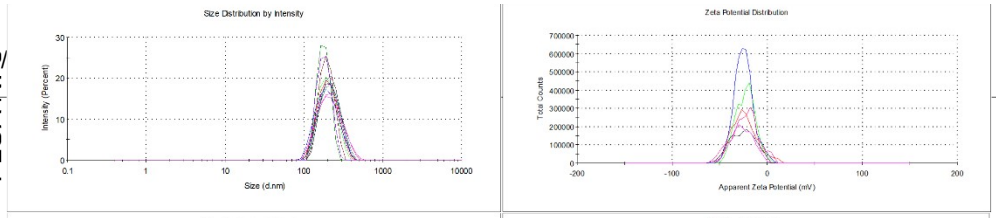
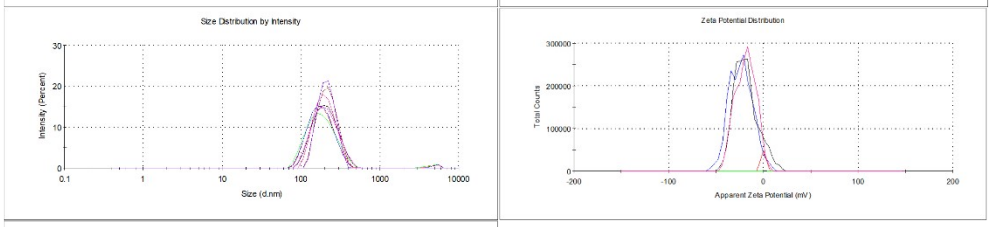
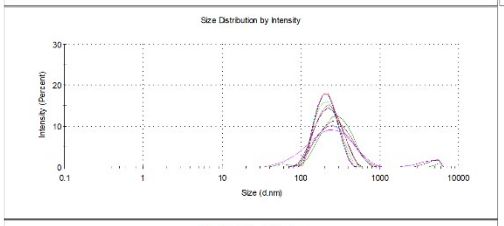
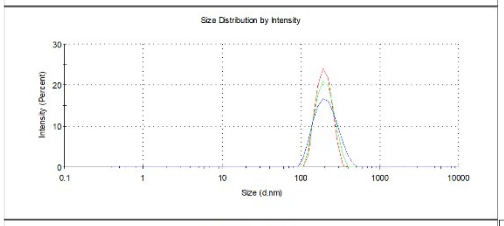
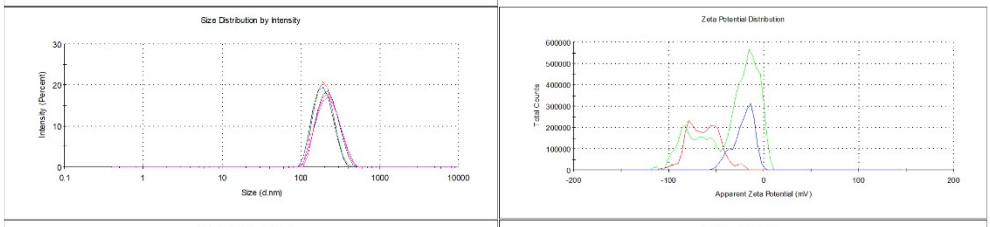
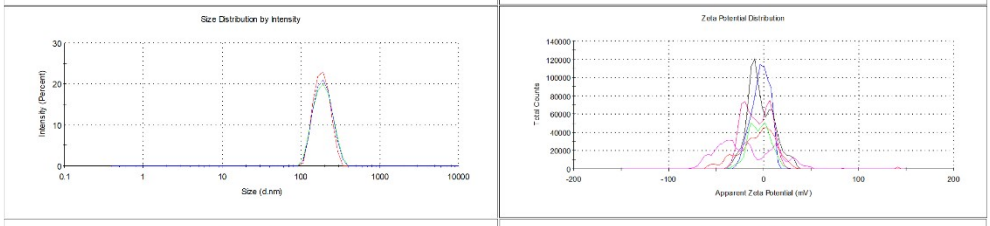
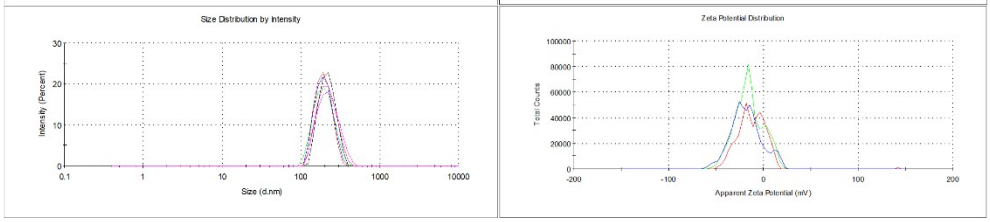
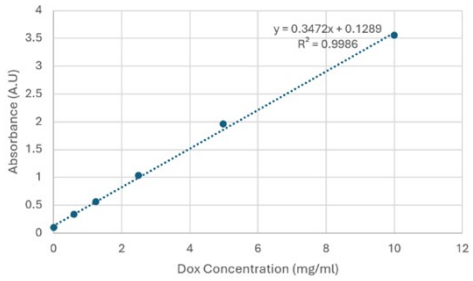
Dox Concentration (mg/	NPs
PLGA NPs	
PLGA-Tz	
PLGA-RhB	
PLGA-RhB-Tz	
PLGA-Dox	
PLGA-Dox-9Tz	
PLGA-Dox-21Tz	

