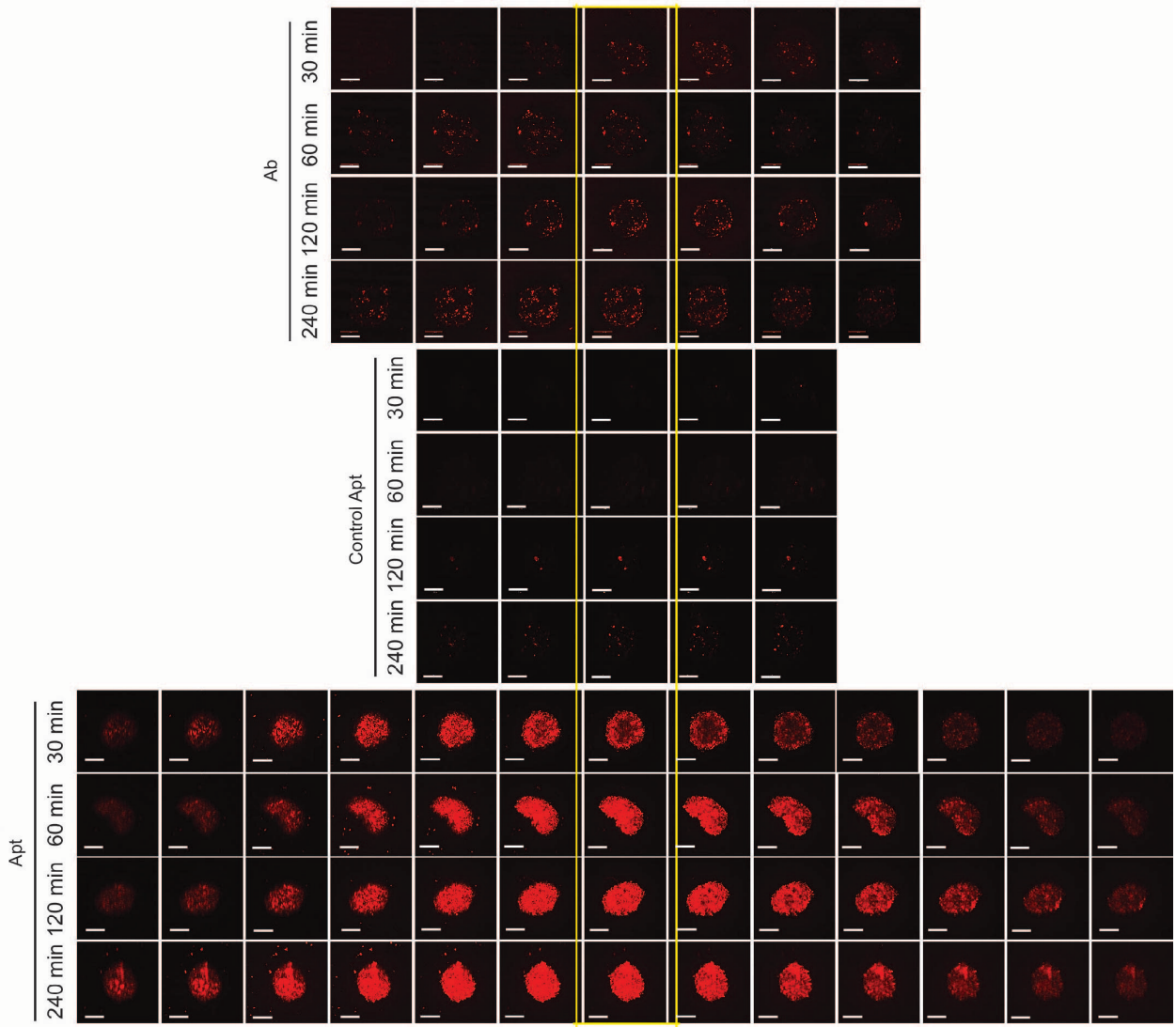
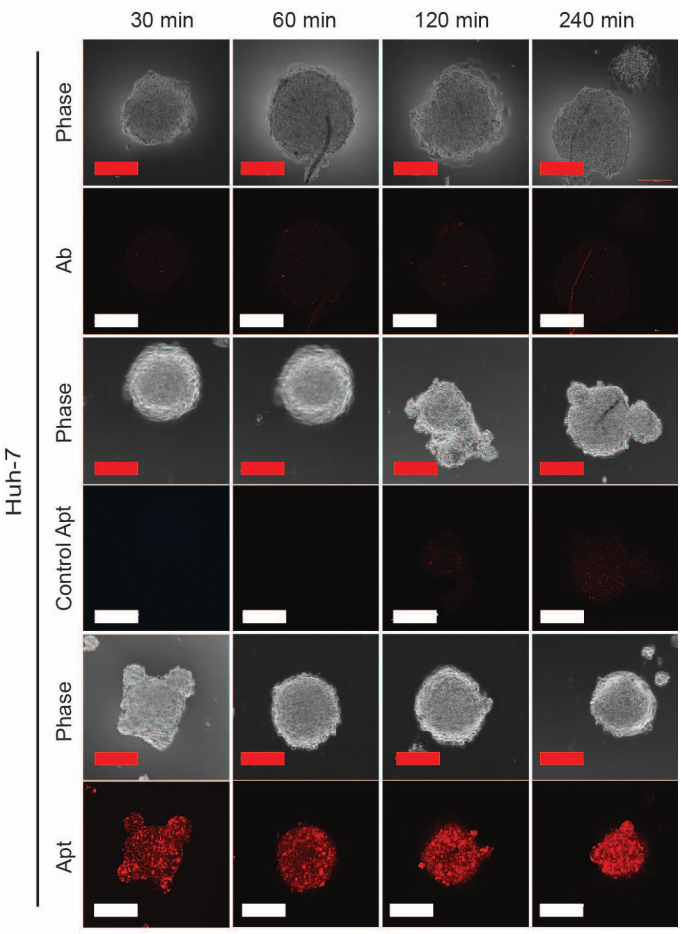
Supplementary Figures and Legends:

