Supplymentary Data
Figure. S1

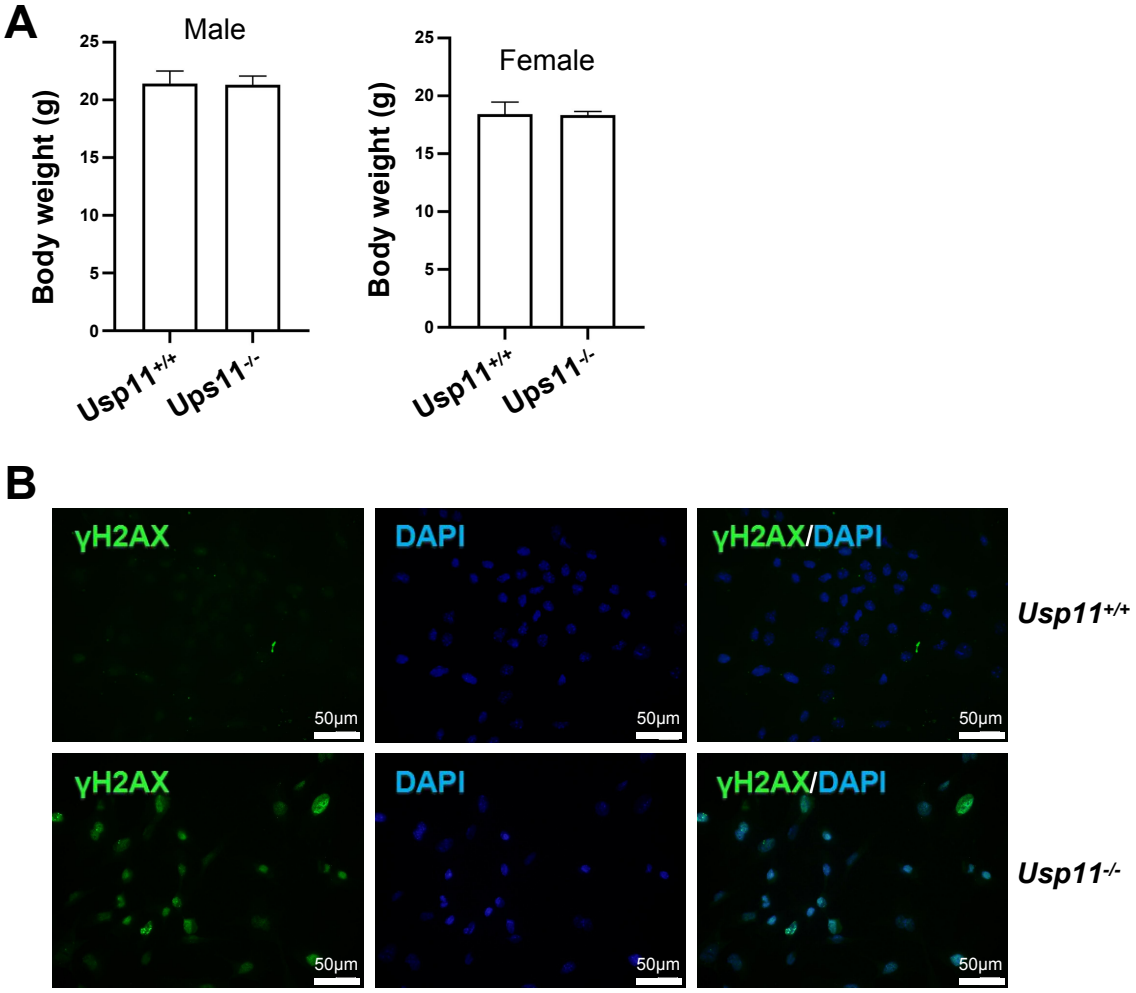