Absorbance (AU)	0.084	0.330	0.560	1.026	1.946	3.555	2.042

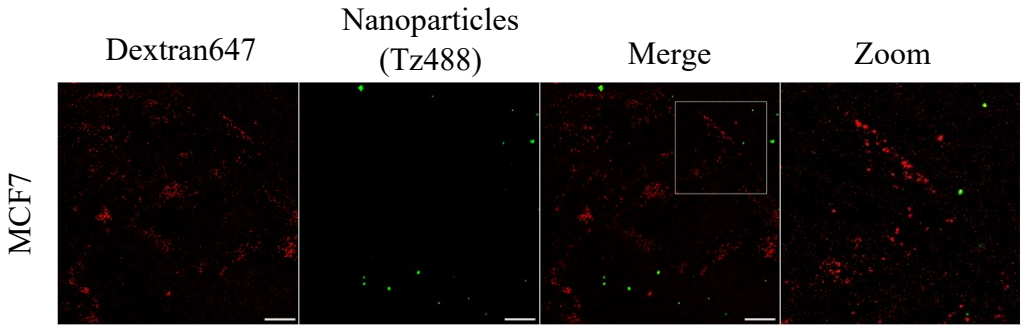
$$Encapsulation\ Efficiency = \frac{Encapsulated\ Doxorubicin}{Loading\ Doxorubicin} \times 100$$

