Figure S1

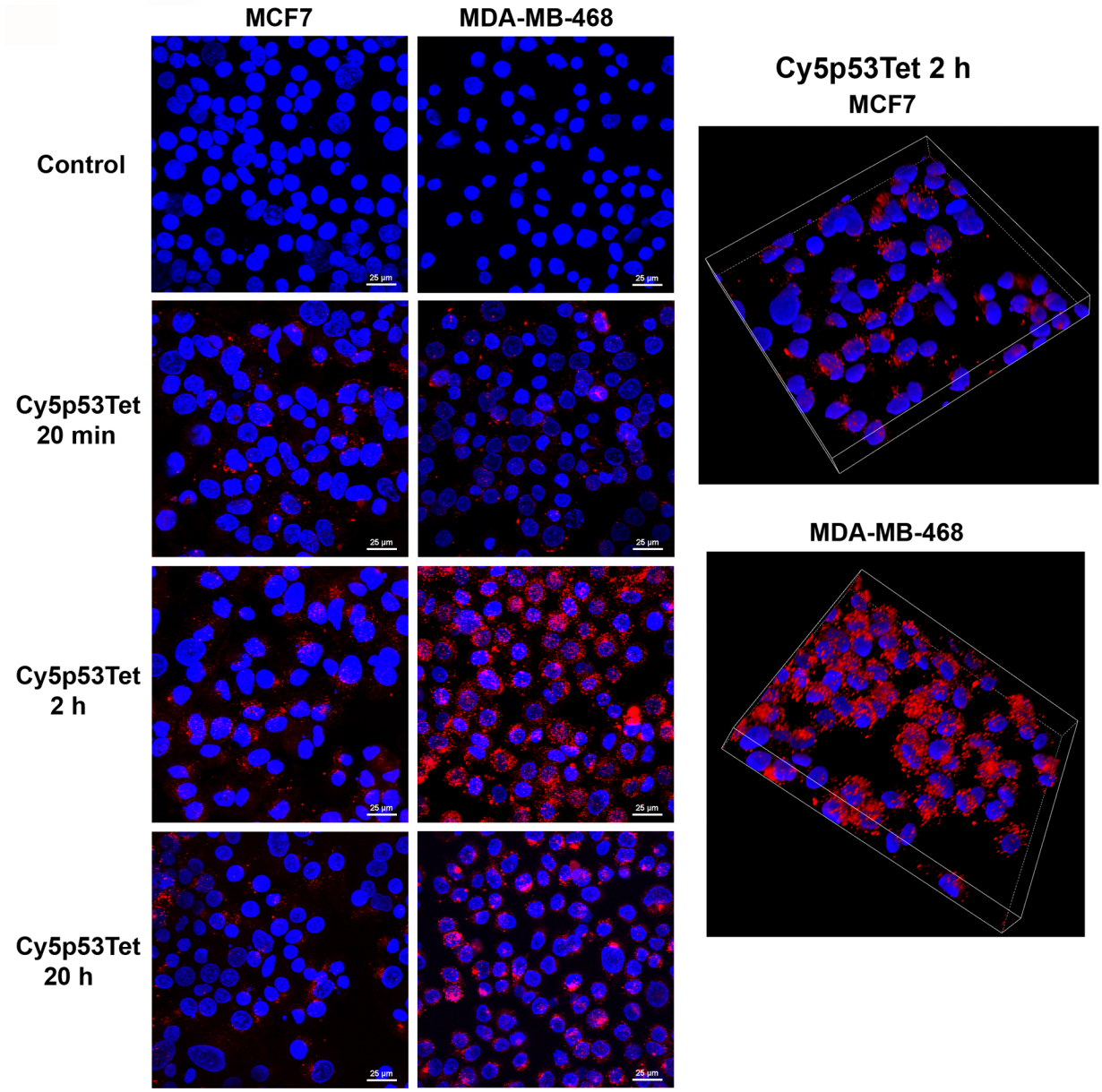

Figure S1. Higher uptake of Cy5p53Tet in MDA-MB-468 TNBC cells than in ER-positive MCF7 cells. Live cell imaging staining of MCF7 and MDA-MB-468 cells after 20 min, 2 h, and 20 h of incubation with 500 nM Cy5p53Tet (red). Hoechst staining (blue) was used to stain the nucleus. 3D model of Cy5p53Tet staining in MCF7 and MDA-MB-468 cells at 2 h generated by Nikon Elements software.