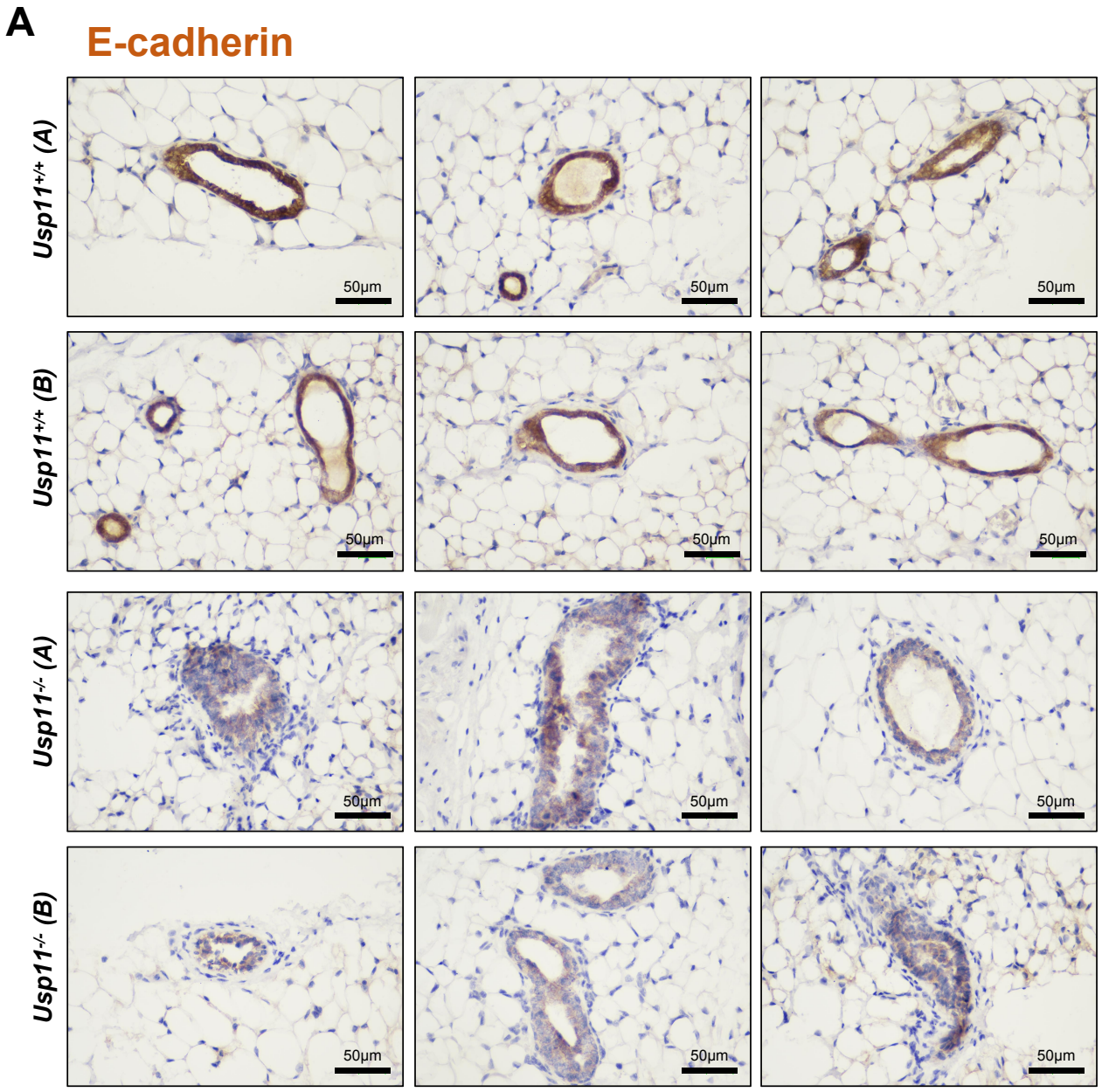


