32,857,706	70.96%	32,835,077	70.91%	53.92	93.62%	79.98%
	Tumor	95,398,474	85,263,403	89.38%	71,355,210	74.80%	71,293,146	74.73%	120.48	96.09%	87.12%
B62-0	Blood	44,384,037	39,027,182	87.93%	33,997,333	76.60%	33,975,303	76.55%	57.54	93.97%	81.44%
	Tumor	40,626,585	35,735,130	87.96%	32,033,281	78.85%	32,012,141	78.80%	54.91	93.71%	80.91%
B63	Blood	51,875,901	46,180,626	89.02%	35,815,977	69.04%	35,800,566	69.01%	59.78	94.60%	81.64%
	Tumor	65,200,088	57,893,496	88.79%	45,438,709	69.69%	45,416,048	69.66%	75.82	95.05%	83.30%
B64	Blood	52,803,660	47,168,486	89.33%	35,414,529	67.07%	35,402,991	67.05%	58.72	94.49%	81.10%
	Tumor	59,111,245	52,792,786	89.31%	41,410,464	70.06%	41,393,102	70.03%	69.58	94.83%	82.67%
B65	Blood	47,674,102	42,537,638	89.23%	33,139,874	69.51%	33,129,044	69.49%	54.58	94.47%	81.14%
	Tumor	50,599,805	45,186,876	89.30%	35,760,281	70.67%	35,747,928	70.65%	59.10	94.47%	81.20%
B66-0	Blood	57,736,322	51,378,470	88.99%	42,532,843	73.67%	42,511,993	73.63%	71.36	94.84%	83.29%
	Tumor	43,046,702	38,361,170	89.12%	32,254,784	74.93%	32,240,370	74.90%	54.20	93.51%	80.25%
B66	Blood	57,579,002	51,165,953	88.86%	41,093,677	71.37%	41,075,861	71.34%	68.28	94.68%	82.53%
	Tumor	46,757,595	41,486,539	88.73%	34,906,578	74.65%	34,894,479	74.63%	58.50	94.03%	81.04%

B68	Blood	49,754,669	44,002,011	88.44%	37,266,518	74.90%	37,250,511	74.87%	62.79	94.44%	82.39%
	Tumor	50,945,337	45,315,819	88.95%	39,067,520	76.69%	39,047,111	76.65%	66.07	94.13%	82.07%
B70	Blood	42,232,983	37,389,630	88.53%	32,049,110	75.89%	32,036,603	75.86%	54.19	94.38%	81.61%
	Tumor	99,480,442	88,649,068	89.11%	71,259,056	71.63%	71,224,108	71.60%	118.68	96.73%	87.89%
B71	Blood	53,324,333	47,541,007	89.15%	38,993,264	73.12%	38,981,421	73.10%	64.98	94.46%	81.94%
	Tumor	93,956,748	83,795,096	89.18%	68,324,649	72.72%	68,290,593	72.68%	114.07	96.09%	86.50%
B73	Blood	56,788,999	50,365,739	88.69%	42,012,047	73.98%	41,991,665	73.94%	70.59	94.93%	83.35%
	Tumor	42,550,519	37,685,591	88.57%	32,655,630	76.75%	32,640,529	76.71%	55.17	93.83%	80.80%
B74	Blood	47,108,015	41,692,624	88.50%	36,200,647	76.85%	36,183,149	76.81%	61.03	93.89%	81.39%
	Tumor	42,878,186	37,888,642	88.36%	33,530,275	78.20%	33,513,007	78.16%	57.01	93.58%	80.49%
B77	Blood	37,458,705	33,247,122	88.76%	28,287,865	75.52%	28,278,892	75.49%	47.30	93.03%	78.23%
	Tumor	34,070,890	30,246,295	88.77%	26,534,101	77.88%	26,524,182	77.85%	44.84	92.62%	77.08%
B78	Blood	47,592,512	42,451,404	89.20%	34,445,131	72.38%	34,435,251	72.35%	57.88	94.72%	81.65%
	Tumor	61,619,658	55,300,355	89.74%	44,514,899	72.24%	44,497,727	72.21%	74.60	95.35%	83.57%
B79	Blood	48,181,622	43,365,266	90.00%	35,344,134	73.36%	35,327,711	73.32%	59.72	86.61%	76.76%
	Tumor	67,388,031	60,610,312	89.94%	48,508,822	71.98%	48,488,839	71.95%	80.81	87.52%	78.04%
B80-0	Blood	47,754,749	42,286,920	88.55%	36,089,699	75.57%	36,072,069	75.54%	61.35	94.66%	82.45%
	Tumor	52,649,903	46,224,412	87.80%	40,178,117	76.31%	40,151,099	76.26%	68.86	94.46%	82.27%
B80-11	Blood	54,957,784	49,367,950	89.83%	41,333,136	75.21%	41,314,816	75.18%	70.04	86.75%	77.64%
	Tumor	43,149,143	38,741,707	89.79%	33,111,771	76.74%	33,098,262	76.71%	56.40	85.88%	76.57%
B80-13	Blood	46,716,227	42,031,132	89.97%	34,086,150	72.96%	34,074,349	72.94%	57.14	86.13%	76.35%
	Tumor	43,464,970	39,111,213	89.98%	32,681,825	75.19%	32,668,975	75.16%	55.36	86.01%	76.36%
B80-1	Blood	51,366,325	46,248,876	90.04%	37,019,911	72.07%	37,001,671	72.03%	62.36	87.10%	77.22%
	Tumor	77,700,562	69,656,632	89.65%	59,387,746	76.43%	59,291,998	76.31%	103.60	89.27%	79.52%
B80-3	Blood	52,900,369	47,707,993	90.18%	39,527,588	74.72%	39,508,896	74.69%	66.62	86.34%	77.14%
	Tumor	47,580,024	42,747,958	89.84%	37,241,920	78.27%	37,218,337	78.22%	64.14	86.00%	77.00%
B80-4	Blood	72,059,203	64,646,618	89.71%	54,710,786	75.92%	54,672,965	75.87%	93.04	87.89%	78.94%
	Tumor	43,080,107	38,376,526	89.08%	34,067,348	79.08%	34,034,576	79.00%	59.19	85.78%	76.35%
B80-5	Blood	40,539,502	36,231,560	89.37%	30,950,258	76.35%	30,935,602	76.31%	53.04	86.11%	76.34%
	Tumor	43,622,631	38,856,682	89.07%	33,715,224	77.29%	33,694,960	77.24%	57.63	85.85%	76.37%
B80-7	Blood	46,955,908	41,660,525	88.72%	33,856,054	72.10%	33,844,276	72.08%	56.68	94.54%	81.71%
	Tumor	46,002,639	40,708,101	88.49%	33,918,835	73.73%	33,905,013	73.70%	56.84	94.40%	81.70%
B80-8	Blood	41,165,810	36,666,755	89.07%	32,716,876	79.48%	32,685,268	79.40%	56.76	85.37%	76.07%
	Tumor	59,154,275	52,961,585	89.53%	44,904,109	75.91%	44,876,163	75.86%	75.62	86.36%	77.63%
B80	Blood	61,184,451	54,594,265	89.23%	44,686,046	73.03%	44,660,658	72.99%	75.02	87.15%	77.63%
	Tumor	43,229,595	38,688,321	89.49%	33,162,462	76.71%	33,141,004	76.66%	56.41	85.80%	75.93%
B81-1	Blood	56,554,773	50,837,069	89.89%	42,193,903	74.61%	42,165,274	74.56%	71.40	87.00%	77.59%
	Tumor	40,868,414	36,597,935	89.55%	32,075,954	78.49%	32,040,109	78.40%	55.36	85.65%	75.75%
B81-2	Blood	36,913,695	32,487,150	88.01%	28,983,222	78.52%	28,948,992	78.42%	47.56	85.45%	75.22%
	Tumor	53,226,251	46,604,084	87.56%	40,605,308	76.29%	40,548,256	76.18%	65.60	86.82%	77.26%