Figure S2

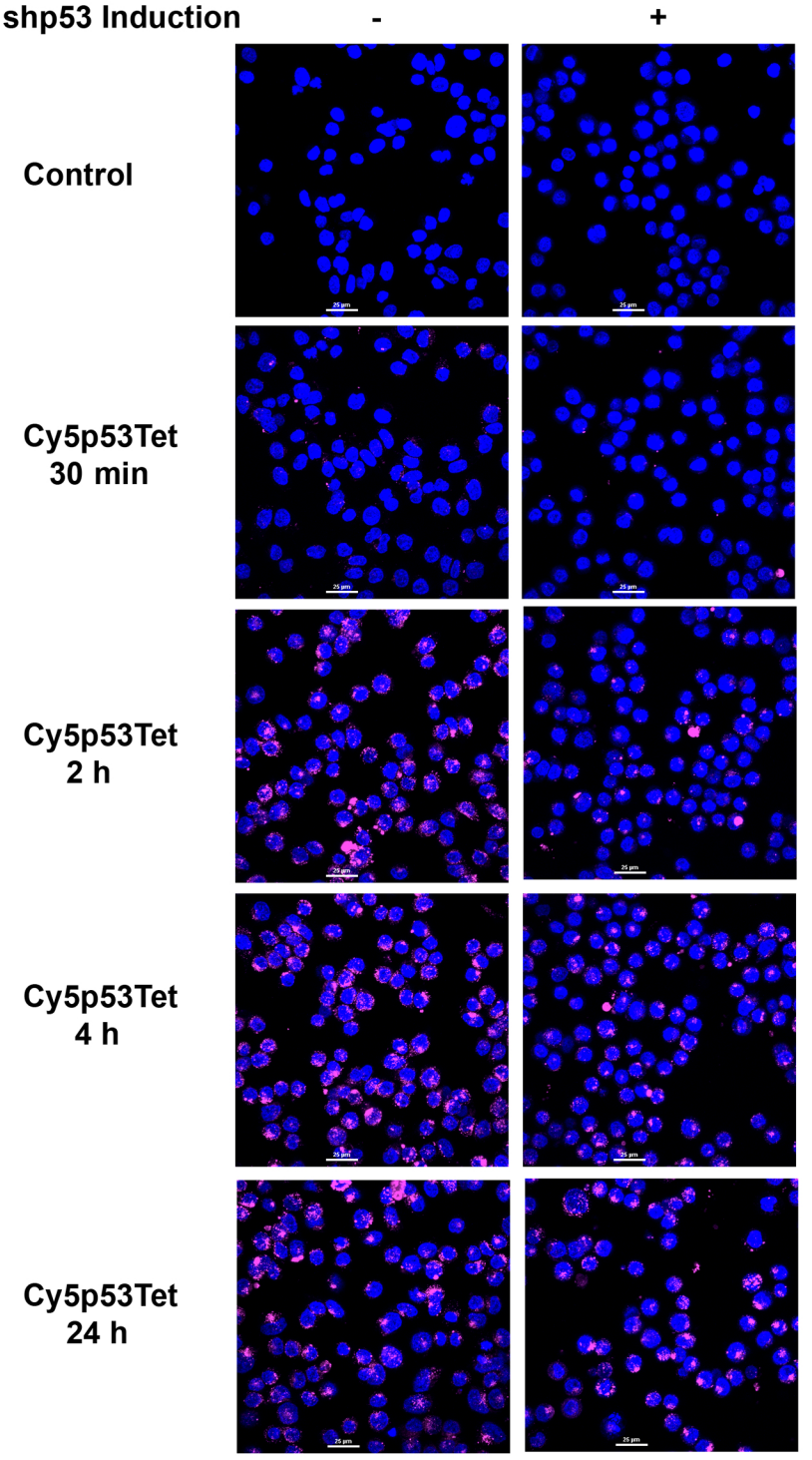

Figure S2. Cy5p53Tet signal reduction upon the depletion of mtp53 R273H. Live cell imaging staining of MDA-MB-468 shp53 cells after 30 min, 2 h, 4 h, or 24 h of incubation with 500 nM Cy5p53Tet (red). Hoechst staining (blue) was used to stain the nucleus.

