12.05 pm **Multimodal in vivo evaluation of a surface-converting nanoparticle platform**

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Active targeting of nanoparticles through surface functionalization with ligands such as antibodies, peptides or nucleic acids has shown significant advantages in preclinical cancer nanotherapy studies. However, in the bloodstream, targeting moieties present on the nanoparticle surface may cause elevated recognition by the mononuclear phagocyte system and thereby compromise nanoparticle pharmacokinetic characteristics. To overcome this limitation, we have developed a new lipid-PLGA nanoparticle platform, which is decorated with RGD peptides but is shielded by a matrix metalloproteinase-2 (MMP2) cleavable polyethylene glycol (PEG) coating to prevent NP/cell interaction in the bloodstream. Once the nanoparticles accumulate within the tumor microenvironment and are exposed to MMP2, the enzymatic cleavage of the PEG polymers leads to the surface exposure of the targeting peptides.

Using an in vivo multimodal imaging strategy involving nuclear, magnetic resonance and optical imaging approaches in an orthotopic murine breast cancer model, we observed that this new enzyme specific surface-converting coating strategy led to prolonged blood circulation and passive accumulation of the nanoparticles in the rim of the tumors. Subsequent ex vivo flow cytometry measurements revealed that our surface-converting nanoparticles exhibited higher tumor cells targeting efficiency compare to control nanoparticles. These results demonstrate that our surface-converting coating ensures a high cell-targeting specificity without compromising favorable nanoparticle pharmacokinetics. We believe that this highly modular strategy can easily be tailored for other types of cancer or inflammatory conditions.