B81	Blood	45,223,712	40,893,009	90.42%	32,352,278	71.54%	32,338,910	71.51%	53.88	85.57%	75.11%
	Tumor	51,725,700	46,536,914	89.97%	40,533,216	78.36%	40,493,870	78.29%	69.89	86.24%	77.27%
B82	Blood	43,219,455	38,790,632	89.75%	32,688,652	75.63%	32,672,045	75.60%	55.34	85.55%	75.91%
	Tumor	54,231,825	48,351,469	89.16%	42,066,143	77.57%	42,026,790	77.49%	72.85	87.02%	77.44%
B83	Blood	42,524,603	38,144,439	89.70%	31,709,663	74.57%	31,700,417	74.55%	53.19	85.16%	75.08%
	Tumor	46,340,605	41,386,217	89.31%	35,012,201	75.55%	34,997,919	75.52%	59.23	85.80%	76.14%
B84	Blood	51,466,199	45,692,836	88.78%	38,374,584	74.56%	38,354,538	74.52%	65.14	94.93%	83.05%
	Tumor	41,980,471	37,165,967	88.53%	32,132,654	76.54%	32,115,215	76.50%	54.82	94.07%	81.05%
B85-0	Blood	43,727,077	39,351,213	89.99%	31,496,885	72.03%	31,484,085	72.00%	53.01	86.43%	76.30%
	Tumor	65,156,567	58,588,691	89.92%	48,507,649	74.45%	48,483,632	74.41%	81.96	87.87%	78.64%
B85-2	Blood	43,680,383	39,185,687	89.71%	32,384,072	74.14%	32,372,214	74.11%	54.49	85.74%	76.13%
	Tumor	75,794,724	67,953,085	89.65%	57,012,635	75.22%	56,982,348	75.18%	96.26	88.11%	78.98%
B86	Blood	48,517,271	43,150,618	88.94%	36,480,290	75.19%	36,434,565	75.10%	61.78	85.26%	75.66%
	Tumor	39,939,558	35,764,275	89.55%	31,534,428	78.96%	31,459,140	78.77%	55.33	84.62%	74.31%
B87	Blood	48,233,225	43,410,182	90.00%	34,563,251	71.66%	34,551,293	71.63%	57.82	85.99%	75.90%
	Tumor	56,078,166	50,364,900	89.81%	41,761,862	74.47%	41,744,193	74.44%	70.36	86.73%	77.67%
B88	Blood	45,446,225	40,336,917	88.76%	33,155,079	72.95%	33,141,679	72.93%	55.66	94.28%	81.36%
	Tumor	51,901,684	46,022,290	88.67%	38,685,408	74.54%	38,664,809	74.50%	65.20	94.62%	82.83%
B89-10	Blood	42,737,041	38,427,418	89.92%	31,909,494	74.66%	31,888,474	74.62%	53.78	85.28%	75.63%
	Tumor	52,939,875	47,612,645	89.94%	40,913,711	77.28%	40,873,397	77.21%	70.27	86.66%	77.62%
B89-11	Blood	43,145,083	38,577,278	89.41%	34,115,952	79.07%	34,090,341	79.01%	58.99	85.43%	76.10%
	Tumor	63,317,759	56,762,216	89.65%	48,251,018	76.20%	48,222,537	76.16%	81.61	86.91%	78.12%
B89-12	Blood	44,789,466	39,821,330	88.91%	33,274,727	74.29%	33,260,599	74.26%	56.19	86.07%	76.47%
	Tumor	46,075,309	40,727,044	88.39%	34,358,188	74.57%	34,340,828	74.53%	57.77	85.81%	76.02%
B89-16	Blood	37,064,434	32,786,731	88.46%	27,068,507	73.03%	27,057,814	73.00%	45.30	92.79%	77.80%
	Tumor	36,707,003	32,584,873	88.77%	27,573,570	75.12%	27,563,693	75.09%	46.24	92.81%	77.81%
B89-1	Blood	44,672,292	39,991,565	89.52%	33,118,493	74.14%	33,104,677	74.11%	55.29	85.38%	76.48%
	Tumor	47,984,607	42,981,923	89.57%	37,367,938	77.87%	37,342,283	77.82%	64.01	85.86%	76.91%
B89-3	Blood	44,269,288	39,825,062	89.96%	34,704,291	78.39%	34,680,718	78.34%	59.85	85.94%	76.74%
	Tumor	64,427,056	58,222,691	90.37%	48,883,491	75.87%	48,857,031	75.83%	82.51	86.93%	78.24%
B89-4	Blood	64,268,656	57,876,221	90.05%	47,353,581	73.68%	47,326,394	73.64%	79.49	87.28%	78.00%
	Tumor	43,563,415	38,924,441	89.35%	33,928,370	77.88%	33,904,517	77.83%	58.16	85.80%	76.27%
B89-5	Blood	45,711,335	41,238,505	90.22%	32,903,604	71.98%	32,892,719	71.96%	55.25	85.87%	75.30%
	Tumor	51,071,723	45,884,850	89.84%	37,998,968	74.40%	37,981,924	74.37%	64.16	86.01%	76.19%
B90	Blood	45,657,227	41,064,299	89.94%	33,674,506	73.76%	33,661,236	73.73%	57.08	86.47%	76.42%
	Tumor	68,786,711	61,951,694	90.06%	50,911,504	74.01%	50,884,458	73.97%	86.35	88.27%	78.50%
B92	Blood	61,870,998	55,787,117	90.17%	45,377,176	73.34%	45,357,565	73.31%	76.07	87.03%	77.51%
	Tumor	42,692,515	38,315,084	89.75%	32,878,976	77.01%	32,866,700	76.98%	56.21	86.19%	76.44%
B96	Blood	73,994,541	66,235,741	89.51%	56,228,608	75.99%	56,172,641	75.91%	96.21	88.58%	79.28%
	Tumor	46,850,444	41,905,812	89.45%	36,847,966	78.65%	36,813,122	78.58%	63.49	86.32%	77.03%

B98	Blood	51,499,739	46,345,229	89.99%	39,159,321	76.04%	39,127,581	75.98%	66.88	86.60%	77.54%
	Tumor	42,977,339	38,698,554	90.04%	33,765,760	78.57%	33,735,896	78.50%	58.03	85.54%	76.65%
B99	Blood	52,741,646	46,929,846	88.98%	40,334,532	76.48%	40,290,346	76.39%	68.68	94.51%	82.86%
	Tumor	140,501,992	125,737,468	89.49%	102,783,026	73.15%	102,642,730	73.05%	172.77	97.28%	89.18%
B9	Blood	246,700,460	178,393,337	72.31%	94,725,338	38.40%	93,902,419	38.06%	123.71	89.05%	72.82%
	Tumor	217,170,245	154,557,672	71.17%	84,691,864	39.00%	83,964,243	38.66%	112.41	88.77%	73.84%

Supplementary Table 3. Predicted somatic mutations in 99 TCC patients (shown in separate excel file).

Supplementary Table 4. A list of all confirmed somatic mutations detected in 99 TCC patients (shown in separate excel file).

Supplementary Table 5. Summary statistics of RNA-Seq data from tumor and normal bladder tissues in 42 TCC patients.

Samples	Total Reads	No. of reads mapping to genome	No. of reads mapping to reference genes	No. of Genes covered by uniquely mapping Reads
B100-T	32,136,512	22,220,602	18,684,233	16,558
B101-T	45,162,546	33,272,540	25,060,095	17,468
B105-0-T	44,308,600	31,973,993	22,528,568	16,985
B105-1-T	53,148,122	39,777,976	29,625,914	17,725
B10-T	44,607,890	34,230,477	18,223,162	16,800
B13-T	45,870,072	34,722,324	22,044,535	17,252
B15-T	45,027,952	34,693,177	19,052,404	16,601
B18-T	38,866,690	28,160,397	16,762,014	16,511
B18-N	36,071,124	28,025,686	21,547,863	16,958
B22-T	39,173,750	28,355,183	15,902,416	16,281
B23-T	49,819,962	37,537,704	25,592,850	17,707
B23-N	52,055,046	39,674,423	33,390,488	17,877
B25-T	36,859,014	28,285,844	16,148,275	17,323
B25-N	36,951,784	28,599,732	22,811,893	17,285
B34-T	48,683,090	38,255,891	19,501,567	17,257
B34-N	42,467,474	32,279,423	26,080,368	17,542
B45-T	24,280,984	14,641,950	8,243,636	14,283
B45-N	39,399,802	30,403,868	21,724,759	17,535
B52-T	40,686,032	30,515,127	19,854,983	17,130
B52-N	44,922,862	34,692,147	28,053,691	17,752
B54-T	55,593,718	42,851,603	28,770,438	17,412
B54-N	29,634,316	22,538,776	13,590,875	16,875
B56-T	31,822,504	23,445,184	13,526,029	16,101
B56-N	35,011,204	23,671,526	25,362,533	16,804
B57-T	35,873,238	27,167,046	12,008,138	16,466
B57-N	48,422,722	34,667,553	30,048,564	17,578
B59-0-T	48,706,270	39,289,423	17,379,940	17,030
B59-1-T	44,833,384	34,411,903	22,868,489	17,119
B59-3-T	41,810,774	30,198,412	26,705,415	17,836
B59-3-N	55,341,118	40,030,997	32,862,783	17,867
B63-T	34,855,462	25,687,776	11,649,829	16,509
B63-N	33,664,610	24,760,675	20,614,369	17,409
B64-T	34,429,512	25,663,947	10,672,005	15,886
B64-N	45,389,434	35,628,279	26,035,941	17,524
B65-T	79,185,814	57,183,218	25,863,508	17,028
B66-0-T	31,366,570	19,999,152	18,237,446	16,205
B66-T	43,573,606	31,962,046	22,243,113	17,185
B68-T	43,147,208	30,350,355	25,624,171	17,226
B68-N	36,360,590	27,926,889	20,170,644	17,127
B70-T	39,003,752	27,425,412	23,812,647	17,126
B71-T	82,664,934	55,033,336	44,716,785	17,782
B71-N	38,770,298	28,254,367	26,745,534	17,625
B73-T	43,343,774	32,401,522	22,277,634	17,226
B73-N	37,603,818	29,667,934	21,127,612	17,420
B74-T	32,319,440	21,679,017	18,182,326	17,147
B77-T	43,852,166	32,569,154	25,201,106	17,517
B77-N	52,264,120	41,156,515	23,187,302	16,927

B80-0-T	47,040,348	32,836,531	33,268,884	17,205
B80-11-T	33,583,952	24,405,375	21,325,969	16,783
B80-13-T	33,536,434	25,800,297	16,606,281	16,552
B80-4-T	27,523,710	17,826,482	16,404,418	16,050
B80-7-T	41,682,426	30,240,334	23,777,238	17,112
B80-8-T	32,783,948	23,655,844	19,838,997	16,503
B85-0-T	37,720,790	25,715,479	25,867,582	16,815
B89-12-T	44,327,176	33,269,524	23,308,964	17,622
B89-4-T	41,874,076	29,036,204	26,338,999	16,632
B89-5-T	34,398,578	26,252,246	13,372,857	16,496
B9-T	43,480,020	30,518,379	25,788,398	17,527

Supplementary Table 6. Genes in 99 TCCs that showed significantly higher mutation rates than the background.