Figure S3

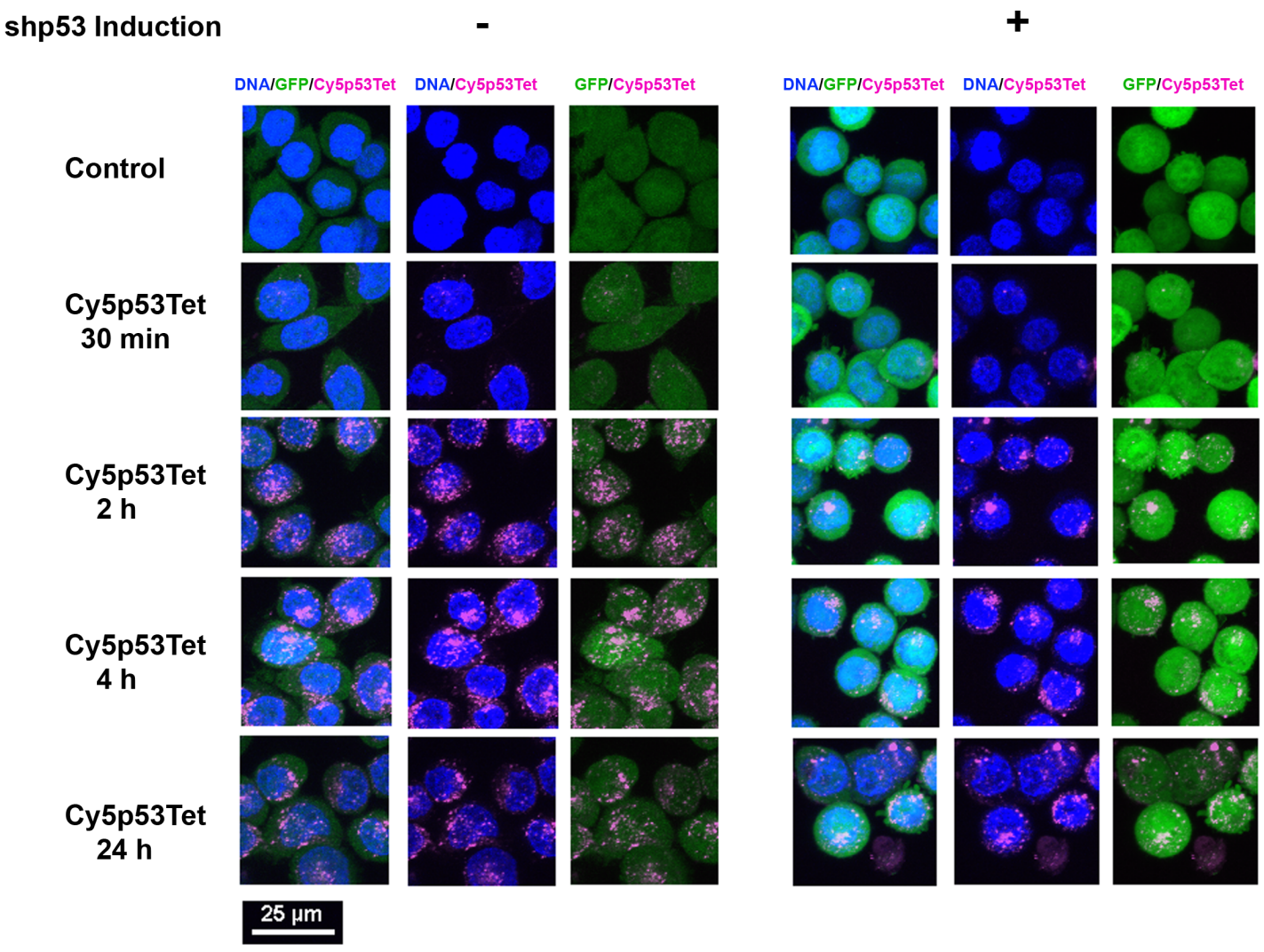

Figure S3. Nuclear penetration of Cy5p53Tet in TNBC. Live cell imaging of Cy5p53Tet (red) in MDA-MB-468 shp53 cells with or without shRNA induction. Cells were imaged by confocal microscopy after 30 min, 2 h, 4 h and 24 h incubation of 500 nM Cy5p53Tet. Hoechst staining (blue) was used to stain the nucleus and GFP (green) was an indicaton of cytoplasm and doxycycline-mediated induction. Three independent experiments with biological replicate were performed.

