Supplementary figure1 Tweak contributes to cancer angiogenesis via stabilization of Fn14 on endothelial cells. A, After transplantation of KU7/GFP cells into the mouse bladder, atelocollagen with either Tweak siRNA or control RNA was transurethrally instilled into the bladder lumen. Bladders were resected 14 d post-instillation, and in situ images captured under fluorescent light and tumor area was measured by GFP expression (upper panel). Expression of Tweak, Fn14, VEGF or ALKBH3 in the bladder cancer samples was examined by western blotting (lower panel)(DV control: Tweak siRNA: Tweak, 1:0.15~0.20; Fn14, 1:0.10~0.40; VEGF, 1:0.18~0.26; ALKBH3, 1:1.10~0.94). B, The immunohistochemistry by Fn14 or CD31 are shown in upper panel. Number of blood vessels (positive for CD31) or Fn14 positive blood vessels per 10 high power fields within cancer foci was counted in lower panel. Columns, mean; bars, SE (#, statistically different from the value of control at p<0.001)

Supplementary figure2 The immunohistochemistry data for ALKBH3 in human urothelial carcinomas of the urinary bladder indicate a correlation with pathological parameter. Immunohistochemistry in A for ALKBH3 expression was done on representative samples of each group. The percentage of immunopositive cells was calculated per 1,000 cells per high-power field. As can be seen, there seems to be a positive correlation between the percentages of ALKBH3 immunopositive cells and tumor stage/grade.

Supplementary figure3 The immunohistochemistry data for Tweak/Fn14 in human urothelial carcinomas of the urinary bladder indicate a correlation with pathological parameter. Immunohistochemistry in A for Tweak/Fn14 expression was done on representative samples of each group. The percentage of immunopositive cells was calculated per 1,000 cells per high-power field. As can be seen, there seems to be a positive correlation between the percentages of Tweak/Fn14
immunopositive cells and tumor stage/grade.

Supplementary figure 4 The immunohistochemistry data for NOX2 in human urothelial carcinomas of the urinary bladder indicate a correlation with pathological parameter. Immunohistochemistry in A for NOX2 expression was done on representative samples of each group. The percentage of immunopositive cells was calculated per 1,000 cells per high-power field. There were no significant correlation between the percentages of NOX2 immunopositive cells and tumor stage/grade.

Supplementary figure 5 A correlation between positive percentages of ALKBH3 at initial diagnosis and pathological parameters including tumor multiplicity (A), tumor size (B) and tumor recurrence within 5 years (C) in human urothelial carcinomas (pT1/pT1, n=47).

Supplementary figure 6 The role of ALKBH3 in progression of human urinary bladder cancer. ALKBH3 contributes to cancer cell survival, angiogenesis and invasion through manipulating upregulating NOX2-ROS signal and Tweak/Fn14-VEGF signal in not only cancer cells but also endothelial cells.