Gene	Non-silent somatic changes		Synonymous mutations	Total mutations	N:S ratio	Number (%) of subjects harboring non-silent mutations	*P*-Value
	Missense	Nonsense, splice site or indel					
UTX	5	27	2	34	32:2	30	0.00E+00
TP53	15	10	0	25	-	24	0.00E+00
ARID1A	4	16	0	20	-	15	0.00E+00
CREBBP	4	13	1	18	17:1	15	0.00E+00
EP300	7	6	0	13	-	13	7.51E-14
HRAS	13	1	0	14	-	13	0.00E+00
RB1	3	10	0	13	-	13	0.00E+00
PIK3CA	14	0	1	15	14:1	12	0.00E+00
FGFR3	12	1	1	14	13:1	11	0.00E+00
STAG2	2	9	0	11	-	11	3.83E-14
SYNE1	7	1	2	10	8:2	8	1.54E-03
ERCC2	6	1	0	7	-	7	1.06E-09
KRAS	8	0	1	9	8:1	7	1.89E-15
MLL	5	2	1	8	7:1	7	5.28E-05
NF1	5	3	0	8	-	7	5.00E-07
SYNE2	6	1	3	10	7:3	7	1.50E-03
ANK3	5	1	0	6	-	6	8.34E-04
CSMD3	6	0	1	7	6:1	6	3.26E-04
ELF3	2	4	0	6	-	6	6.36E-10
ESPL1	5	1	1	7	6:1	6	1.54E-05
LRP2	5	1	0	6	-	6	1.02E-03
ANK2	5	0	0	5	-	5	2.91E-03
ATM	4	1	0	5	-	5	8.28E-04
CHD6	4	1	2	7	5:2	5	5.52E-04
ERBB2	5	0	2	7	5:2	5	1.55E-05
ERBB3	6	0	1	7	6:1	5	1.12E-06
FAT4	5	0	0	5	-	5	6.78E-03
KALRN	5	0	1	6	5:1	5	9.17E-04
LAMA4	5	0	1	6	5:1	5	9.84E-05
MLL3	2	3	1	6	5:1	5	6.80E-03
NCOR1	4	2	0	6	-	5	2.78E-05
NFE2L3	5	2	1	8	7:1	5	2.61E-10
PDZD2	4	1	1	6	5:1	5	6.88E-04
PIK3R4	5	0	0	5	-	5	2.31E-05
TRAK1	3	2	1	6	5:1	5	6.47E-06
TRRAP	5	1	0	6	-	5	3.69E-04
TSC1	1	4	0	5	-	5	9.82E-06

N:S, non-silent : silent mutation; –, no synonymous mutation was identified in this gene.

Supplementary Table 7. *STAG2* mutations detected in discovery (99 tumors) and prevalence (50 tumors) cohorts.

Gene Symbol	Tumor ID	Nucleotide (genomic)[#]	Nucleotide (cDNA)[$]	Codon change	Amino acid chage	Amino acid (protein)	Mutation Type
STAG2	B105	g.chrX:123048109C>T	c.3085C>T	CAG=>TAG	Gln=>Stop	p.Q1029*	nonsense
STAG2	B109	g.chrX:123037893T>C	c.2564T>C	ATT=>ACT	Ile=>Thr	p.I855T	missense
STAG2	B114	g.chrX:123027705G>A	-	-	-	-	spliceSite
STAG2	B18	g.chrX:123045061C>T	c.3034C>T	CGA=>TGA	Arg=>Stop	p.R1012*	nonsense
STAG2	B35	g.chrX:123012651G>A	-	-	-	-	spliceSite
STAG2	B57	g.chrX:122999075G>A	c.306G>A	TGG=>TGA	Trp=>Stop	p.W102*	nonsense
STAG2	B80-3	g.chrX:123024692C>T	c.1777C>T	CAG=>TAG	Gln=>Stop	p.Q593*	nonsense
STAG2	B89-4	g.chrX:123011737G>T	c.914G>T	CGA=>CTA	Arg=>Leu	p.R305L	missense
STAG2	B110	g.chrX:123030112_123030112delA	c.2283_2283delA	-	-	L761fs	Frame-shift_indel
STAG2	B87	g.chrX:123006776insA	c.544insA	-	-	L182fs	Frame-shift_indel
STAG2	B89-16	g.chrX:123024495_123024496delTG	c.1701_1702delTG	-	-	F567fs	Frame-shift_indel
STAG2	267	g.chrX:123006731C>T	c.499C>T	CAG=>TAG	Gln=>Stop	p.Q167*	nonsense
STAG2	267	g.chrX:123006861C>G	c.629C>G	TCA=>TGA	Ser=>Stop	p.S210*	nonsense
STAG2	237	g.chrX:123030188G>T	-	-	-	-	spliceSite
STAG2	71	g.chrX:123052177C>T	c.3349C>T	CAG=>TAG	Gln=>Stop	p.Q1117*	nonsense
STAG2	137	g.chrX:123037883insTCAT	c.2554insTCAT	-	-	A852fs	Frame-shift_indel

#Genomic positions are coordinates in the hg18 UCSC release of the human genome. g., genomic sequence; c., cDNA sequence; p., protein sequence. $ Mutated positions indicate the sites in the protein-coding region of the cDNA sequence. * Stop codon.

Supplementary Table 8. Methylation status of *STAG2* promoter in 30 tumors and matched normal bladder tissue samples.

Sample ID	Number of CpGs successfully sequenced	Number of unmethylated CpGs	Number of methylated CpGs	Methylation rate of CpGs (%)	Methylation rate >10% (T or N)	Log2Ratio (T/N) >1	P-value
B23T	43	43	0	0	No	-	-
B23N	430	429	1	0.23			
B34T	344	340	4	1.16	No	-	-
B34N	430	429	1	0.23			
B45T	430	420	10	2.33	No	-	-
B45N	430	426	4	0.93			
B52T	516	494	22	4.26	No	-	-
B52N	387	387	0	0			
B54T	258	252	6	2.33	No	-	-
B54N	301	301	0	0			
B63T	301	295	6	1.99	No	-	-
B63N	430	427	3	0.7			
B73T	430	421	9	2.09	No	-	-
B73N	430	424	6	1.39			
B77T	430	372	58	13.49	Yes	1.291	2.75421E-13
B77N	430	427	3	0.69			
B83T	430	317	113	26.27	Yes	No	-
B83N	387	161	226	58.38			
B9T	430	427	3	0.7	No	-	-
B9N	430	365	65	15.12			
B16T	430	414	16	3.72	No	-	-
B16N	430	424	6	1.4			
B80T	430	419	11	2.56	No	-	-
B80N	430	417	13	3.03			
B64T	430	420	10	2.34	No	-	-
B64N	430	428	2	0.46			
B68T	430	419	11	2.57	No	-	-
B68N	344	343	1	0.29			
B71T	430	424	6	1.38	No	-	-
B71N	387	386	1	0.25			
B7T	387	297	90	23.25	Yes	5.074	3.80013E-24
B7N	430	427	3	0.69			
B11T	430	280	150	34.77	Yes	4.424	1.57977E-36
B11N	430	423	7	1.62			
B15T	430	406	24	5.59	No	-	-
B15N	430	424	6	1.38			
B21T	430	361	69	16.04	Yes	3.529	2.65328E-14
B21N	430	424	6	1.39			
B25T	430	426	4	0.92	No	-	-
B25N	344	299	45	13.07			
B31T	430	424	6	1.4	No	-	-
B31N	387	385	2	0.51			
B85T	387	227	160	41.28	Yes	1.343	1.80772E-15
B85N	430	360	70	16.27			

B93T	430	164	266	61.86	Yes	No	-
B93N	387	225	162	41.86			
B99T	387	386	1	0.26	No	-	-
B99N	430	408	22	5.21			
B103T	430	387	43	9.99	No	-	-
B103N	430	427	3	0.69			
B123T	301	213	88	29.23	Yes	2.237	4.71074E-16
B123N	387	363	24	6.2			
B27T	430	420	10	2.35	No	-	-
B27N	387	353	34	8.79			
B29T	387	99	288	74.4	Yes	2.930	6.97232E-79
B29N	430	388	42	9.76			
B37T	301	117	184	61.13	Yes	No	-
B37N	430	267	163	37.99			
B49T	430	425	5	1.17	No	-	-
B49N	430	414	16	3.81			

Supplementary Table 9. List of significant focal amplifications and deletions in the TCCs.