$$Encapsulation\ Efficiency = \frac{5.51mg}{10mg} \times 100$$

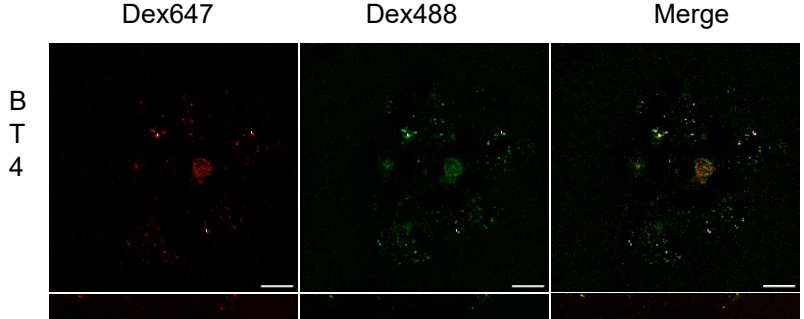
$$Encapsulation\ Efficiency = 55.1\%$$

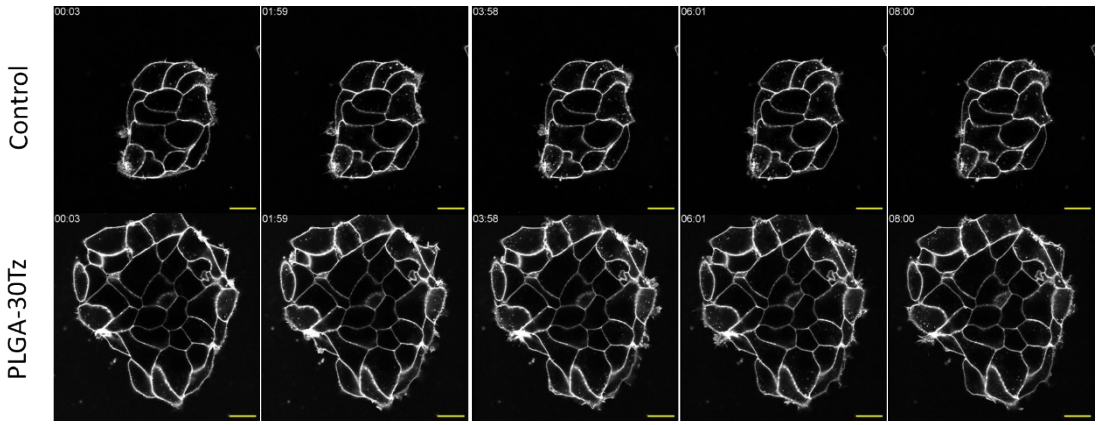


Supplementary Figure 2: Representative example of a calculation to determine encapsulation efficiency of Dox in PLGA NPs. Absorbance (490nm) was measured using a Tecan Infinite M Plex Plate Reader.

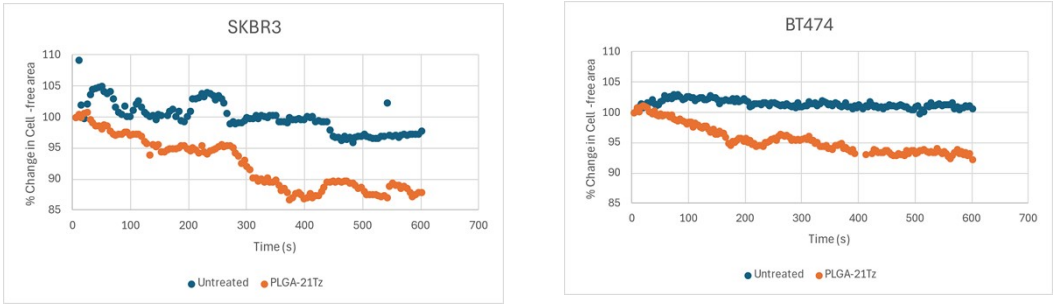


Supplementary Figure 3: HER2-low MCF7 cells treated with the lysosomal marker dextran-647 (Red) for 2 hours before washing and further treatment with PLGA-Tz (green) for 24 hours. Compared with HER2^{++} cells (Figure 3) there is very little evidence of binding and internalisation. Scale bar 20μm





Supplementary Figure 5: BT474 cells pre-treated with CellMask Deep Red were treated with PLGA-21Tz and imaged for 10 minutes capturing plasma membrane reorganisation. Images shown are from frames taken approximately 2 minutes apart. Minor increases in membrane activity are observed, albeit not as dynamic as those seen in the SKBR3 cells. Scale bar 20μm.



Supplementary Figure 6: Change in area over time across cells treated with PLGA-21Tz in Figure 4 and Supplementary Figure 5. Increases in total cell area is reflected by a decrease in cell-free area. In the SKBR3 cells the untreated cells show some variation however it does not substantially deviate from the baseline, in comparison the PLGA-21Tz treated cells show 10% reduction in cell-free area.