Suppl. Fig. 1.



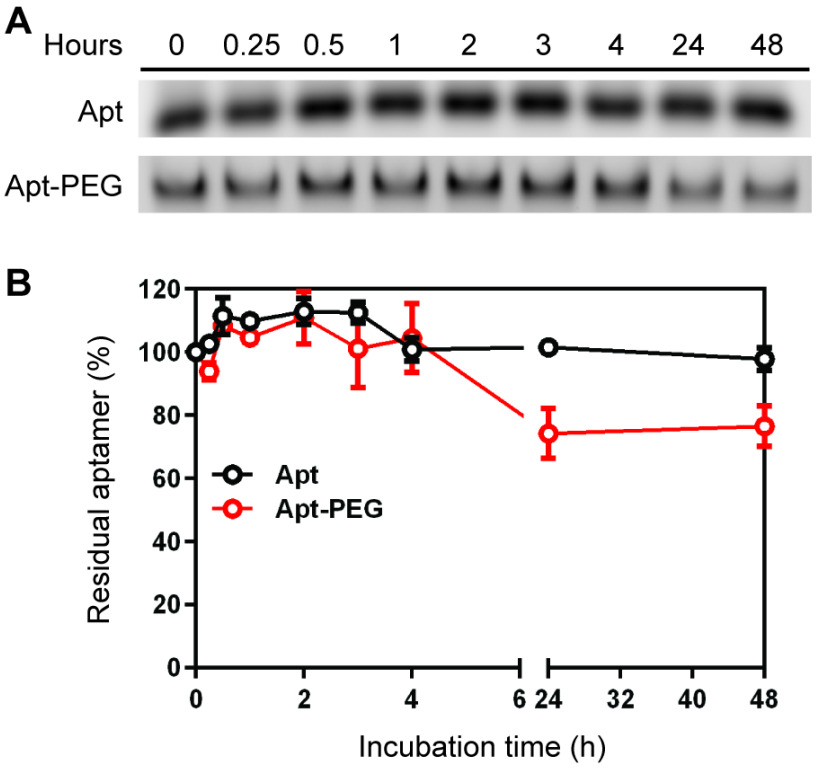
Supplementary Figure 1. EpCAM aptamer penetrates tumorsphere more effectively than the EpCAM antibody. EpCAM aptamer, control aptamer, or EpCAM antibody of the same concentration (100 nM) were incubated with HT29 tumorsphere for up to 240 min at 37 °C. The tumorspheres were then washed three times in PBS and imaged using laser scanning confocal microscopy. The images of the middle z-stack sections (marked by yellow lines) were used for the comparison of tumorsphere penetration. Scale bar: 200 µm.

Suppl. Fig. 2.



Supplementary Figure 2. EpCAM aptamer is retained much longer inside tumorsphere than the EpCAM antibody. EpCAM aptamer, control aptamer, or EpCAM antibody of the same concentration (100 nM) were incubated with Huh-7 tumorsphere for up to 240 min at 37 °C. The tumorspheres were then washed three times in PBS and either imaged using laser scanning confocal microscopy or incubated for further 4 h and 24 h incubation in phenol red-free culture medium. Scale bar: 200 µm.

Suppl. Fig. 3.



Supplementary Figure 3. Modification of EpCAM aptamers exhibits a desirable *in vitro* stability. (a) 5 μM of free EpCAM aptamer and PEGylated aptamer were incubated in 50 % fetal bovine serum (FBS) (V:V = 1:1) for up to 48 hours. Aptamers in serum-aptamer mixtures at the indicated time-points (0, 0.25, 0.5, 1, 2, 3, 4, 24, and 48 hours) were recovered using phenol-chloroform extraction and the full-length aptamer were resolved on a 2.5% agarose gel. (b) The remaining full-length aptamers at each time points were quantified using a LAS-4000 Imaging System (GE Healthcare Life Sciences). Data shown are means ± SEM, n=3.