Chromosome	Start of region	End of region	Amp/Del	Gscore _Max	Gscore _Min	log2 of copy number ratio (Tumor/Normal)	P value	FDR	Gene count	Region _Class	Genes in region	Cancer genes in region
chr1	200,001	600,000	Amplification	0.2727	0.2104	2.0481	0	0	3	exonic	OR4F16,OR4F29,OR4F3	
chr1	1,200,001	1,300,000	Amplification	0.1369	0.0761	1.5999	1.28E-05	0.00379928	9	exonic	ACAP3,AURKAIP1,CPSF3L,DVL1,GLTPD1,MXRA8,PUSL1,SCNN1D,TAS1R3	
chr1	2,200,001	2,500,000	Amplification	0.1421	0.0788	1.5991	7.10E-06	0.00212559	8	exonic	HES5,MORN1,PANK4,PEX10,PLCH2,RER1,SKI,TNFRSF14	TNFRSF14,
chr1	3,400,001	3,500,000	Amplification	0.1156	0.0821	1.5145	0.00014973	0.0267968	1	exonic	MEGF6	
chr1	121,100,001	141,500,000	Deletion	0.1434	0.1194	0.6116	1.75E-06	7.32E-05	0	intergenic	EMBP1(dist=84792),LOC100130000(dist=978653)	
chr1	121,200,001	141,500,000	Amplification	0.1819	0.1819	3.2708	5.00E-08	4.37E-06	0	intergenic	EMBP1(dist=184792),LOC100130000(dist=978653)	
chr1	144,100,001	144,900,000	Amplification	0.1283	0.0828	1.4669	3.53E-05	0.0078532	19	exonic	ANKRD34A,ANKRD35,CD160,GPR89A,GPR89C,HFE2,ITGA10,LIX1L,NBPF11,NBPF24,NUDT17,PDZK1,PEX11B,PIAS3,POLR3C,POLR3GL,RBM8A,RNF115,TXNIP	
chr1	153,200,001	153,500,000	Amplification	0.1480	0.0758	1.4699	3.48E-06	0.000675328	23	exonic	ADAM15,CKS1B,CLK2,DCST1,DCST2,DPM3,EFNA1,EFNA3,EFNA4,FAM189B,FLAD1,GBA,KRTCAP2,LENEP,MTX1,MUC1,PYGO2,SCAMP3,SHC1,SLC50A1,THBS3,TRIM46,ZBTB7B	MUC1,
chr1	159,100,001	159,600,000	Amplification	0.1764	0.0884	1.4814	9.00E-08	3.05E-05	24	exonic	ADAMTS4,APOA2,ARHGAP30,B4GALT3,DEDD,F11R,FCER1G,ITLN1,ITLN2,KLHDC9,MPZ,NDUFS2,NIT1,NR1I3,PCP4L1,PFDN2,PPOX,PVRL4,SDHC,TOMM40L,TSTD1,UFC1,USF1,USP21	SDHC,
chr2	9,800,001	9,900,000	Amplification	0.1033	0.0762	1.8055	0.00056964	0.00767945	0	intergenic	YWHAQ(dist=111444),TAF1B(dist=1022)	
chr2	127,500,001	127,600,000	Amplification	0.0951	0.0951	1.6108	0.00134903	0.0190943	1	exonic	BIN1	
chr2	213,100,001	213,300,000	Deletion	0.1035	0.0800	0.6139	0.00047728	0.0168163	1	exonic	ERBB4	
chr2	215,900,001	216,300,000	Deletion	0.1003	0.0797	0.6504	0.00072431	0.0323261	2	exonic	ATIC,FN1	ATIC,
chr2	223,900,001	224,700,000	Deletion	0.1276	0.0799	0.6349	1.76E-05	0.0011334	5	exonic	AP1S3,MRPL44,SCG2,SERPINE2,WDFY1	
chr2	233,100,001	234,000,000	Deletion	0.1334	0.0808	0.6433	7.45E-06	0.00018525	14	exonic	ATG16L1,C2orf82,CHRND,CHRNG,DGKD,EFHD1,EIF4E2,GIGYF2,INPP5D,KCNJ13,NEU2,NGEF,SAG,TIGD1	
chr2	239,600,001	239,800,000	Deletion	0.1064	0.0833	0.6551	0.00032108	0.0101678	1	exonic	HDAC4	
chr2	242,300,001	242,400,000	Deletion	0.1020	0.0793	0.6574	0.00057992	0.0232881	3	exonic	D2HGDH,GAL3ST2,ING5	
chr3	12,800,001	13,700,000	Amplification	0.1422	0.0768	1.6868	7.08E-06	0.000263986	6	exonic	CAND2,FBLN2,HDAC11,IQSEC1,NUP210,RPL32	
chr3	16,400,001	16,500,000	Amplification	0.0870	0.0755	1.5849	0.00307768	0.0386816	1	exonic	RFTN1	
chr3	49,800,001	50,600,000	Deletion	0.1116	0.0968	0.6438	0.00016076	0.00207253	29	exonic	C3orf18,C3orf45,C3orf54,CACNA2D2,CAMKV,CDHR4,CYB561D2,GNAI2,GNAT1,HEMK1,HYAL1,HYAL2,HYAL3,IFRD2,MON1A,MST1R,NAT8,NPRL2,RASSF1,RBM5,RBM6,SEMA3B,SEMA3F,SLC38A3,TMEM115,TRAIP,TUSC2,UBA7,ZMYND10	
chr3	52,800,001	52,900,000	Deletion	0.1045	0.0885	0.6276	0.0004136	0.00801666	6	exonic	ITIH1,ITIH3,ITIH4,MUSTN1,TMEM110,TMEM110-MUSTN1	
chr3	57,900,001	58,000,000	Deletion	0.0913	0.0913	0.6329	0.00228393	0.0445719	1	exonic	FLNB	
chr4	1,700,001	1,800,000	Amplification	0.1412	0.0780	1.5853	7.81E-06	0.000285204	3	exonic	FGFR3,LETM1,TACC3	FGFR3,
chr4	2,500,001	2,600,000	Deletion	0.0926	0.0926	0.6500	0.00193823	0.0394009	1	splicing	FAM193A	
chr4	181,900,001	182,400,000	Deletion	0.1082	0.0795	0.6154	0.0002539	0.00299402	1	ncRNA	NCRNA00290	
chr4	190,300,001	190,600,000	Deletion	0.1019	0.0794	0.6329	0.00058222	0.0105348	0	intergenic	LOC401164(dist=539945),HSP90AA4P(dist=31293)	
chr5	1,100,001	1,200,000	Amplification	0.1797	0.0931	1.7196	7.00E-08	4.88E-06	1	exonic	SLC12A7	
chr5	6,800,001	8,200,000	Amplification	0.1133	0.0778	1.8127	0.00019175	0.0169024	5	exonic	ADCY2,C5orf49,FASTKD3,MTRR,PAPD7	
chr5	10,600,001	11,200,000	Amplification	0.1174	0.0851	1.7526	0.00012201	0.0105227	3	exonic	ANKRD33B,CTNND2,DAP	
chr5	14,100,001	14,500,000	Amplification	0.1208	0.0780	1.8624	8.40E-05	0.00598915	1	exonic	TRIO	
chr5	21,200,001	21,400,000	Amplification	0.1254	0.0799	1.7086	4.93E-05	0.00233611	0	intergenic	CDH18(dist=1175891),GUSBP1(dist=95346)	
chr5	36,800,001	37,300,000	Amplification	0.1548	0.0778	1.6858	1.45E-06	8.03E-05	2	exonic	C5orf42,NIPBL	
chr5	53,700,001	54,000,000	Deletion	0.1102	0.0810	0.6093	0.00019487	0.00457547	2	exonic	HSPB3,SNX18	