Figure S1. Analysis of Usp11 knock-out mice and DNA damage in mammary epithelial cells

(A) Quantification of body weight from 8-week-old male (left) and female (right) mice. The results were presented as mean ± SEM. N = 4 for male *Usp11*$^{+/+}$ mice; N = 4 for male *Usp11*$^{-/-}$ mice; N = 5 for female *Usp11*$^{+/+}$ mice; N = 6 for female *Usp11*$^{-/-}$ mice. (B) Representative immunofluorescent staining of γH2AX in primary mammary epithelial cells isolated from 5-week-old *Usp11*$^{+/+}$ and *Usp11*$^{-/-}$ female mice.

Supplymentary Data
Figure. S2



Supplymentary Data
Figure. S2

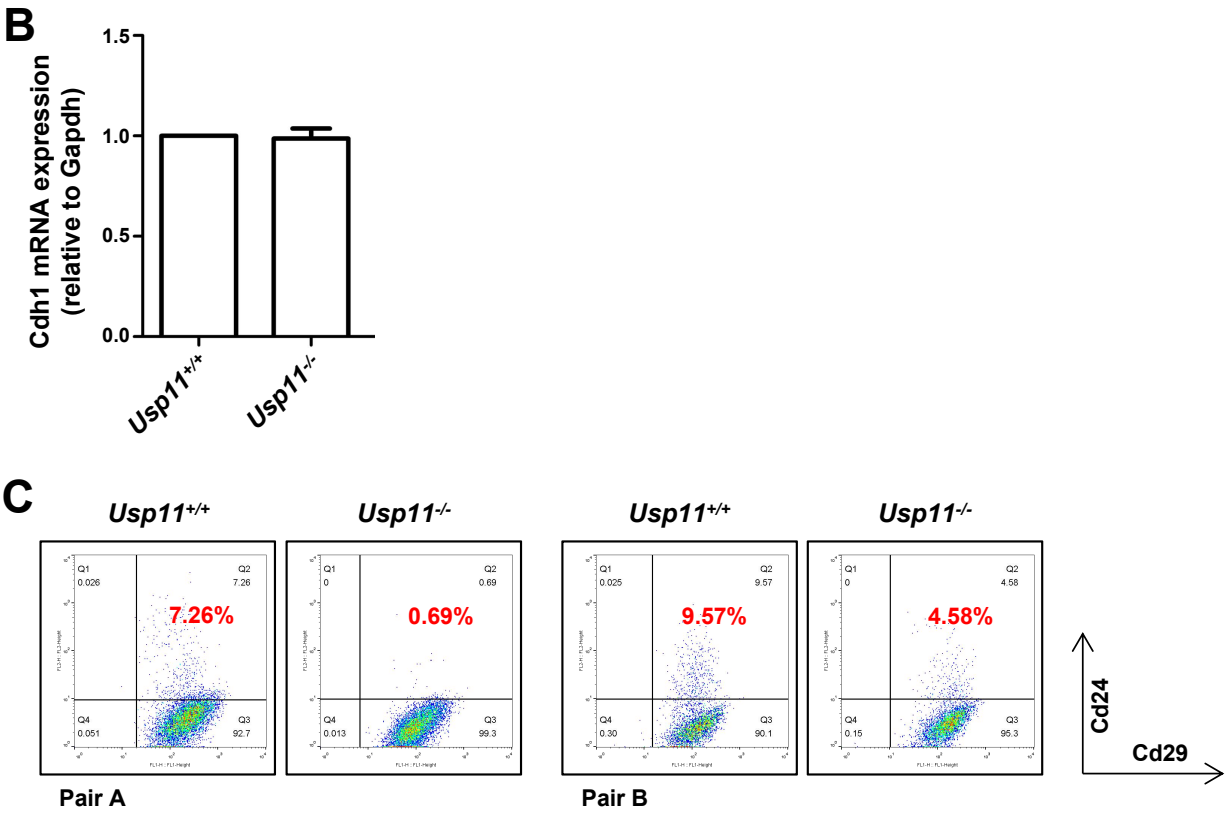


Figure S2. Analysis of luminal features of mammary epithelial cells in Usp11 knock-out mice

(A) Representative IHC staining of E-cadherin in mammary glands from 5-week-old *Usp11*$^{+/+}$ and *Usp11*$^{-/-}$ female mice. (B) qRT-PCR analysis of mRNA expression of Cdh1 in *Usp11*$^{+/+}$ and *Usp11*$^{-/-}$ MECs. Gapdh was used as an internal control. The results represent the mean ± SEM of three individual samples. (C) FACS analysis of Cd24 and Cd29 expression in in intro cultured *Usp11*$^{+/+}$ and *Usp11*$^{-/-}$ MECs.

