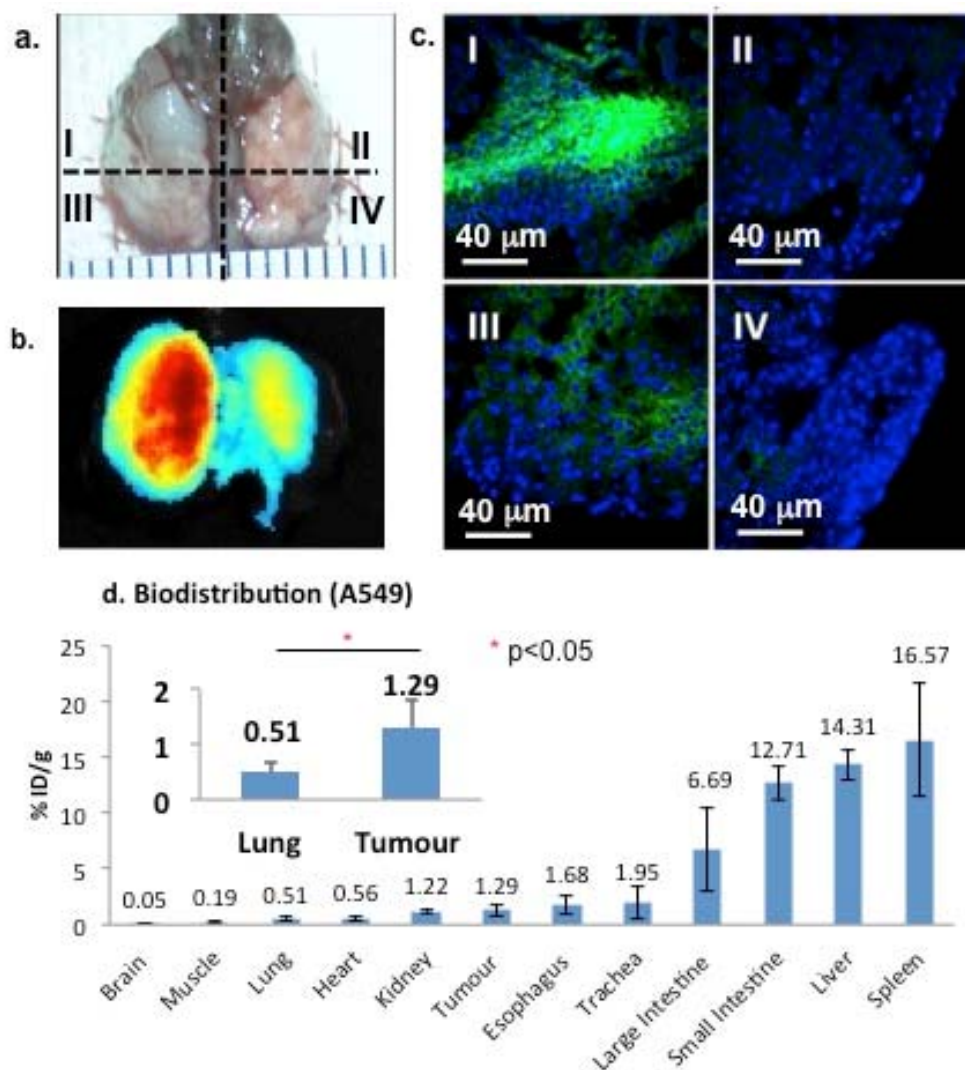
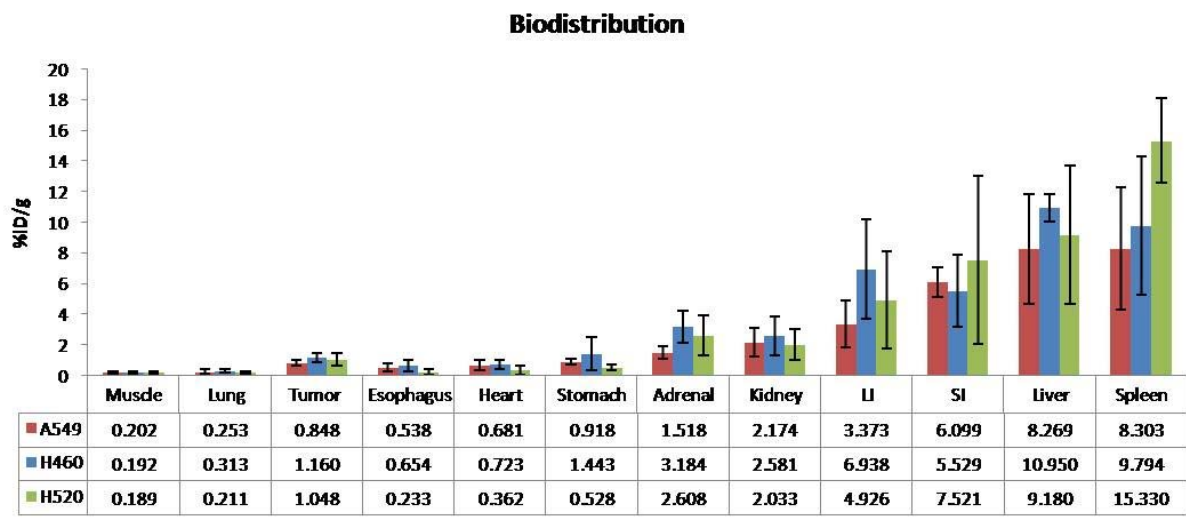