chr5	68,900,001	70,700,000	Deletion	0.1665	0.0837	0.5919	6.00E-08	7.04E-06	8	exonic	GTF2H2,GTF2H2C,GTF2H2D,NAIP,SERF1A,SERF1B,SMN1,SMN2	
chr5	79,400,001	79,900,000	Deletion	0.1044	0.0858	0.6140	0.00042397	0.0124565	6	exonic	ANKRD34B,FAM151B,SERINC5,SPZ1,THBS4,ZFYVE16	
chr5	82,600,001	82,700,000	Deletion	0.0997	0.0793	0.6229	0.00077572	0.0244819	1	exonic	XRCC4	
chr5	97,300,001	97,800,000	Deletion	0.0961	0.0817	0.6144	0.00123558	0.0417587	0	intergenic	RIOK2(dist=755240),RGMB(dist=332899)	
chr6	20,500,001	21,300,000	Amplification	0.2078	0.1061	2.1267	0	0	2	exonic	CDKAL1,E2F3	
chr6	58,900,001	61,900,000	Amplification	0.2288	0.2288	2.4036	0	0	0	intergenic	GUSBP4(dist=504318),MTRNR2L9(dist=441967)	
chr6	58,900,001	61,900,000	Deletion	0.3003	0.3003	0.4972	0	0	0	intergenic	GUSBP4(dist=504318),MTRNR2L9(dist=441967)	
chr7	1,400,001	1,500,000	Deletion	0.0872	0.0872	0.5967	0.00379159	0.0467039	2	exonic	INTS1,MICALL2	
chr7	1,400,001	1,500,000	Amplification	0.1443	0.0836	1.5574	5.66E-06	0.000219346	2	exonic	INTS1,MICALL2	
chr7	2,500,001	2,700,000	Amplification	0.1165	0.1088	1.6893	0.00013506	0.00305029	4	exonic	BRAT1,IQCE,LFNG,TTYH3	
chr7	61,100,001	61,200,000	Deletion	0.1216	0.1216	0.5897	4.05E-05	0.000697298	0	intergenic	NONE(dist=NONE),LOC643955(dist=1189105)	
chr7	101,900,001	102,100,000	Amplification	0.0932	0.0923	1.5645	0.00164798	0.0489199	8	exonic	LRWD1,POLR2J,POLR2J2,POLR2J3,RASA4,SPDYE2,SPDYE2L,UPK3BL	
chr7	149,100,001	149,200,000	Amplification	0.0987	0.0987	1.5350	0.00093549	0.0211011	2	exonic	SSPO,ZNF862	
chr8	6,600,001	8,100,000	Deletion	0.2064	0.1068	0.6017	0	0	35	exonic	AGPAT5,DEFA1,DEFA1B,DEFA3,DEFA4,DEFA5,DEFA6,DEFB1,DEFB103A,DEFB103B,DEFB104A,DEFB104B,DEFB105A,DEFB105B,DEFB106A,DEFB106B,DEFB107A,DEFB107B,DEFB4A,DEFB4B,FAM90A10,FAM90A13,FAM90A14,FAM90A18,FAM90A19,FAM90A20,FAM90A5,FAM90A7,FAM90A8,FAM90A9,LOC100132396,SPAG11A,SPAG11B,XKR5,ZNF705G	
chr8	27,800,001	28,400,000	Deletion	0.1411	0.0828	0.6185	2.45E-06	0.00144424	6	exonic	C8orf80,ELP3,FBXO16,PNOC,SCARA5,ZNF395	
chr8	30,100,001	31,000,000	Deletion	0.1287	0.0806	0.6310	1.51E-05	0.00228325	11	exonic	DCTN6,GSR,GTF2E2,LEPROTL1,LOC100507341,MBOAT4,PPP2CB,PURG,RBPMS,TEX15,UBXN8	
chr8	34,400,001	34,900,000	Deletion	0.1120	0.0811	0.6056	0.00015212	0.00877978	0	intergenic	DUSP26(dist=823020),UNC5D(dist=312517)	
chr8	44,000,001	47,000,000	Amplification	0.2637	0.1364	1.6547	0	0	0	intergenic	POTEA(dist=662516),NCRNA00293(dist=871673)	
chr8	44,000,001	47,000,000	Deletion	0.1893	0.1893	0.5225	0	0	0	intergenic	POTEA(dist=662516),NCRNA00293(dist=871673)	
chr8	81,700,001	83,300,000	Amplification	0.1542	0.0829	1.5157	1.59E-06	0.0256112	12	exonic	CHMP4C,FABP12,FABP4,FABP5,FABP9,IMPA1,PAG1,PMP2,SLC10A5,SNX16,ZFAND1,ZNF704	
chr8	98,900,001	103,600,000	Amplification	0.2126	0.1065	1.5269	0	0	26	exonic	ANKRD46,C8orf47,COX6C,FBXO43,GRHL2,HRSP12,KCNS2,LAPTM4B,MATN2,NCALD,NIPAL2,OSR2,PABPC1,POLR2K,POP1,RGS22,RNF19A,RPL30,RRM2B,SNX31,SPAG1,STK3,UBR5,VPS13B,YWHAZ,ZNF706	COX6C,
chr8	105,300,001	108,500,000	Amplification	0.2005	0.1015	1.5459	0	0	8	exonic	ABRA,ANGPT1,DPYS,LRP12,OXR1,RIMS2,TM7SF4,ZFPM2	
chr8	118,500,001	120,900,000	Amplification	0.1580	0.0852	1.4714	9.30E-07	0.00681566	9	exonic	COLEC10,ENPP2,EXT1,MAL2,MED30,NOV,SAMD12,TAF2,TNFRSF11B	EXT1,
chr8	126,400,001	127,000,000	Amplification	0.1724	0.0911	1.5249	1.20E-07	0.00138312	2	exonic	NSMCE2,TRIB1	
chr8	128,100,001	130,600,000	Amplification	0.1841	0.1016	1.5265	5.00E-08	0.00031048	2	exonic	MYC,POU5F1B	MYC,
chr8	133,600,001	134,600,000	Amplification	0.1805	0.0972	1.4987	7.00E-08	0.00069549	8	exonic	LRRC6,NDRG1,PHF20L1,SLA,ST3GAL1,TG,TMEM71,WISP1	NDRG1,
chr8	144,400,001	144,800,000	Amplification	0.2259	0.1132	1.5401	0	0	14	exonic	C8orf73,EEF1D,GLI4,GSDMD,MAFA,NAPRT1,PYCRL,RHPN1,TIGD5,TOP1MT,TSTA3,ZC3H3,ZFP41,ZNF696	
chr9	9,200,001	9,900,000	Deletion	0.1697	0.0973	0.6111	5.00E-08	0.000625467	1	splicing	PTPRD	
chr9	21,700,001	22,700,000	Deletion	0.6461	0.3343	0.3271	0	0	4	exonic	CDKN2A,CDKN2B,DMRTA1,MTAP	CDKN2A, CDKN2B
chr9	23,300,001	25,600,000	Deletion	0.2259	0.1130	0.5563	0	0	1	exonic	ELAVL2	
chr9	36,500,001	36,600,000	Deletion	0.1384	0.0834	0.6391	3.48E-06	0.0218682	1	exonic	MELK	
chr9	40,900,001	41,100,000	Deletion	0.1905	0.0961	0.5570	0	0	0	intergenic	ZNF658(dist=117889),FAM75A5(dist=211107)	
chr9	44,900,001	45,200,000	Deletion	0.1369	0.0810	0.5865	4.41E-06	0.0402509	1	ncRNA	FAM27C	
chr9	45,700,001	45,800,000	Deletion	0.1441	0.0901	0.5704	1.61E-06	0.0131911	0	intergenic	FAM27A(dist=81722),KGFLP1(dist=823421)	
chr9	67,300,001	67,400,000	Deletion	0.1546	0.0801	0.6263	3.50E-07	0.00803985	1	ncRNA	FAM27B	
chr9	68,200,001	68,300,000	Deletion	0.1434	0.0800	0.6414	1.74E-06	0.0146344	0	intergenic	LOC100132352(dist=61809),PGM5P2(dist=70064)	
chr9	69,300,001	69,400,000	Deletion	0.1351	0.0852	0.6435	5.71E-06	0.0432052	0	intergenic	LOC100133920(dist=345232),FOXD4L5(dist=65527)	
chr9	118,200,001	118,500,000	Deletion	0.1646	0.0827	0.6157	8.00E-08	0.00093188	2	exonic	ASTN2,TRIM32	
chr9	123,100,001	123,800,000	Deletion	0.1407	0.0803	0.6138	2.58E-06	0.0164342	4	exonic	DAB2IP,GSN,STOM,TTLL11	
chr9	126,900,001	127,200,000	Deletion	0.1610	0.0907	0.6080	1.70E-07	0.00391017	5	exonic	GAPVD1,HSPA5,PPP6C,RABEPK,SCAI	
chr9	131,800,001	131,900,000	Deletion	0.1351	0.0829	0.6109	5.75E-06	0.0445611	2	exonic	FNBP1,GPR107	FNBP1,
chr9	132,700,001	133,000,000	Deletion	0.1372	0.0877	0.6135	4.22E-06	0.0262327	6	exonic	ABL1,AIF1L,FIBCD1,LAMC3,NUP214,QRFP	ABL1,NUP214,
chr9	136,400,001	136,500,000	Amplification	0.0969	0.0969	1.6255	0.0011219	0.0162981	1	exonic	RXRA	
chr9	138,300,001	138,600,000	Deletion	0.1752	0.0945	0.6063	2.00E-08	0.00023677	10	exonic	C9orf163,CARD9,DNLZ,GPSM1,INPP5E,NOTCH1,PMPCA,SDCCAG3,SEC16A,SNAPC4	NOTCH1,

