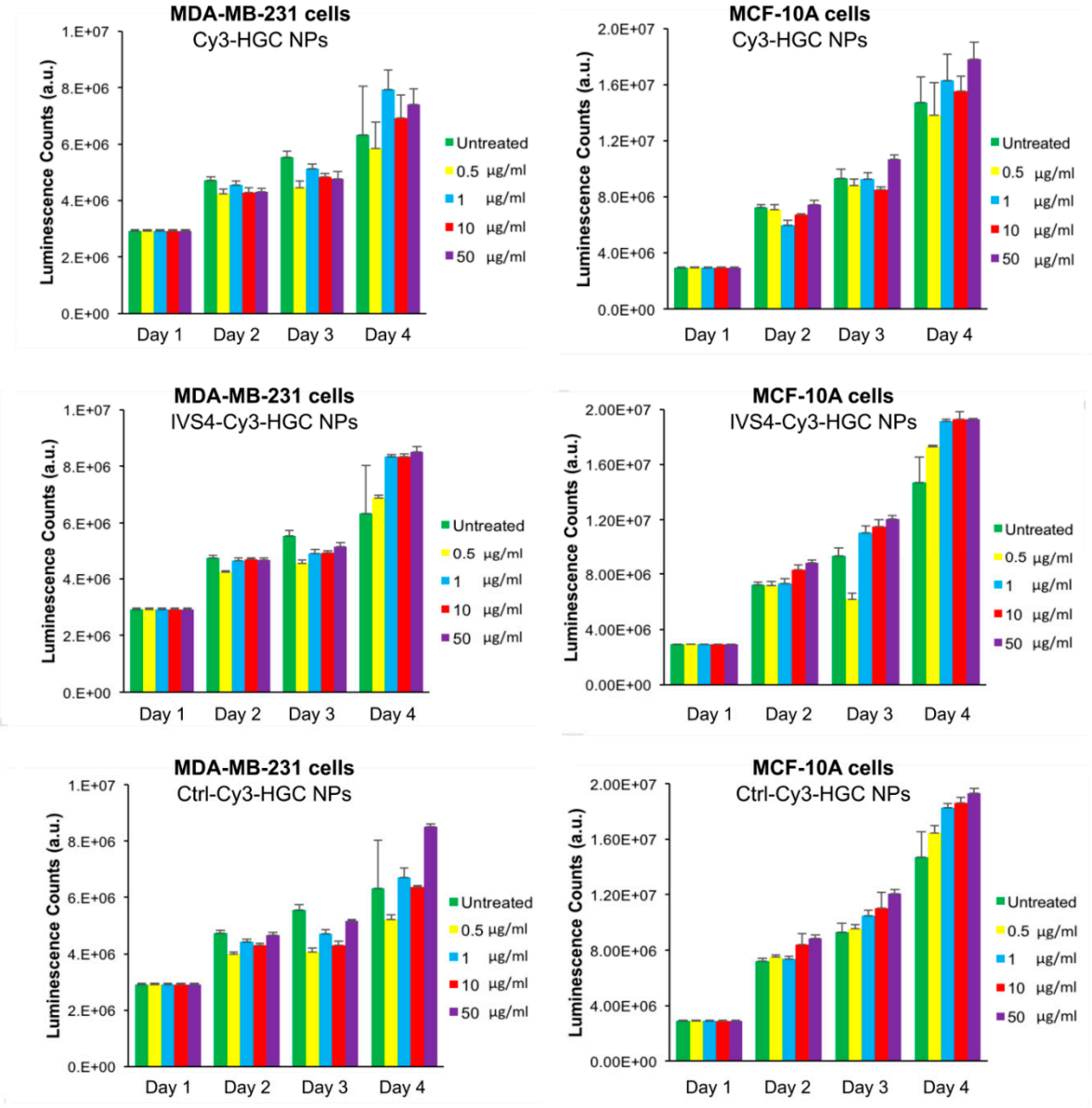
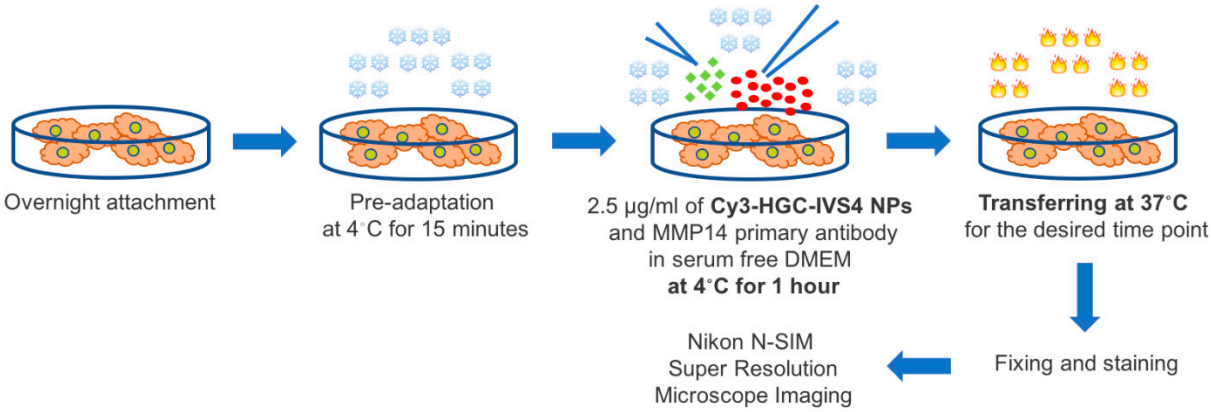
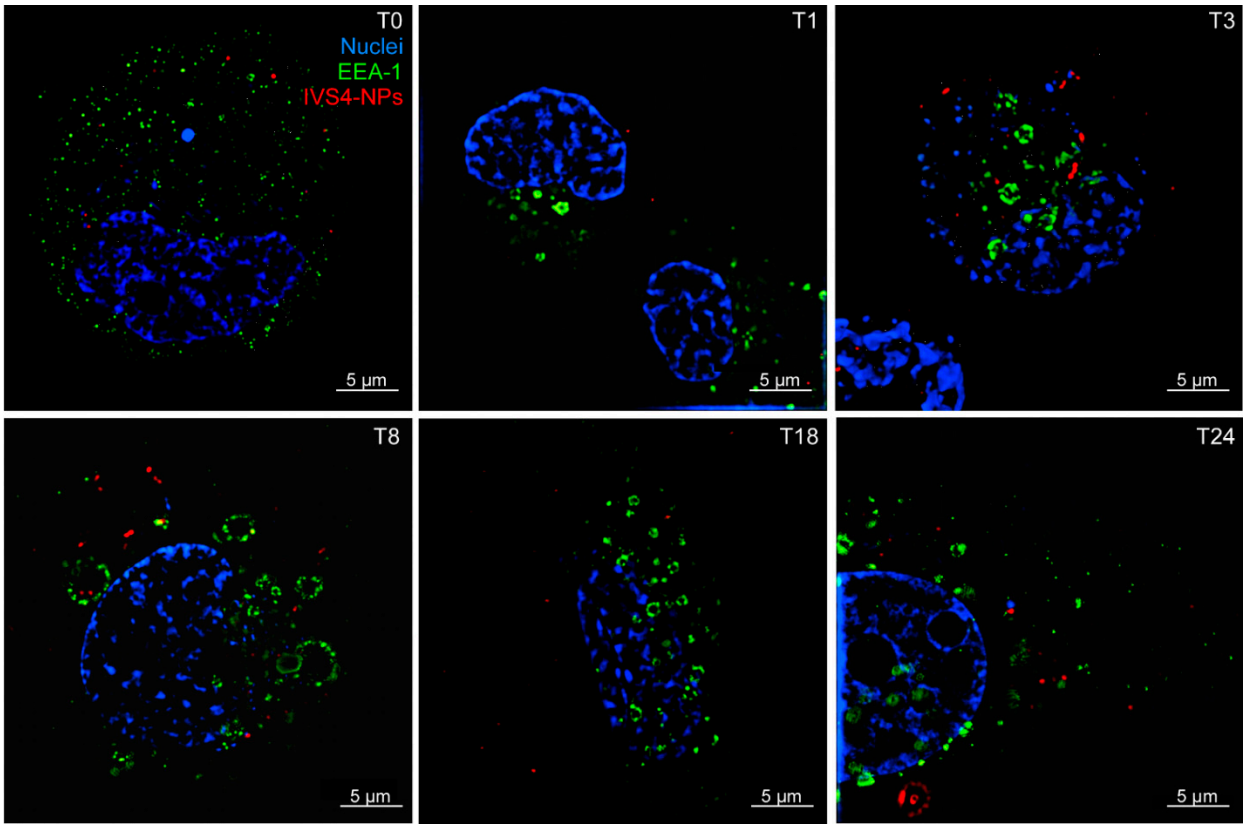
Supplemental Materials