Figure S4

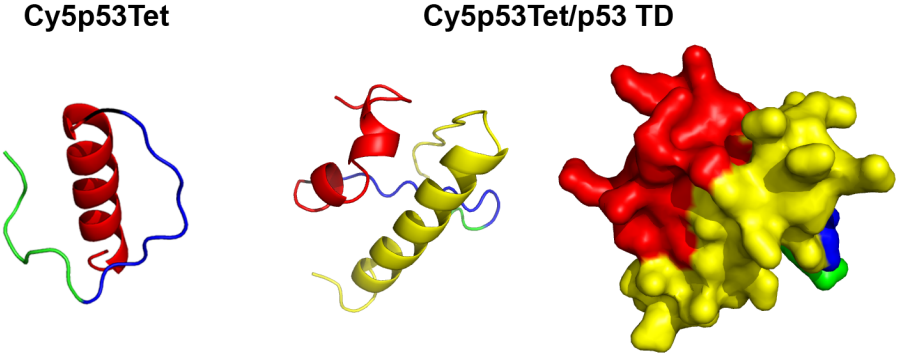

Figure S4. Prediction of p53TD and Cy5p53Tet complex by the protein–peptide globe docking method CABS-dock. (Left) Cy5p53Tet peptide structure model was generated using RPBS Mobyle portal PEP-FOLD [1, 2]. (Right) Cartoon representations of the Cy5p53Tet. Cy5p53Tet-p53TD complex built by CABS-dock [3]. Secondary structure were demonstrated and colored: HIV-1 TAT (green), p53TD β strand (blue) and p53TD α helix (red), p53TD (yellow). The analysis by CABS-dock simulation runs, using a ligand RMSD cutoff of 5.5 Angstrom, elicited a top-scored model of p53TD-Cy5p53Tet complex (average RMSD=1.63) that represents a high-quality prediction. The best docking model was displayed by PyMOL.

[1] C. Alland, F. Moreews, D. Boens, M. Carpentier, S. Chiusa, M. Lonquety, N. Renault, Y. Wong, H. Cantalloube, J. Chomilier, J. Hochez, J. Pothier, B.O. Villoutreix, J.F. Zagury, P. Tufféry, RPBS: a web resource for structural bioinformatics, Nucleic acids research, 33 (2005) W44-49.
[2] A. Lamiable, P. Thevenet, J. Rey, M. Vavrusa, P. Derreumaux, P. Tuffery, PEP-FOLD3: faster de novo structure prediction for linear peptides in solution and in complex, Nucleic acids research, 44 (2016) W449-454.
[3] M. Kurcinski, M. Jamroz, M. Blaszczyk, A. Kolinski, S. Kmiecik, CABS-dock web server for the flexible docking of peptides to proteins without prior knowledge of the binding site, Nucleic acids research, 43 (2015) W419-424.