chr9	138,300,001	138,600,000	Amplification	0.1007	0.0886	1.6376	0.00075507	0.00973439	10	exonic	C9orf163,CARD9,DNLZ,GPSM1,INPP5E,NOTCH1,PMPCA,SDCCAG3,SEC16A,SNAPC4	NOTCH1,
chr10	5,500,001	5,700,000	Amplification	0.1138	0.0772	1.5360	0.00018228	0.00320709	2	exonic	CALML3,CALML5	
chr10	11,900,001	12,100,000	Amplification	0.0903	0.0753	1.6276	0.00222382	0.0290549	2	exonic	C10orf47,UPF2	
chr10	38,800,001	38,900,000	Deletion	0.1099	0.1099	0.6563	0.00020278	0.0284399	0	intergenic	LOC399744(dist=18914),NONE(dist=NONE)	
chr10	39,200,001	41,700,000	Deletion	0.1390	0.1390	0.6047	3.26E-06	0.000104345	0	intergenic	LOC399744(dist=418914),LOC441666(dist=447320)	
chr10	104,900,001	105,100,000	Deletion	0.1068	0.0801	0.6383	0.00030316	0.0402019	4	exonic	INA,LOC729020,NT5C2,PCGF6	
chr10	109,900,001	110,100,000	Deletion	0.1052	0.0809	0.6261	0.00037959	0.0485748	0	intergenic	SORCS1(dist=985545),XPNPEP1(dist=1514514)	
chr10	118,400,001	118,600,000	Deletion	0.1058	0.0819	0.6331	0.00034922	0.044568	3	exonic	C10orf82,ENO4,HSPA12A	
chr10	121,000,001	121,200,000	Deletion	0.1125	0.0803	0.6490	0.0001426	0.00682089	1	exonic	GRK5	
chr10	126,300,001	126,400,000	Deletion	0.1100	0.0801	0.6453	0.00019988	0.0125515	1	exonic	FAM53B	
chr10	129,700,001	129,800,000	Deletion	0.1119	0.0805	0.6517	0.0001538	0.00882	2	exonic	MKI67,PTPRE	
chr10	132,400,001	132,500,000	Deletion	0.1348	0.0810	0.6345	5.93E-06	0.00067074	0	intergenic	GLRX3(dist=531365),MIR378C(dist=150841)	
chr10	134,700,001	135,000,000	Deletion	0.1332	0.0883	0.6271	7.75E-06	0.0015497	8	exonic	ADAM8,CALY,GPR123,KNDC1,TUBGCP2,UTF1,VENTX,ZNF511	
chr11	1,800,001	2,000,000	Deletion	0.1734	0.0884	0.6453	2.00E-08	3.08E-06	5	exonic	LSP1,MRPL23,SYT8,TNNI2,TNNT3	
chr11	28,700,001	30,200,000	Deletion	0.1543	0.0804	0.6390	3.80E-07	0.000113409	1	exonic	KCNA4	
chr11	42,700,001	43,000,000	Deletion	0.1270	0.0798	0.6415	1.94E-05	0.00229161	0	intergenic	LOC100507205(dist=468185),HNRNPKP3(dist=239630)	
chr11	48,700,001	48,800,000	Deletion	0.1073	0.0837	0.6228	0.0002873	0.0137866	0	intergenic	OR4A47(dist=232151),LOC120824(dist=153626)	
chr11	50,600,001	50,900,000	Deletion	0.1019	0.0796	0.6394	0.00058175	0.0272734	0	intergenic	LOC646813(dist=263623),OR4A5(dist=367954)	
chr11	51,500,001	54,500,000	Deletion	0.1213	0.1213	0.6101	4.20E-05	0.00325385	0	intergenic	OR4C46(dist=127214),TRIM48(dist=286234)	
chr11	65,100,001	65,200,000	Amplification	0.1076	0.1076	1.6499	0.00036224	0.0310422	6	exonic	EHBP1L1,KCNK7,MAP3K11,PCNXL3,RELA,SIPA1	
chr11	66,900,001	67,000,000	Amplification	0.1137	0.1137	1.6976	0.00018366	0.0136201	10	exonic	CABP4,CARNS1,CORO1B,GPR152,PPP1CA,PTPRCAP,RAD9A,RPS6KB2,TBC1D10C,TMEM134	
chr11	67,500,001	67,600,000	Amplification	0.1294	0.0924	1.6589	3.12E-05	0.00302629	5	exonic	ALDH3B1,CHKA,NDUFS8,TCIRG1,UNC93B1	
chr11	68,300,001	68,600,000	Amplification	0.1472	0.1124	2.1124	3.95E-06	0.000188008	6	exonic	CPT1A,IGHMBP2,MRGPRD,MRGPRF,MRPL21,TPCN2	
chr11	68800001	69800000	Amplification	0.2962	0.1577	2.4104	0	0	9	exonic	ANO1,CCND1,FADD,FGF19,FGF3,FGF4,MYEOV,ORAOV1,PPFIA1	CCND1
chr11	70,100,001	70,200,000	Amplification	0.1110	0.0755	1.9096	0.00024912	0.0193804	1	exonic	SHANK2	
chr11	76,500,001	76,600,000	Amplification	0.1335	0.0797	1.5652	1.93E-05	0.00119029	2	exonic	CAPN5,MYO7A	
chr12	67500001	68200000	Amplification	0.1195	0.0766	4.6954	9.72E-05	0.00202412	5	exonic	CPM,CPSF6,LYZ,MDM2,YEATS4	MDM2
chr12	123,400,001	123,500,000	Amplification	0.0921	0.0921	1.5863	0.00185306	0.035737	1	exonic	NCOR2	
chr12	131,600,001	131,700,000	Amplification	0.1111	0.0860	1.5232	0.00024714	0.00484512	2	exonic	FBRSL1,LOC100507055	
chr13	45,300,001	45,400,000	Deletion	0.0905	0.0827	0.5803	0.00249731	0.0335471	1	exonic	SIAH3	
chr13	47300001	50600000	Deletion	0.1271	0.0800	0.5089	1.93E-05	0.000394704	23	exonic	ARL11,CAB39L,CDADC1,CYSLTR2,DLEU7,EBPL,FNDC3A,ITM2B,KCNRG,KPNA3,LPAR6,MED4,MLNR,NUDT15,PHF11,RB1,RCBTB1,RCBTB2,RNASEH2B,SETDB2,SPRYD7,SUCLA2,TRIM13	RB1
chr13	112,700,001	113,100,000	Amplification	0.1021	0.0997	1.6579	0.0006538	0.00863379	8	exonic	CUL4A,F10,F7,GRTP1,LAMP1,MCF2L,PCID2,PROZ	
chr13	113,700,001	113,900,000	Amplification	0.0936	0.0933	1.6982	0.00157974	0.0217515	1	exonic	RASA3	
chr14	104,200,001	104,300,000	Amplification	0.1208	0.1208	1.7545	8.39E-05	0.00183107	3	exonic	ADSSL1,INF2,SIVA1	
chr14	104,700,001	104,800,000	Amplification	0.1092	0.1092	1.8090	0.00030514	0.00570223	4	exonic	BRF1,BTBD6,JAG2,NUDT14	
chr15	39,900,001	40,000,000	Deletion	0.0959	0.0959	0.6399	0.00126835	0.0107853	6	exonic	EHD4,JMJD7,JMJD7-PLA2G4B,MAPKBP1,PLA2G4B,SPTBN5	
chr15	39,900,001	40,000,000	Amplification	0.0824	0.0824	1.6289	0.00490254	0.0485958	6	exonic	EHD4,JMJD7,JMJD7-PLA2G4B,MAPKBP1,PLA2G4B,SPTBN5	
chr16	500,001	700,000	Deletion	0.1321	0.1198	0.5678	8.99E-06	0.000217389	16	exonic	C16orf11,C16orf13,FAM195A,FBXL16,JMJD8,NHLRC4,PIGQ,RAB11FIP3,RAB40C,RHBDL1,RHOT2,SOLH,STUB1,WDR24,WDR90,WFIKKN1	
chr16	1,000,001	1,200,000	Amplification	0.1393	0.0753	1.6278	9.72E-06	0.000343625	3	exonic	C1QTNF8,CACNA1H,SSTR5	
chr16	1,100,001	1,300,000	Deletion	0.1139	0.0845	0.5970	0.00011726	0.00318546	5	exonic	CACNA1H,TPSAB1,TPSB2,TPSD1,TPSG1	
chr16	3,500,001	3,900,000	Deletion	0.1068	0.0890	0.5499	0.00030581	0.0143671	6	exonic	CLUAP1,CREBBP,DNASE1,NLRC3,SLX4,TRAP1	CREBBP,
chr16	4,700,001	4,800,000	Deletion	0.1003	0.0815	0.6376	0.00071731	0.0321988	6	exonic	ANKS3,C16orf71,GLYR1,ROGDI,SEPT12,ZNF500	
chr16	16,300,001	16,400,000	Deletion	0.1098	0.1098	0.5218	0.00020418	0.00733001	7	ncRNA	MIR3179-1,MIR3179-2,MIR3179-3,MIR3180-1,MIR3180-2,MIR3180-3,PKD1P1	
chr16	28,200,001	28,500,000	Amplification	0.1294	0.0788	1.7154	3.11E-05	0.00169391	7	exonic	APOBR,CCDC101,CLN3,EIF3CL,IL27,NUPR1,SBK1	
chr16	33,100,001	33,200,000	Deletion	0.1085	0.1085	0.4560	0.0002447	0.0100238	3	exonic	LOC653550,TP53TG3,TP53TG3B	
chr16	87,000,001	87,100,000	Amplification	0.1347	0.0955	1.5644	1.67E-05	0.000607023	2	exonic	ZFPM1,ZNF469	
chr17	12,900,001	13,400,000	Deletion	0.1424	0.0793	0.6356	2.04E-06	0.00144424	1	exonic	HS3ST3A1	
chr17	18,900,001	19,100,000	Deletion	0.1866	0.0938	0.6206	0	0	1	exonic	GRAPL	
chr17	21,200,001	21,300,000	Deletion	0.1154	0.0813	0.6217	9.54E-05	0.00546864	2	exonic	KCNJ12,KCNJ18	
chr17	22,200,001	22,300,000	Deletion	0.1907	0.1907	0.4367	0	0	0	intergenic	MTRNR2L1(dist=251883),MIR4522(dist=345063)	

chr17	22,200,001	22,300,000	Amplification	0.1858	0.1858	1.8317	2.00E-08	3.65E-06	0	intergenic	MTRNR2L1(dist=251883),MIR4522(dist=345063)	
chr17	35,000,001	35,200,000	Amplification	0.1798	0.1538	2.1730	7.00E-08	5.84E-06	10	exonic	C17orf37,ERBB2,GRB7,IKZF3,NEUROD2,PGAP3,PNMT,PPP1R1B,STARD3,TCAP	ERBB2,
chr17	55,200,001	55,600,000	Amplification	0.1350	0.0867	1.8032	1.60E-05	0.00402003	6	exonic	CA4,HEATR6,RNFT1,RPS6KB1,TUBD1,VMP1	
chr17	56,600,001	57,100,000	Amplification	0.1630	0.0889	2.0052	4.80E-07	0.0001712	5	exonic	BCAS3,C17orf82,NACA2,TBX2,TBX4	
chr17	71,000,001	71,100,000	Amplification	0.1228	0.0763	1.4252	6.70E-05	0.0160515	4	exonic	CASKIN2,KIAA0195,LLGL2,TSEN54	
chr17	74,600,001	74,700,000	Amplification	0.1324	0.0766	1.4176	2.19E-05	0.00644872	1	exonic	RBFOX3	
chr17	77,000,001	77,100,000	Amplification	0.1715	0.0859	1.5020	1.20E-07	3.29E-05	2	exonic	ACTG1,BAHCC1	
chr17	78,600,001	78,774,742	Amplification	0.1398	0.0821	1.5355	9.23E-06	0.00238811	2	exonic	B3GNTL1,METRNL	
chr18	75,300,001	75,400,000	Deletion	0.0943	0.0843	0.6157	0.00155909	0.0128852	1	exonic	NFATC1	
chr18	76,100,001	76,117,153	Deletion	0.0891	0.0891	0.6958	0.00300632	0.0388875	1	exonic	PARD6G	
chr19	24,400,001	32,400,000	Deletion	0.1013	0.1013	0.5769	0.00063097	0.00599025	0	intergenic	LOC100101266(dist=261912),LOC148189(dist=573241)	
chr19	34,900,001	35,000,000	Amplification	0.0986	0.0986	1.7085	0.00093705	0.0323433	1	exonic	CCNE1	CCNE1,
chr19	38,400,001	38,500,000	Amplification	0.0975	0.0975	1.5270	0.00106185	0.0446322	2	exonic	CEBPA,SLC7A10	CEBPA,
chr19	40,900,001	41,000,000	Amplification	0.1025	0.0805	1.5079	0.00062472	0.0154512	9	exonic	ARHGAP33,C19orf55,HSPB6,IGFLR1,LIN37,MLL4,PRODH2,PSENEN,U2AF1L4	
chr19	43,200,001	43,700,000	Amplification	0.1339	0.0757	1.5491	1.85E-05	0.000583043	14	exonic	C19orf33,CATSPERG,DPF1,FAM98C,GGN,KCNK6,PPP1R14A,PSMD8,RASGRP4,RYR1,SIPA1L3,SPINT2,SPRED3,YIF1B	
chr19	47,400,001	47,600,000	Amplification	0.1151	0.0814	1.4882	0.00015804	0.00343477	11	exonic	CIC,CNFN,DEDD2,ERF,GSK3A,LIPE,MEGF8,PAFAH1B3,PRR19,TMEM145,ZNF526	CIC,
chr20	29,300,001	30,300,000	Amplification	0.1416	0.0791	1.4307	7.40E-06	0.000592246	24	exonic	BCL2L1,C20orf160,COX4I2,DEFB115,DEFB116,DEFB118,DEFB119,DEFB121,DEFB123,DEFB124,DUSP15,FOXS1,HCK,HM13,ID1,MYLK2,PDRG1,PLAGL2,POFUT1,REM1,TM9SF4,TPX2,TTLL9,XKR7	
chr20	31,700,001	31,800,000	Amplification	0.1167	0.0763	1.3952	0.0001314	0.0135026	6	exonic	C20orf134,C20orf144,E2F1,NECAB3,PXMP4,ZNF341	
chr20	35,900,001	36,000,000	Amplification	0.1121	0.0756	1.4224	0.00022012	0.0220331	2	exonic	CTNNBL1,VSTM2L	
chr20	42,200,001	42,900,000	Amplification	0.1549	0.0790	1.5951	1.43E-06	7.93E-05	13	exonic	ADA,C20orf111,FITM2,GDAP1L1,HNF4A,JPH2,KCNK15,PKIG,R3HDML,RIMS4,SERINC3,TTPAL,WISP2	
chr20	48,200,001	48,500,000	Amplification	0.1211	0.0790	1.4593	8.13E-05	0.00815913	3	exonic	CEBPB,TMEM189,TMEM189-UBE2V1	
chr20	55,400,001	55,500,000	Amplification	0.1280	0.0763	1.4531	3.70E-05	0.00337376	1	exonic	RBM38	
chr20	61,500,001	61,600,000	Amplification	0.1789	0.0914	1.5778	7.00E-08	4.88E-06	2	exonic	EEF1A2,KCNQ2	
chr21	10,300,001	13,300,000	Deletion	0.1367	0.1367	0.6258	4.52E-06	0.000122702	0	intergenic	BAGE(dist=179193),ANKRD30BP2(dist=32358)	
chr21	10,300,001	13,300,000	Amplification	0.1305	0.0968	1.6485	2.70E-05	0.00075693	0	intergenic	BAGE(dist=179193),ANKRD30BP2(dist=32358)	
chr21	44,500,001	44,600,000	Amplification	0.1263	0.0821	1.5496	4.46E-05	0.00132236	5	exonic	AIRE,C21orf2,DNMT3L,PFKL,TRPM2	
chr21	45,700,001	45,800,000	Amplification	0.1066	0.1066	1.5437	0.00040253	0.0109323	2	exonic	COL18A1,SLC19A1	
chr22	17,000,001	17,100,000	Amplification	0.1173	0.1173	1.6643	0.00012391	0.0045712	1	exonic	USP18	
chr22	18,500,001	18,700,000	Amplification	0.1295	0.0752	1.5081	3.07E-05	0.000988382	3	exonic	DGCR6L,RTN4R,ZDHHC8	
chr22	20,100,001	20,200,000	Deletion	0.0972	0.0972	0.6363	0.00108273	0.025184	2	exonic	HIC2,TMEM191C	
chr22	20,100,001	20,200,000	Amplification	0.1043	0.0790	1.5075	0.00051629	0.0209543	2	exonic	HIC2,TMEM191C	
chr22	41,000,001	41,100,000	Deletion	0.0964	0.0964	0.6384	0.00118751	0.0337941	1	ncRNA	LOC388906	
chr22	44,700,001	44,800,000	Deletion	0.1212	0.1212	0.6104	4.28E-05	0.0016838	1	exonic	WNT7B	
chr22	49,000,001	49,100,000	Amplification	0.1338	0.0784	1.5297	1.87E-05	0.000586747	6	exonic	FAM116B,HDAC10,MAPK11,MAPK12,PLXNB2,TUBGCP6	
chr22	49,000,001	49,100,000	Deletion	0.1326	0.0864	0.6250	8.32E-06	0.000202871	6	exonic	FAM116B,HDAC10,MAPK11,MAPK12,PLXNB2,TUBGCP6	
chrX	58,600,001	61,600,000	Deletion	0.1275	0.1275	0.5279	1.80E-05	0.000372289	0	intergenic	ZXDA(dist=646209),SPIN4(dist=883832)	
chrX	152,400,001	152,700,000	Amplification	0.1598	0.0821	1.5616	7.60E-07	4.09E-05	10	exonic	ABCD1,ATP2B3,BCAP31,BGN,DUSP9,FAM58A,PLXNB3,PNCK,SLC6A8,SRPK3	