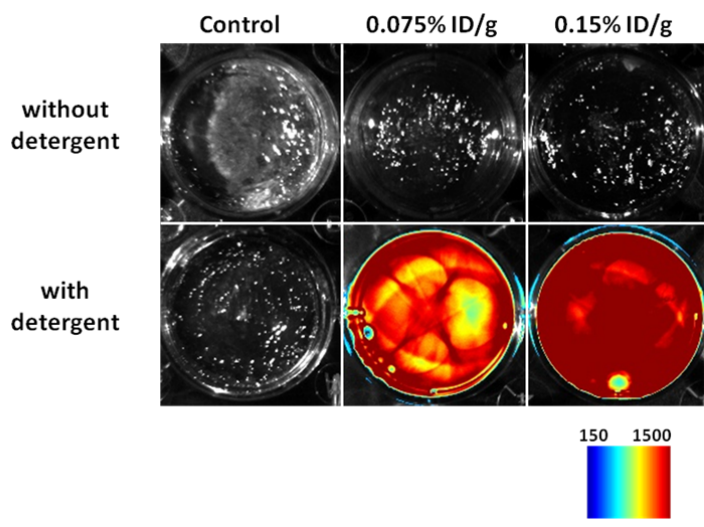
Supplementary Figures



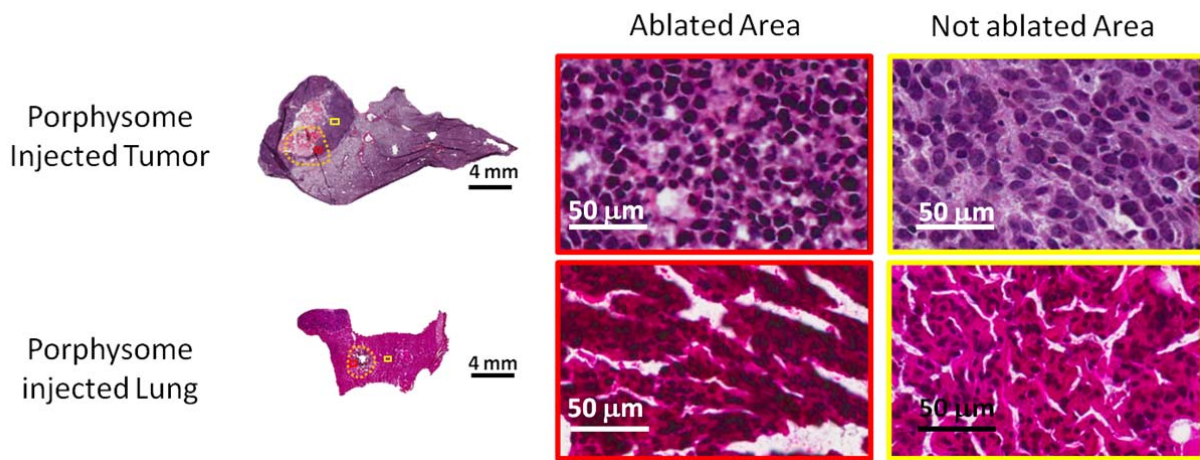
**Figure S1** Porphysome accumulation in mouse orthotopic A549 cancer at 24 h post injection. **(A)**, *ex vivo* white light image of resected lungs; **(B)**, fluorescence image (575-605 nm excitation filter and >645 nm long pass detection filter); **(C)**, confocal fluorescence microscopy (Ex: 633 nm, Em: 645-695nm) of the four sections indicated in **(A)**; **(D)**, porphysome concentration in different organs at 24 h post IV injection: means  $\pm$  S.D. (n=5). The insert shows tumor and normal lung on an expanded scale. \* represents  $p < 0.05$ .



