Supplementary Figure 1

Distribution of somatic mutations detected by exome sequencing in the ESCC patient cohort.

The average, median and range of mutation numbers in each category are shown.
Supplementary Figure 2

Landscape of somatic copy number alterations detected by exome sequencing in the ESCC patient cohort.

Chromosomes are arranged circularly end to end, with the cytobands frequently affected marked in the outer rim. The inner space displays copy number data inferred from whole-exome sequencing, with red dots indicating copy number gains and blue dots indicating copy number losses. Amplifications are arranged as inward radiations in proportion to the fold change.
Supplementary Figure 3

Substitution composition of smokers and non-smokers in the ESCC exome.

(a) Comparison of the average substitution rates at non-CpG dinucleotides and at CpG dinucleotides between smokers and non-smokers. Most of the excessive substitution of C>T over C>A/G occurred at CpG dinucleotides. (b) Comparison of the average rates of all possible single-base substitutions between ESCC smokers ($n = 77$) and non-smokers ($n = 36$). Error bars indicate s.e.m. No significant difference was found between smokers and non-smokers.
Supplementary Figure 4

Distribution of non-silent mutations or SCNAs of known cancer genes.

(a) Mapping of cancer signaling pathways in ESCC, indicated by the number of mutations per capita and by the fraction of tumors carrying at least one mutation in the corresponding pathway. (b) Fraction of tumors carrying mutations in known oncogenes and tumor suppressor genes (TSGs). Pathway definition and gene classification are as shown in Supplementary Table 14.
Supplementary Figure 5

Recurrently mutated COSMIC Cancer Census genes in ESCC cell lines.
Supplementary Figure 6

Somatic alterations of RB1, NOTCH1, CCND1 and MIR548K correlate with clinical features.

(a) Mutation spectrum of RB1 (n = 10). (b) RB1 mutation was associated with younger age of onset of ESCC (P = 0.010, Student’s t test, two-tailed). (c) Mutation spectrum of NOTCH1 (n = 16). (d) NOTCH1 mutation was associated with older age of onset of ESCC (P = 0.001, Student’s t test, two-tailed). Amplifications of (e) CCND1 and (f) MIR548K were associated with poor overall survival (P = 0.006 and P = 0.022, log-rank test).
Supplementary Figure 7

Western blot confirmation of p300 knockdown efficiency in KYSE-150 and KYSE-450 cells.
Supplementary Figure 8

Representative fields of immunohistochemistry results.

The proteins of interest are designated in rows. Immunoreactivity scores are listed above. p-YAP1, phosphorylated YAP1.
Supplementary Figure 9

Somatic alterations in the PI3K-Ras and Notch pathways in ESCC.

Genes are shown along with the percentage of samples with alterations, including somatic mutations (blue), homozygous deletions (green) and amplifications (red).