Supplementary Table 10. Gene fusion candidates predicted by RNA-Seq in the 42 TCCs.

Case/Tumor ID	Upstream gene	Chromosome of upstream gene	Strand of upstream gene	Genomic breakpoint of upstream gene	Downstream gene	Chromosome of downstream gene	Strand of downstream gene	Genomic breakpoint of downstream gene	Number of paired end reads spanning the breakpoint (Tumor/Normal)	Number of reads split by the breakpoint (Tumor/Normal)
B56	ACTR6	chr12	+	99,122,966	MYL6	chr12	+	54,841,438	216/5	180/6
B77	ASXL1	chr20	+	30,420,587	DUSP8	chr11	-	1,543,740	9/0	9/0
B89-4-CA	BPIFB1	chr20	+	31,325,121	IDO2	chr8	+	39,963,711	6/NA	6/NA
B23	C6orf106	chr6	-	34,772,201	RNF144B	chr6	+	18,507,709	7/0	5/0
B105-1-CA	CDKAL1	chr6	+	21,309,484	MBOAT1	chr6	-	20,260,979	11/NA	12/NA
B65-CA	CPSF6	chr12	+	67,942,609	FUS	chr16	+	31,107,147	9/NA	8/NA
B100-CA	FGFR3	chr4	+	1,778,504	TACC3	chr4	+	1,700,278	112/NA	118/NA
B59	FGFR3	chr4	+	1,778,459	TACC3	chr4	+	1,711,227	446/0	411/0
B15-CA	GPR21	chr9	+	124,837,783	ARMC10	chr7	+	102,527,273	7/NA	7/NA
B105-0-CA	LRFN3	chr19	+	41,119,938	AP1M2	chr19	-	10,548,976	7/NA	8/NA
B9-CA	LSM14A	chr19	+	39,377,386	PDCD2L	chr19	+	39,604,264	37/NA	71/NA
B65-CA	MDM1	chr12	-	67,011,154	FCF1	chr14	+	74,272,380	65/NA	54/NA
B101-CA	NAPA	chr19	-	52,709,912	KCNIP3	chr2	+	95,403,771	13/NA	12/NA
B89-4-CA	NEAT1	chr11	+	64,968,369	ARMC10	chr7	+	102,527,277	7/NA	6/NA
B65-CA	NUP107	chr12	+	67,415,391	MDM1	chr12	-	67,011,268	164/NA	80/NA
B9-CA	PLEKHA7	chr11	-	16,992,112	RPS13	chr11	-	17,055,600	15/NA	17/NA
B15-CA	PTBP1	chr19	+	755,438	PALM	chr19	+	677,138	11/NA	13/NA
B89-4-CA	PTGES	chr9	-	131,540,511	ARMC10	chr7	+	102,527,271	28/NA	8/NA
B9-CA	RAB2A	chr8	+	61,592,366	CLVS1	chr8	+	62,451,718	7/NA	8/NA
B56	RBM19	chr12	-	112,837,158	TMPRSS12	chr12	+	49,538,834	5/0	5/0
B59	RBM47	chr4	-	40,241,196	C6orf145	chr6	-	3,672,895	10/0	12/0
B89-12-CA	RPL31	chr2	+	100,988,965	AFF3	chr2	-	99,710,022	29/NA	20/NA
B89-12-CA	RPSAP58	chr19	+	23,737,776	NCALD	chr8	-	102,997,262	8/NA	7/NA
B80-8-CA	SARS	chr1	+	109,568,193	GPSM2	chr1	+	109,262,758	8/NA	15/NA
B9-CA	SEC24B	chr4	+	110,574,607	CCDC109B	chr4	+	110,823,187	17/NA	21/NA
B89-5-CA	SEMA5A	chr5	-	9,598,696	NDUFS6	chr5	+	1,855,435	13/NA	18/NA
B9-CA	STARD3	chr17	+	35,047,010	SCFD2	chr4	-	53,481,794	7/NA	12/NA
B66-CA	SUV420H1	chr11	-	67,703,513	DPP3	chr11	+	66,019,253	18/NA	6/NA
B65-CA	TRAK1	chr3	+	42,176,969	ZNF692	chr1	-	247,119,143	6/NA	5/NA
B71	UCK2	chr1	+	164,063,793	DNM3-AS1	chr1	-	170,380,200	246/3	352/5
B105-1-CA	USP12	chr13	-	26,643,729	ELF1	chr13	-	40,454,418	13/NA	19/NA
B57	ZNF320	chr19	-	58,073,310	APOL1	chr22	+	34,992,919	7/0	6/0

NA indicates the morphologically normal bladder tissues were not available

Supplementary Table 11. Pathways that are significantly enriched with genetic alterations in TCC.

