**Supplementary Information**

**RNA interference**

For siRNA experiments, 19 nucleotide siRNA duplexes with 3’dTdT overhangs were synthesized by Dharmacon (GE healthcare, Lafayette, CO). For siRNA transfection, cells were transfected with 50 nM siRNA using DharmaFECT 1 siRNA transfection reagent (Dharmacon) according to the manufacturer’s instructions. The siRNA oligonucleotide sequences were as follows: Luciferase control (siLUC), 5’- CUUACGCUGAGUACUUCG A -3’; Np63, 5’- CAATGCCCAGACTCAATTT -3’; STXBP4#1, 5’- CCTGGAGGAGACTGTTATA -3’; STXBP4#2, 5’- CCGACAACATTCAGCCAGAAA -3’; PDGFR, 5’- CGAGACTCCTGTAACCTTA -3’; XAGE1B, 5’- GCGUCAAGGUGAAGAUAAU -3’; DPP4, 5’- UCAGUAAAGAGGCGAAGUA -3’; EPHA3, 5’- GAUCGGACCUCCAGAAAUA -3’.

For shRNA experiments, shRNAs for Luciferase (LUC), Np63, STXBP4 and PDGFR oligonucleotides were annealed at 90°C for 15 min, 70°C for 30 min, 25°C for 30 min, and then cloned into the pLKO.1 puro lentiviral shRNA expression vector between Age I - Eco RI sites. All constructs were verified by DNA sequencing (Genewiz). Oligonucleotide target sequences used for shRNAs were follows: Np63, 5’- CAATGCCCAGACTCAATTT -3’; STXBP4, 5’- CCTGGAGGAGACTGTTATA -3’; PDGFR, 5’- CGAGACTCCTGTAACCTTA -3’.

**Quantitative real-time PCR**

Primers used were as follows: *STXBP4*, forward 5’- GGCCCATTGGTATATATTCAGG -3’ and reverse 5’- GGCTTCAAACGACCATCCT -3’; *ΔNp63*, forward 5’- GGAAAACAATGCCCAGACTC -3’ and reverse 5’- CTGCTGGTCCATGCTGTTC -3’ ; *PDGFRA*, forward 5’- CCACCTGAGTGAGATTGTGG -3’ and reverse 5’- TCTTCAGGAAGTCCAGGTGAA -3’; *PDGFRB*, forward 5’- CATCTGCAAAACCACCATTG -3’ and reverse 5’- GAGACGTTGATGGATGACACC -3’; *VEGFR1* (*FLT1*), forward 5’- CAGCATACCTCACTGTTCAAGG -3’ and reverse 5’- CCACACAGGTGCATGTTAGAG -3’; *VEGFR2* (*KDR*), forward 5’- GCTCAAGACAGGAAGACCAAG -3’ and reverse 5’- GGTGCCACACGCTCTAGG -3’; *VEGFR3* (*FLT4*), forward 5’- AAGATGTTTGCCCAGCGTAG -3’ and reverse 5’- GCACTGTGGCATGAGGTCT -3’.

**Supplementary Figures Legends**

**Supplementary Figure 1.** STXBP4 expression is correlated with poor prognosis in patients with tumors expressing high ΔNp63 levels. (A, B) A total of 87 samples of lung SCC were classified into 2 subgroups based on the expression of ΔNp63, high ΔNp63 (n=30) and low ΔNp63 (n=57). And then, Kaplan-Meier analysis defined according to STXBP4 expression. A statistically significant differences in OS and PFS were observed among the patients [OS (A), *P* < 0.01; PFS (B), *P* < 0.01]. *P*-values were obtained by log-rank test. (C, D) A total of 87 samples of lung SCC were classified into 2 subgroups based on the expression of STXBP4, high STXBP4 (n=52) and low STXBP4 (n=35). And then, Kaplan-Meier analysis defined according to ΔNp63 expression. *P*-values were obtained by log-rank test [OS (C), *P* = 0.99; PFS (D), *P* = 0.84].

**Supplementary Figure 2.** Causal networks associated with STXBP4 expression in lung SCC. The canonical pathway analysis characterized two signaling pathways as the functional relationship of STXBP4-positivity, including “Cellular Movement” and “Cell Morphology”.

**Supplementary Figure 3.** Depletion of PDGFR suppresses the growth of lung SCC. The lung SCC cells, RERF-LC-Sq1, were treated with siRNAs for Luciferase (siLUC) as a control, PDGFR, XAGE1B, DPP4 or EPHA3. The cell growth rate was measured at 72 hrs after siRNA transfection using CCK-8 reagent (Dojindo, Tokyo, Japan) according to the manufacturer’s instruction.

**Supplementary Figure 4.** *PDGFRA* mRNA was significantly correlated with *STXBP4* in the gene expression profiles of lung SCC patients. (A) Scatter plot of relative mRNA expression levels between *Np63* and *STXBP4*. A total of 52 available samples with high RNA integrity number (RIN > 2.0) were used for transcriptome profiling by real-time RT-PCR. (B) A total of 488 lung SCC cases in the datasets of The Cancer Genome Atlas (TCGA), were classified into 2 groups based on the expressions of *STXBP4* mRNAs (High: high *STXBP4*, Low: low *STXBP4*). The z-score of each gene expression was analyzed. *P*-value was obtained by Student’s T-test.

**Supplementary Figure 5.** *PDGFRA* expression is upregulated in STXBP4-transduced lung SCC cells. (A) STXBP4 or Np63 induces *PDGFRA* expression in lung SCC cell line, RERF-LC-Sq1. The cells were retrovirally transduced with empty vector control (Mock), Np63 or STXBP4. The mRNA levels of *PDGFRA* were determined by real-time RT-PCR. (C) RERF-LC-Sq1 cells transduced as in (B), were subjected to immunoblotting using indicated antibodies.

**Supplementary Figure 6.** STXBP4-depletion inhibits SCC tumorigenesis and modulates PDGF signaling *in vivo*. (A) The lung SCC cell line, EBC-1, were treated with siRNAs for Luciferase (siLUC) as a control, STXBP4, Np63 or PDGFR. Total RNAs were quantified by real-time RT-PCR analysis and the induction levels of *PDGFRA* were determined by the relative Ct method. (B) EBC-1 cells depleted as in (A), were subjected to immunoblotting using indicated antibodies. (C) The growth of EBC-1 cells after shRNA mediated STXBP4, Np63 or PDGFR, knockdown was monitored by soft agar colony formation assays. Standard deviations (SD) are plotted. \**P* < 0.05. (D) Representative images of xenografts from subcutaneously transplanted with lentivirally shRNA transduced Luciferase as a control (shLUC), STXBP4, Np63 or PDGFR knockdown EBC-1 cells (n = 6 for each knockdown). The results of six independent injections of knockdown cells are shown. Fourteen days after implantation, the length (L) and width (W) of the tumor mass were measured, and the tumor volume (TV) was calculated using the equation: TV = (L x W2)/2. \**P* < 0.05.

**Supplementary Figure 7.** STXBP4 promotes tumorigenesis through PDGFRA in lung SCC. (A) STXBP4 promotes SCC tumorigenesis through PDGFR in a *Np63*-dependent manner. The growth of STXBP4 expressing EBC-1 cells after depletion of luciferase as a control (shLUC), Np63 or PDGFR, were monitored by soft agar colony formation assays. Standard deviations (SD) are plotted. \**P* < 0.05. (B) STXBP4-depletion induces SCC tumorigenesis through PDGFR in lung SCC cells.The growth of STXBP4-depleted RERF-LC-Sq1 cells after induction of PDGFR was monitored by soft agar colony formation assays.