Supplymentary Data
Figure. S3

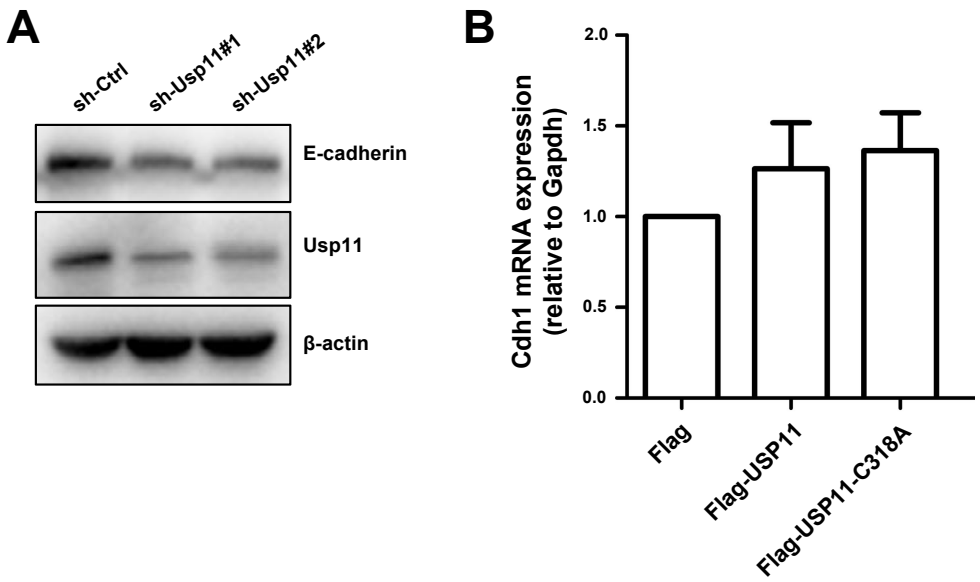
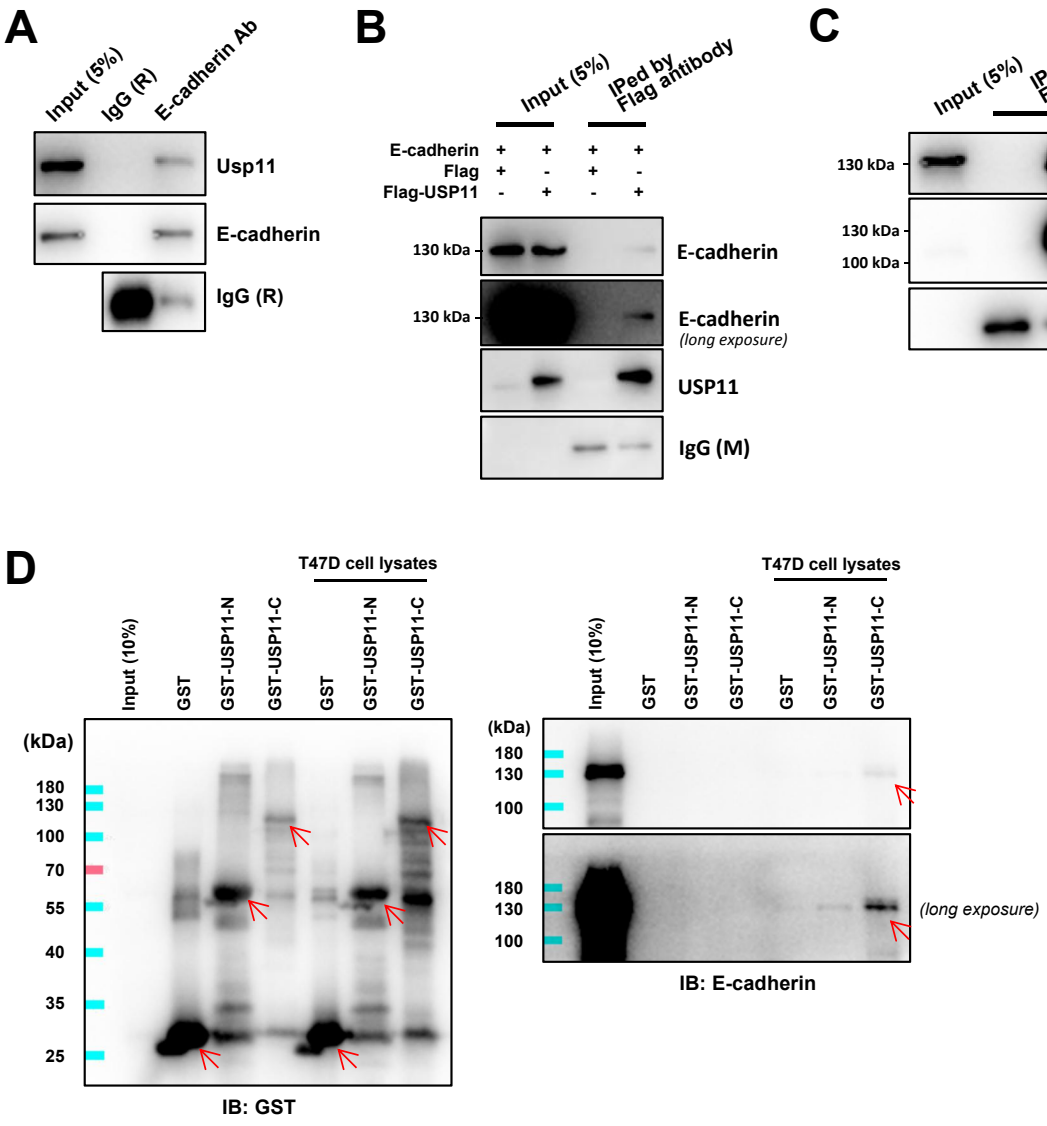


Figure S3. Knock-down or over-expression of Usp11 in mouse mammary epithelial and tumor cells

(A) Western blotting analysis of the protein expression of E-cadherin and Usp11 in sh-Ctrl, sh-Usp11#1, or sh-Usp11#2 lentivirus infected HC11 cells. β-actin was used as an internal control. (B) qRT-PCR analysis of Cdh1 in mouse mammary tumor cells infected with Flag, Flag-USP11, and Flag-USP11-C318A. Gapdh was used as an internal control. The results represent the mean ± SEM of three individual samples.

Supplymentary Data
Figure. S4



Supplymentary Data
Figure. S4

Figure S4. The interaction of Usp11 and E-cadherin

(A) Immunoprecipitations were performed in mouse mammary tumor cell lysates using anti-E-cadherin antibody or IgG. The expression of Usp11 and E-cadherin in input and immunoprecipitated samples were detected by western blotting. (B) HEK293T cells were transfected with Flag or Flag-USP11 for 48 h, then immunoprecipitations were performed in the mixture of HEK293T and T47D cell lysates using anti-Flag antibody. The expression of E-cadherin and USP11 in input and immunoprecipitated samples were detected by western blotting. (C) Human T47D cells were transfected with Flag or Flag-USP11 for 48h, then immunoprecipitations were performed in these cell lysates using anti-Flag antibody. The expression of E-cadherin and USP11 in input and immunoprecipitated samples were detected by western blotting. (D) Purified GST or GST tagged N-terminal and C-terminal fragments of USP11 were used to interact with E-cadherin in T47D cell lysates, and the eluted proteins were analyzed by western blotting using GST or E-cadherin primary antibody.