Figure S5

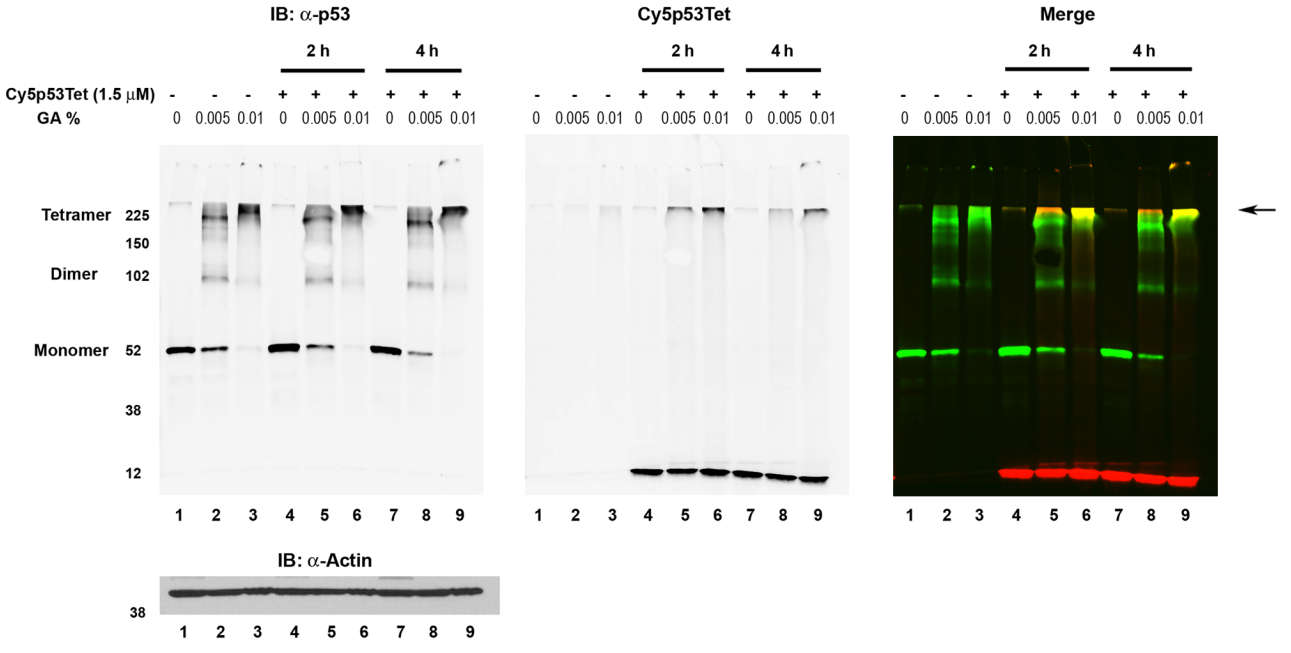

Figure S5. Glutaraldehyde cross-link assay validated Cy5p53Tet binding to tetrameric mtp53 R273H. MDA-MB-468 cells incubated with 1.5 μM Cy5p53Tet for 2 or 4 h and 100 μg of cell lysates were treated with increasing amounts of glutaraldehyde (0, 0.005% and 0.01%) for 20 min at room temperature. Western blot was carried out to detect mtp53 oligomer using anti-p53 antibody (left panel). Cy5p53Tet signal was detected using the Cy5 channel (middle panel). Merged mtp53 (green) and Cy5p53Tet (red) image suggest that a high molecular weight signal (yellow, indicate with arrow) was a mtp53/Cy5p53Tet complex (right panel).

Figure S6

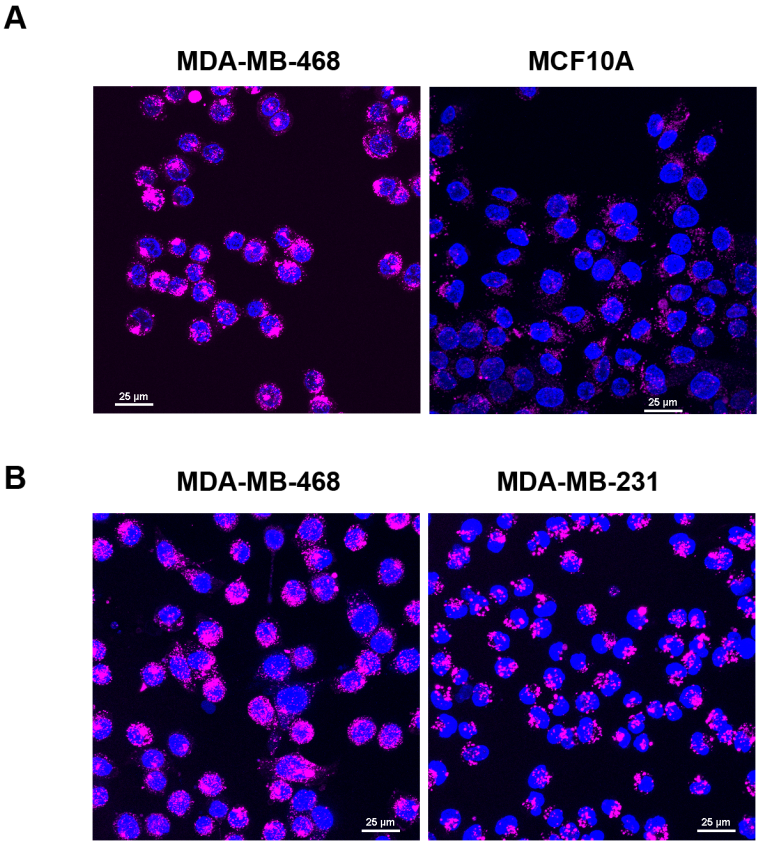

Figure S6. Different intracellular distributions of the Cy5p53Tet between TNBC and normal mammary epithelial cells. (A) Live cell imaging staining of TNBC MDA-MB-468 cells and normal mammary epithelial MCF10A cells after 3 h of incubation with 500 nM Cy5p53Tet (red). **(B)** Live cell imaging staining of TNBC MDA-MB-231 and MDA-MB-468 cells after 2 h of incubation with 500 nM Cy5p53Tet (red). Hoechst staining (blue) was used to stain the nucleus.