Pathway name	The number of reference genes in the category	Number of genes in the gene set and also in the category	Expected number in the category	Ratio of enrichment	*P* value from hypergeometric test	FDR
MAPK signaling pathway	269	31	6.05	5.12	1.38E-13	1.92E-12
Cell cycle	128	21	2.88	7.29	1.29E-12	1.63E-11
ErbB signaling pathway	87	17	1.96	8.69	9.61E-12	1.11E-10
ECM-receptor interaction	84	16	1.89	8.47	5.86E-11	6.01E-10
Calcium signaling pathway	178	21	4	5.24	7.53E-10	6.16E-09
Regulation of actin cytoskeleton	216	23	4.86	4.73	9.18E-10	7.09E-09
Insulin signaling pathway	137	18	3.08	5.84	2.14E-09	1.49E-08
Neurotrophin signaling pathway	126	17	2.83	6	3.95E-09	2.61E-08
Long-term potentiation	70	13	1.57	8.26	5.09E-09	3.22E-08
Axon guidance	129	17	2.9	5.86	5.69E-09	3.41E-08
Notch signaling pathway	47	11	1.06	10.4	5.89E-09	3.41E-08
GnRH signaling pathway	101	15	2.27	6.6	8.50E-09	4.73E-08
TGF-beta signaling pathway	87	14	1.96	7.15	9.19E-09	4.91E-08
Endocytosis	187	20	4.21	4.75	1.05E-08	5.41E-08
Purine metabolism	151	16	3.4	4.71	3.46E-07	1.50E-06
p53 signaling pathway	69	11	1.55	7.09	3.93E-07	1.66E-06
Adherens junction	77	11	1.73	6.35	1.22E-06	4.99E-06
Vascular smooth muscle contraction	115	13	2.59	5.02	2.07E-06	7.99E-06
RNA polymerase	29	7	0.65	10.73	2.89E-06	1.08E-05
Ubiquitin mediated proteolysis	138	14	3.1	4.51	3.10E-06	1.10E-05
Long-term depression	70	10	1.57	6.35	3.72E-06	1.29E-05
Phosphatidylinositol signaling system	76	10	1.71	5.85	7.92E-06	2.62E-05
Wnt signaling pathway	151	14	3.4	4.12	8.89E-06	2.87E-05
Oocyte meiosis	114	12	2.56	4.68	1.06E-05	3.35E-05
Pyrimidine metabolism	98	11	2.2	4.99	1.34E-05	4.14E-05
mTOR signaling pathway	52	8	1.17	6.84	2.00E-05	5.91E-05
Chemokine signaling pathway	190	15	4.27	3.51	2.95E-05	8.20E-05
Gap junction	90	10	2.02	4.94	3.58E-05	9.76E-05
VEGF signaling pathway	76	9	1.71	5.26	5.27E-05	0.0001
Glycosaminoglycan degradation	21	5	0.47	10.58	8.60E-05	0.0002
Progesterone-mediated oocyte maturation	86	9	1.93	4.65	0.0001	0.0002
Tight junction	134	11	3.01	3.65	0.0002	0.0005
Leukocyte transendothelial migration	118	10	2.65	3.77	0.0003	0.0007
B cell receptor signaling pathway	75	8	1.69	4.74	0.0003	0.0007
Lysine degradation	44	6	0.99	6.06	0.0004	0.0009
NOD-like receptor signaling pathway	62	7	1.39	5.02	0.0005	0.0011
PPAR signaling pathway	69	7	1.55	4.51	0.0009	0.002
RIG-I-like receptor signaling pathway	71	7	1.6	4.38	0.0011	0.0024
Basal transcription factors	36	5	0.81	6.17	0.0012	0.0026
Lysosome	117	9	2.63	3.42	0.0014	0.0029
Jak-STAT signaling pathway	155	10	3.49	2.87	0.0028	0.0056

Nucleotide excision repair	44	5	0.99	5.05	0.003	0.0059
T cell receptor signaling pathway	108	8	2.43	3.29	0.0031	0.006
Tyrosine metabolism	46	5	1.03	4.83	0.0036	0.0069
Apoptosis	88	7	1.98	3.54	0.0037	0.007
Natural killer cell mediated cytotoxicity	137	9	3.08	2.92	0.004	0.0074

Supplementary Table 12A. *STAG2* exons primers for screening of *STAG2* in additional 50 TCCs.

STAG2 EXON	PRIMER
STAG2-3F	5'GCACTGGGGAATTTAACTTTTG3'
STAG2-3R	5'CAGAGCCTTGATGAGTGCTG3'
STAG2-4F	5'TCTTGTGTGTTTGGTAACGTGC3'
STAG2-4R	5'GCTTACCATACCAATCAGCTCC3'
STAG2-5F	5'GGACACCACAAAGAGGCTGT3'
STAG2-5R	5'TGCAATTAGAAAAATCAGAGCTACA3'
STAG2-6F	5'TTGACTTCCATAGTTTCCACATTC3'
STAG2-6R	5'AAAGTGCTAACAACATCTCTTTAGGTG3'
STAG2-7F	5'AGTAAAGTGAGTCAGGTAGAAATGGC3'
STAG2-7R	5'CATGCCCAGCCTAATGCTTAC3'
STAG2-8F	5'GGATTTATTGGAGAAGAAAGGTGAG3'
STAG2-8R	5'AATTCGCAGGAGGGATGG3'
STAG2-9F	5'CATTTGTAGCAGCTGCATCTTTC3'
STAG2-9R	5'TGTTGGGCAAATAGTTTGAAATG3'
STAG2-10F	5'CCAATCAAATATTTCAGGTATTAAGGG3'
STAG2-10R	5'TGACTCAGTGGCACTAATGGAG3'
STAG2-11F	5'GTGAGCAAAGGCTGGGATATG3'
STAG2-11R	5'GGAGGCTTCCAGAAATGTGTC3'
STAG2-12F	5'TCTGAAGGAATGCTATGGTATGAAA3'
STAG2-12R	5'TGTCAAGGGTCATAGACACAATTC3'
STAG2-13F	5'TTTACCAGTCGGTTCAAGGTTAG3'
STAG2-13R	5'TTCTATGGTTCCTTCTTCCTGTG3'
STAG2-14F	5'GGACGTTACTAAAAGCACCTGTT3'
STAG2-14R	5'CCCAGCCTACATTTCCCTTT3'
STAG2-15F	5'TGTGCCATGTTGGATGATATTG3'
STAG2-15R	5'GGGTGGCTCTCCATTCTATTC3'
STAG2-16F	5'GCAAGCAAACTAAGGCAGTTTC3'
STAG2-16R	5'ATAAAGAATGTTGACAGCAATTACATC3'
STAG2-17F	5'GGCAGATTCTGTTTACAGGCAG3'
STAG2-17R	5'TCAAATTTCTCAAATTGCTAATGC3'
STAG2-18F	5'ACCATCTGAAGGTAGAGTTGGTTAG3'
STAG2-18R	5'AAAGCATTATAATATTCTGTGAGGCA3'
STAG2-19F	5'TGGCCCTTCCTCAGTTATTAGC3'
STAG2-19R	5'CAAAGGGAAGCATCATTACCG3'
STAG2-20F	5'CCATGGTGGTATGGTCATGTAG3'
STAG2-20R	5'CTGCTAGGGACTATCACCAAGAC3'
STAG2-21F	5'CCCAGCCATATTGCCTTAAAT3'
STAG2-21R	5'CCCACAACGACAACAACAAAT3'
STAG2-22F	5'CGTTGTGGGGGCATTTTA3'
STAG2-22R	5'GCAAGTTGCCAAAGGATTACA3'

STAG2-23F	5'AAATGGAGACATGCCTGAGC3'
STAG2-23R	5'AACCACAGATTATGCCACCTTC3'
STAG2-24F	5'TTAAGGCTGCAATTTGGTGAG3'
STAG2-24R	5'CAAGATATTTCTGCTTTGCTCAAT3'
STAG2-25F	5'GCCTTATACAAATATAAGCATTCGTTG3'
STAG2-25R	5'GCTGGAATATATACCTGTGTTTCACG3'
STAG2-26F	5'TGGAGTGATTCAGTTCCATTTG3'
STAG2-26R	5'CCTTAAAGAATTCAATGGCAGC3'
STAG2-27F	5'GGTTTCAGTAACATTCTTTCCTGC3'
STAG2-27R	5'ACTTTGCCCAATTTCAACTGC3'
STAG2-28F	5'CAGTGCCTCATTTATTGAACACC3'
STAG2-28R	5'AATTGAGATAGCACTGTAACTGGTTC3'
STAG2-29F	5'GCTTGGCAAAGGAAGTAGTGAG3'
STAG2-29R	5'AATGCAATCCTACAATTCTGTGTG3'
STAG2-30F	5'ATGCCTATGCTCGCACAACTA3'
STAG2-30R	5'TTTGTAAGCTATTATTGAACACATCTCA3'
STAG2-31F	5'CAGGGACTGCCCCTTACATA3'
STAG2-31R	5'TTGCCTTGCTTCCTCTTGTT3'
STAG2-32F	5'TCCAATGCAGACTGAACATCA3'
STAG2-32R	5'TGCTTTTCTGTTGGAAAGACC3'
STAG2-33F	5'AGAGAGCCACATACTGCTGCC3'
STAG2-33R	5'GGATCTACCACCTTCACCAACC3'
STAG2-34F	5'TGTGTCAGGTACACTTGGAATCAC 3'
STAG2-34R	5'CCTCCCACTGAAATCCTGC3'
STAG2-35F	5'TGAGGTAAGTAGCATCTTGATTAGTCC3'
STAG2-35R	5'CCTCAATGCACTTGATCTTGG3'

Supplementary Table 12B. Bisulfite PCR primers used in STAG2 promoter methylation analysis.

Bisulfite PCR primers	
STAG2 F	5’-GGGAATTAGGGTTATAGGTTTTTTATAGGGGTGTG-3’
STAG2 R	5’- CTAACTCCCAACCCTCCCACCCAAC-3’

Supplementary Table 13. Real time quantitative PCR primers for validation of amplifications of *CCND1*, *ERBB2* and *DHFR*, and deletions of *CDKN2A/B*.

Real Time PCR Primers	
CCND1 F	5' CTGCGAGGAACAGAAGTGCG 3'
CCND1 R	5' GGATGGAGTTGTCGGTGTAGATG 3'
CDKN2A/2B F	5' GAAGTCTTGGTCCTGATGTCCCC 3'
CDKN2A/2B R	5' CGGCTCTTCTGCACAACTCAACT 3'
DHFR F	5' AGGGACCAGGTTGGATTAGGC 3'
DHFR R	5' AGGGCAAGGAAGTCTTCACAGC 3'
ERBB2 F	5' CTGCTGGACATTGACGAGACA 3'
ERBB2 R	5' TTGATGGGCACCTGGGAG 3'

Supplementary Table 14. The detailed information on positions and sequences of RT-PCR and PCR primers in experiment of *FGFR3-TACC3* confirmation in B59

Primer	**Sequence**	**Position (hg18)**
P1 F	5' AGAGGCCCACCTTCAAGCA 3'	1,778,395-1,778,413
P1 R	5' TCCTCAGCTCCCGGTTCTC 3'	1,711,245-1,711,263
P3 F	5' GGCTGTTCCCGAATAAGGC 3'	1,778,295-1,778,313
P3 R	5' CAAGTCAGCAGGCAGGCG 3'	1,711,193-1,711,210
P4 F	5' CCGCCAACTGCACACACG 3'	1,778,187-1,778,204
P4 R	5' AGGAAGTTCAGAAGCAGAAG 3'	1,712,351-1,712,370