Supplymentary Data
Figure. S5

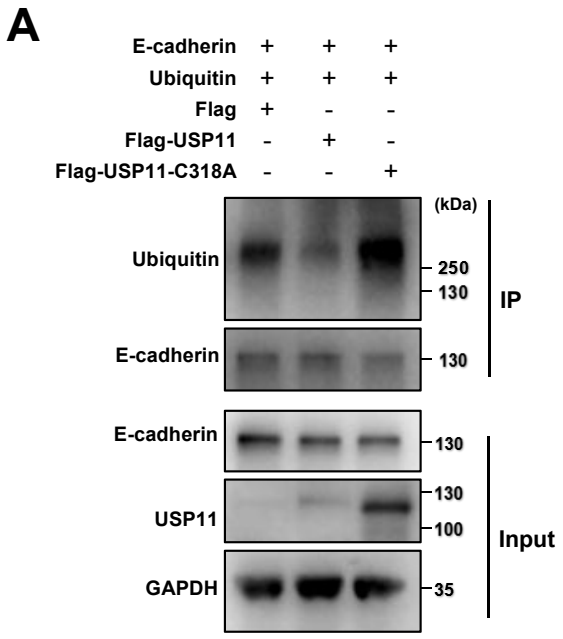
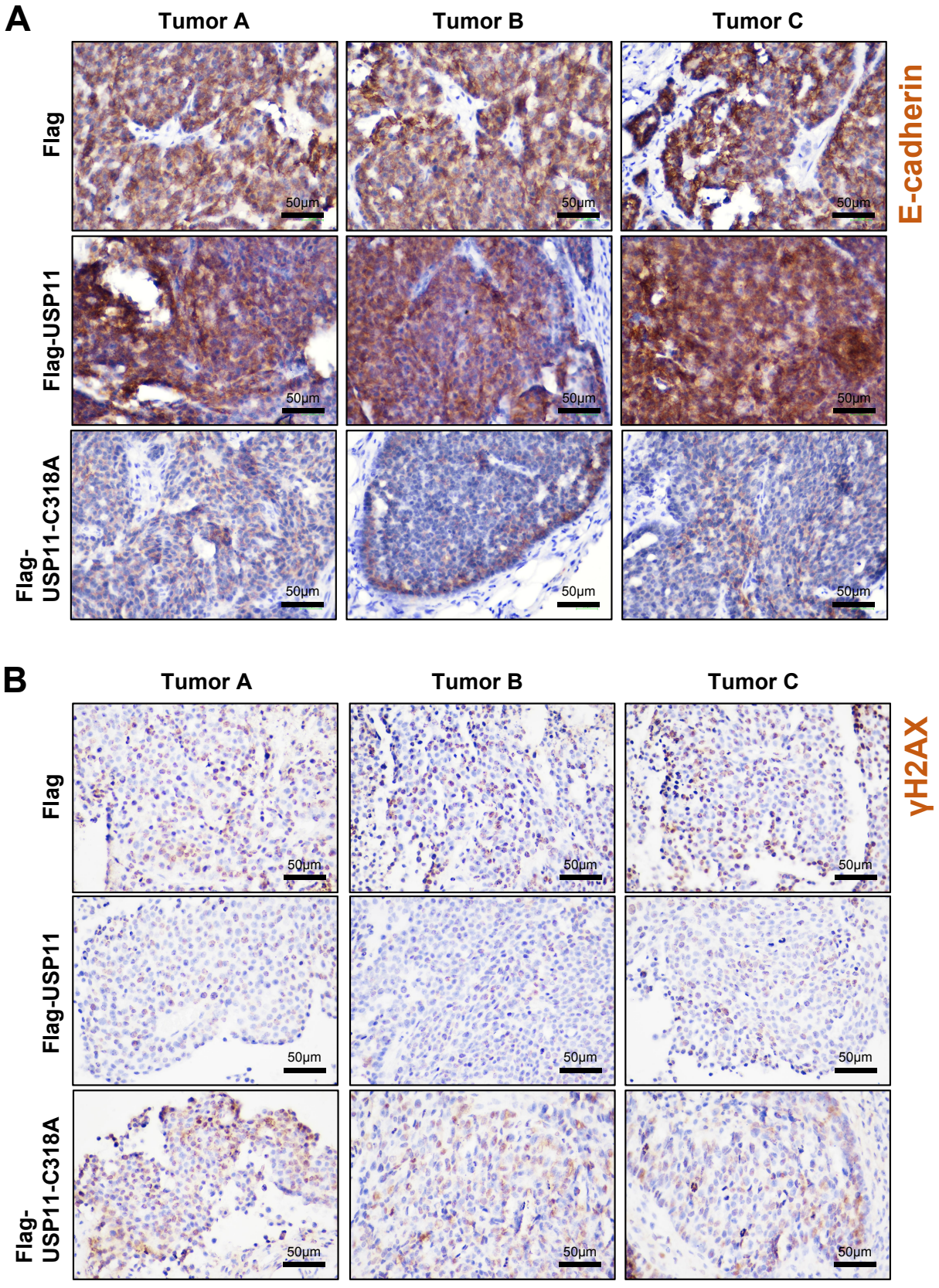


Figure S5. Deubituitination of E-cadherin by USP11

(A) HEK293T cells were transfected with Flag, Flag-USP11 or Flag-USP11-C318A plasmids along with E-cadherin and Ubiquitin plasmids for 48h, then immunoprecipitations were performed in these cell lysates using anti-E-cadherin antibody or IgG. The expression of Ubiquitin and E-cadherin in immunoprecipitated samples and the expression of E-cadherin and USP11 in input samples were detected by western blotting. GAPDH was used as an internal control for input sample.