Figure S7

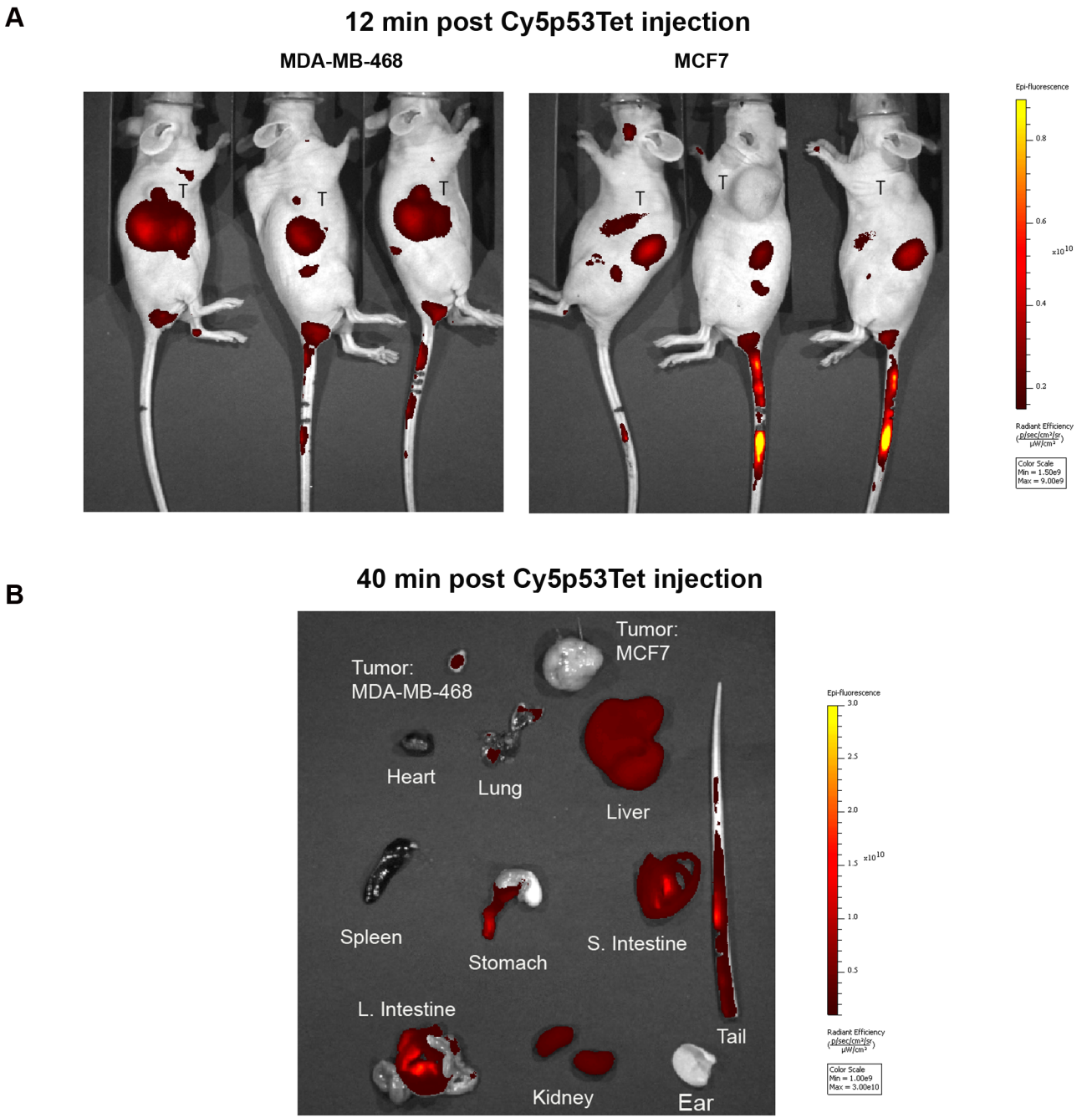

Figure S7. Cy5p53Tet signal in whole animal and healthy organs. (A) *In vivo* NIRF imaging of Cy5p53Tet uptake in mice bearing bilateral MCF7 and MDA-MB-468 xenograft models. Image acquired 12 min post-injection is shown. The tumor is marked by a "T". **(B)** *Ex vivo* NIRF imaging of Cy5p53Tet uptake in MDA-MB-468 and MCF7 tumors and organs. Image acquired 40 min post-injection is shown.