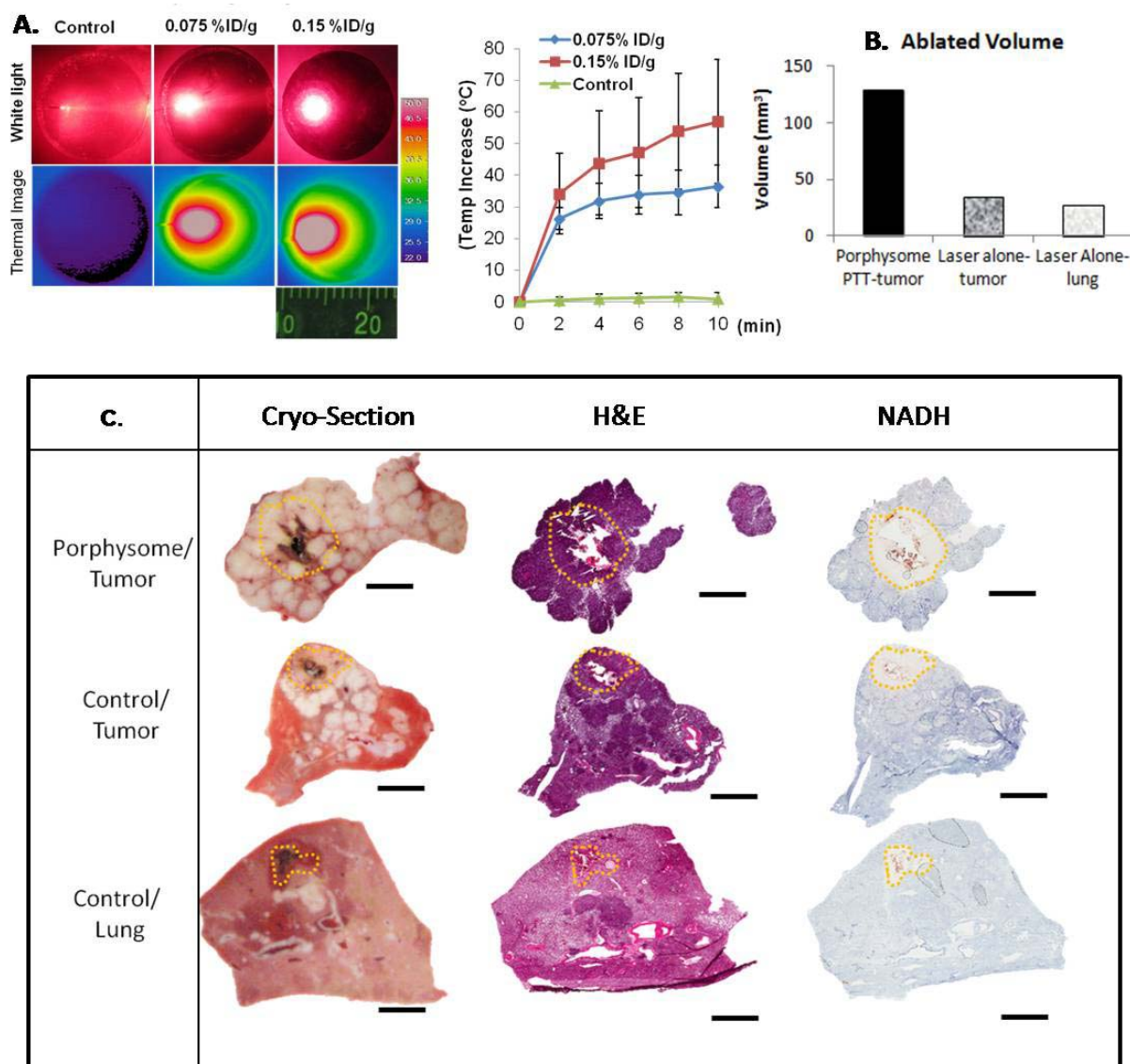
**Figure S2.** Biodistribution of porphyrins in mice bearing each of the three subtypes of human lung cancer at 48 h post-IV injection: means  $\pm$  S.D. (n=4).