Supplymentary Data
Figure. S6



Supplymentary Data
Figure. S6

Figure. S6. IHC analysis of the gene expression in xenograft tumors.

(A, B) Tumors generated by mouse mammary tumor cells stably expressing Flag, Flag-USP11 and Flag-USP11-C318A were analyzed with antibodies against E-cadherin (A) and γH2AX (B). Representative IHC staining results from three individual tumors are shown.

Supplymentary Data
Figure. S7

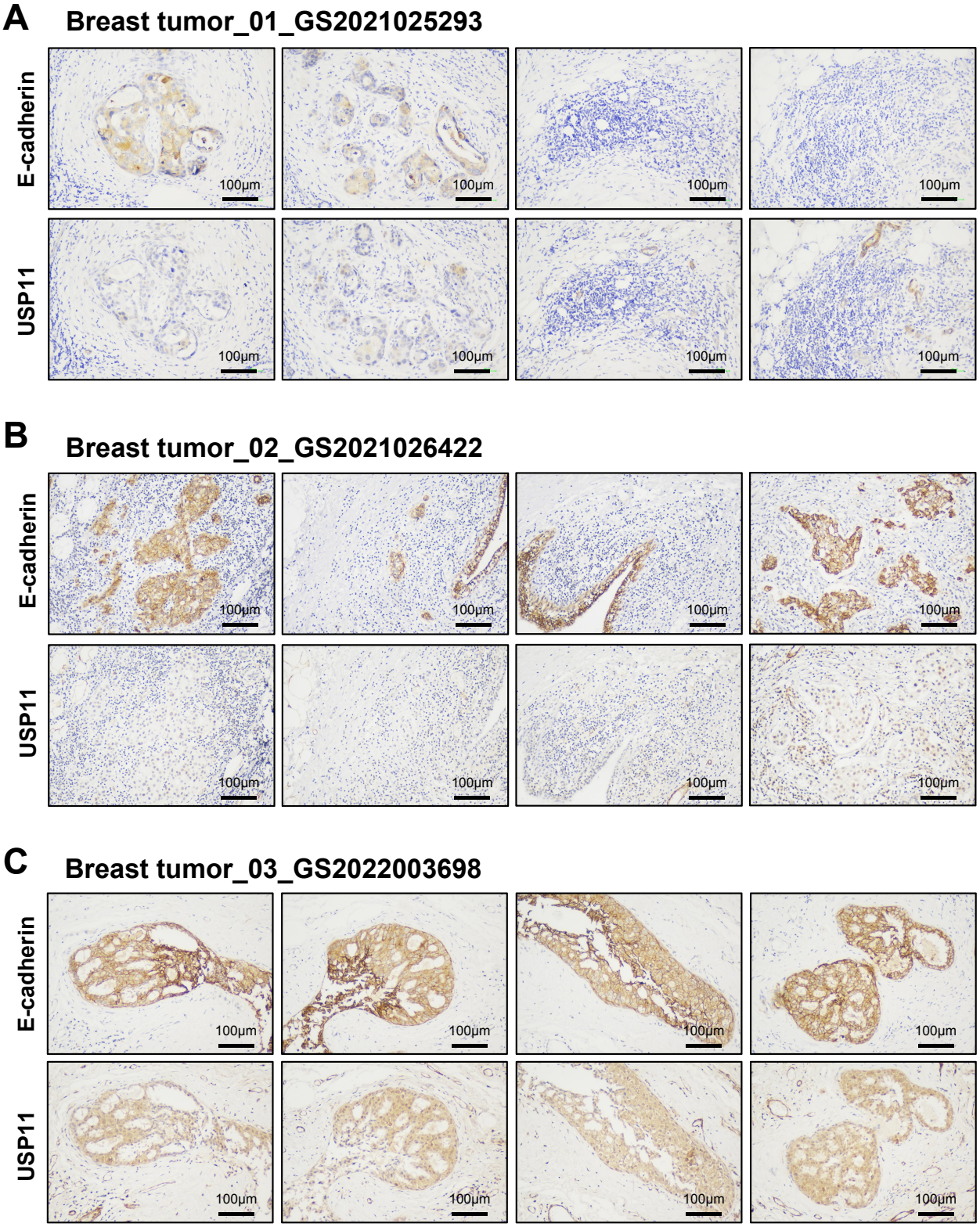


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Figure. S7

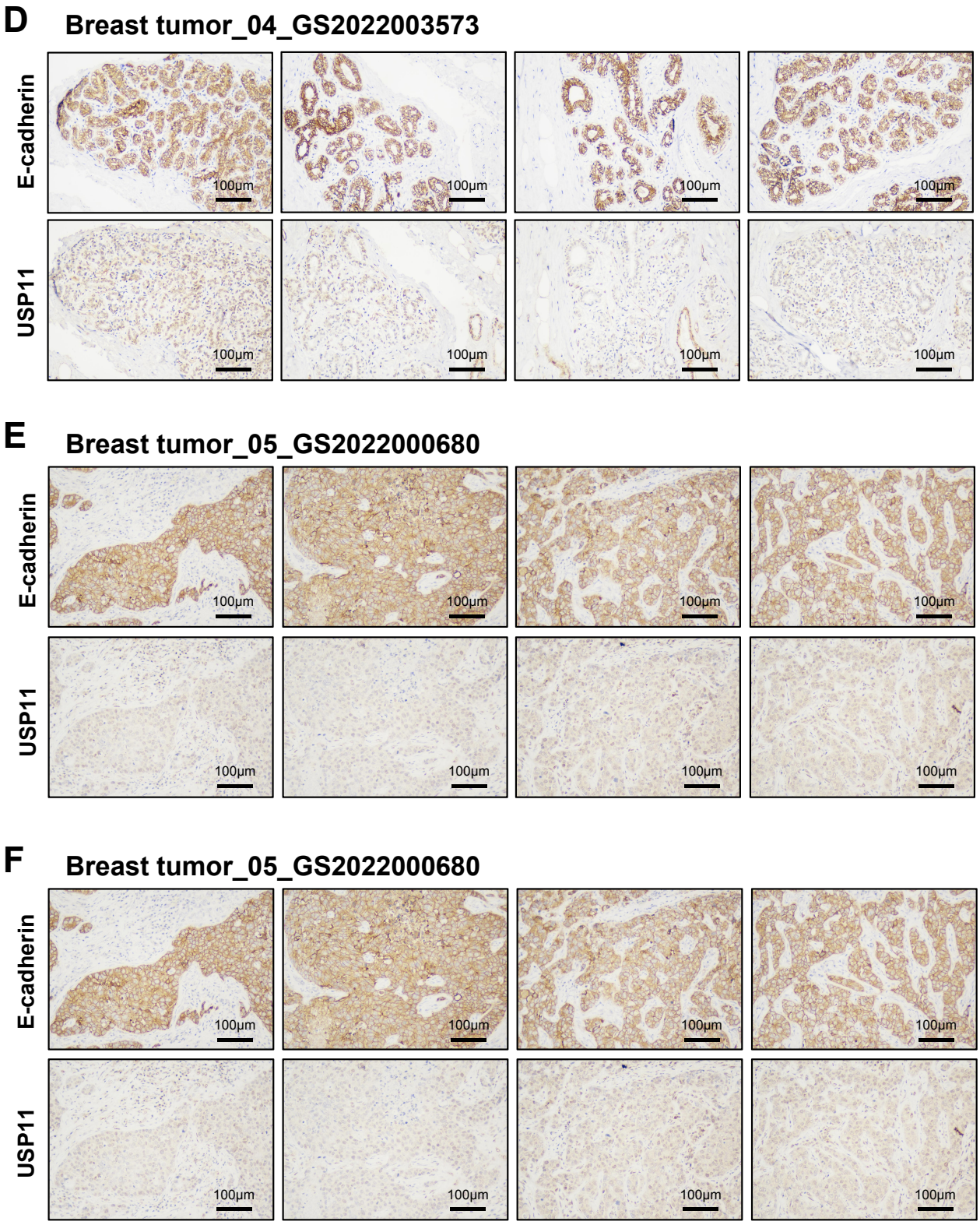

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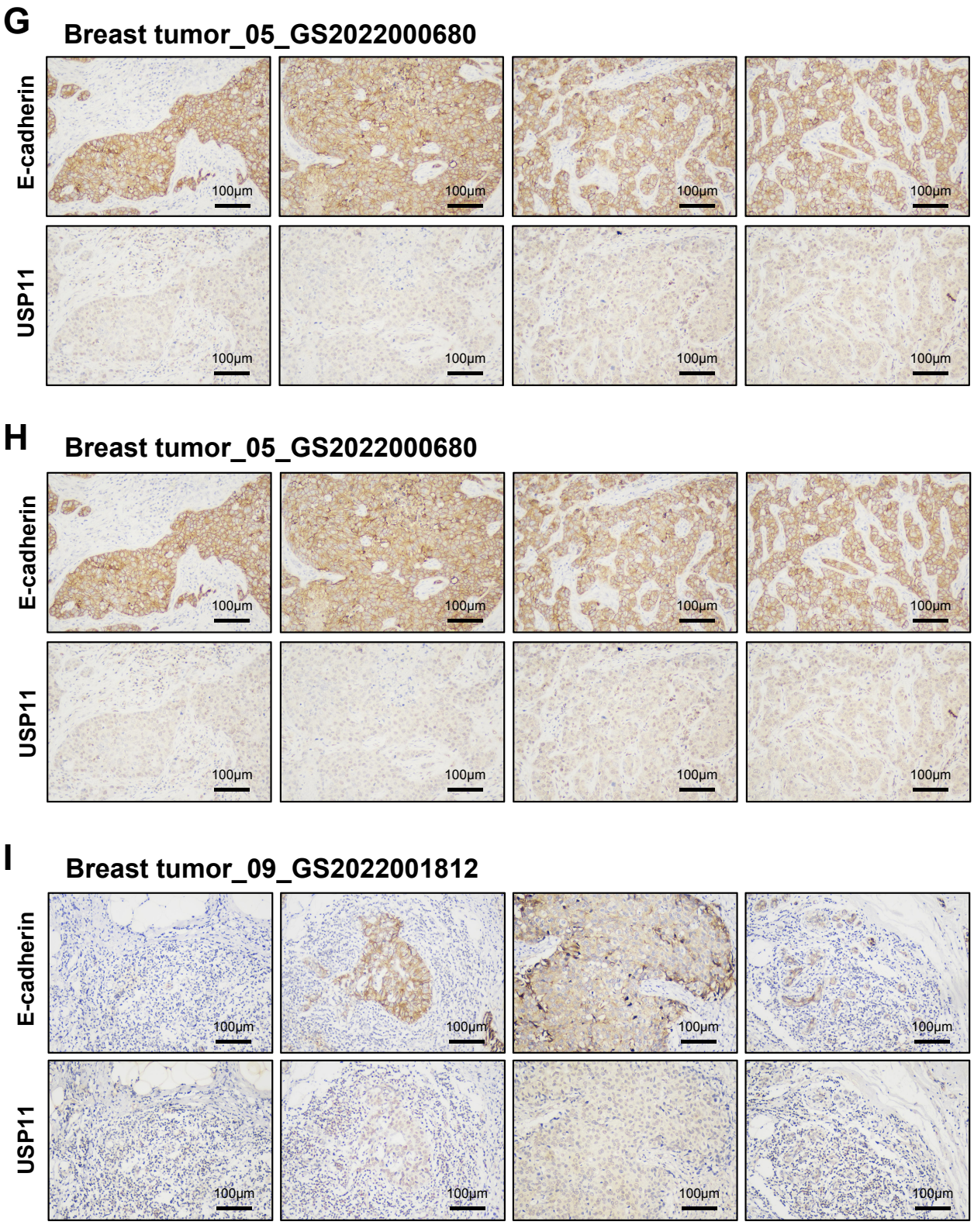
Figure. S7