Supplementary Figure S1. Cell viability of cancerous and non-cancerous breast cancer cells treated with empty NP vehicles. Cell viability of MDA-MB-231 cells and MCF-10A cells treated with different nanoparticles (NPs), continuously, for up to 3 days. Error bars refer to the standard error of a representative experiment performed with triplicates.



Supplementary Figure S2. Schematic of the experimental protocol for the in vitro endocytosis assay. Flow diagram depicting the plating, the treatment and the post processing of the internalization mechanism experiment. MDA-MB-231 cells were treated with 2.5 µg/ml of IVS4-Cy3-HGC NPs and with the primary antibody for MMP-14. After a pre-adaptation step at 4 °C for 15 minutes, cells were incubated at 4 °C for 1 hour with the functionalized NPs and the primary antibody to slow down the internalization process and endocytic recycling. Subsequently, cells were washed with cold PBS to remove unbound NPs and transferred to a 37 °C incubator. At specific time points samples were fixed, stained, and prepared for Super-resolution Illumination Microscopy.



Supplementary Figure S3. Super-resolution structured illumination microscopy images of MDA-MB-231 cells show that the endosomal structure (green channel) swelled in size from 0 to 8 hours post-delivery, and then began to decrease again. IVS4-NPs (red channel) appeared to be entrapped inside the endosomes up until 8 hours, after which they were no longer co-localized.