**Figure S3.** Porphyrin fluorescence images in phantoms at 0, 29 and 58 nM concentration, with and without dissociation using 1% Triton-100.

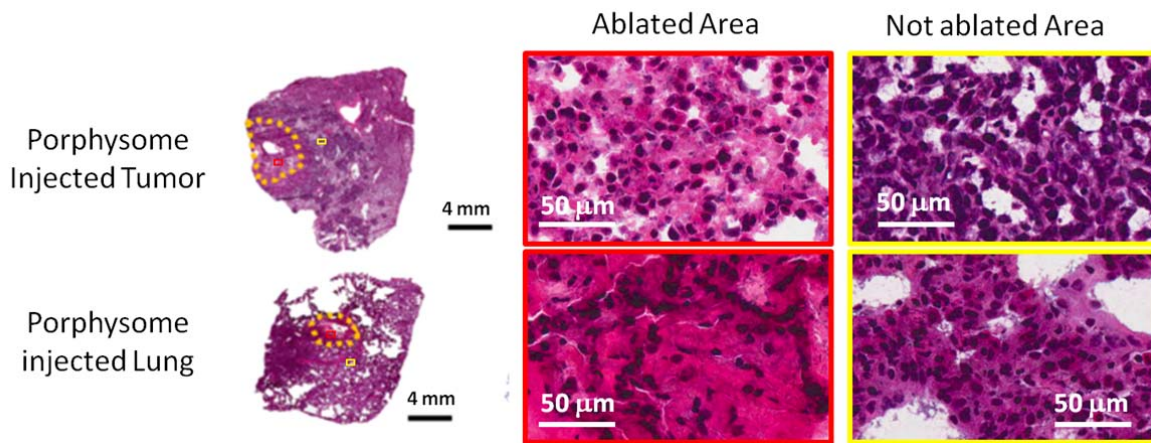


**Figure S4.** Gross sections (left) and high-resolution (20X) H&E stained tissues (tumor *versus* lung) following transbronchial PTT at 250 mW in rabbit with IV-administration of 20 mg/kg porphysomes.



**Figure S5.** *In vivo* transpleural porphysome-enabled fluorescence localization and PTT in the rabbit model using a straight-cut fiber at 500 mW/cm. **(A)** White-light and thermal camera images and corresponding temperature-time curves during PTT in phantoms using a straight-cut fiber at 500 mW laser output power and for different porphysome concentrations. n=3 for each group. The white light images show the effect of the porphysome absorption and scattering of the treatment light in the otherwise optically-transparent phantom material; **(B)** corresponding ablated volume in VX2 tumor in rabbit using the same laser irradiation at 48h after IV injection of 20 mg/kg porphysomes (n=2) or

control with no porphysome administration (Tumor without porphysomes: n=2), lung without porphysomes: n=1); (C) examples of corresponding gross histology: the orange dotted line was identified based on NADH stained slide, indicating the ablated area (scale bars: 4mm).



**Figure S6.** Gross sections (left) and high-resolution (20X) H&E stained tissues (tumor *versus* lung) following transpleural PTT at 500 mW/cm in rabbit with IV-administration of 20 mg/kg porphysome. The cells were considered as thermally killed based on deep eosinophilic-staining cytoplasm and hyperchromatic nuclei with loss of nuclear detail.