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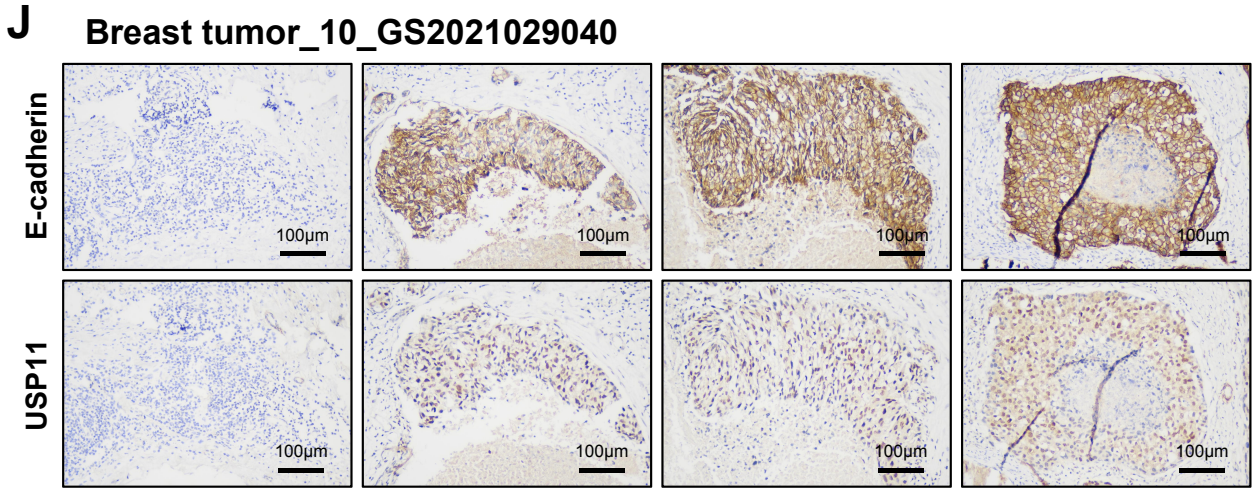

Figure S7. IHC analysis of human breast cancer samples.

(A-J) Representative IHC staining of E-cadherin and USP11 in human breast cancers. Representative results from four individual sub-tumor nodules/foci of each tumor sample are shown.