Fate Controllable Clickable Albumin nanoplatform by Distinct Glycation for in-vivo Cell Targeting

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Despite extensive research in the field nano medicine, delivery efficiency of nano particles (NPs) were generally found to be low in the pooled data analysis. One of the reasons for this poor targeting ability using nanoparticles is a short circulating half-life as a result of fast removal of NPs by the reticular endothelial system (RES). In this regard, albumin is one of the most attractive nano platforms because it is not immunogenic and exist in blood flow for a long time without being removed by RES. But in many reported albumin nano platform research, circulation half-life was short and varied. The surface chemistry of NP can determine the immune response and biodistribution. So un-controlled surface chemistry and size change of albumin NPs through the additional functional group or drug loading were possible factors of the immune response and shortening circulation half-life. To circumvent these problems, we recently reported a click chemistry-based nanoplatform in which a clickable albumin nanoplatform (CAN) was easily functionalized for in vivo imaging with sufficient circulation half-life. Moreover, as the physical and radiochemical properties of albumin were maintained to some extent during functionalization, the potency of HSA in vivo may be further amplified by the EPR effect, as well as the secreted protein acidic and rich in cysteine (SPARC) produced in the local metastatic microenvironment, thereby facilitating cellular internalization of HSA within the metastatic sites[1,2,3]. To specifically target tumor-associated macrophages (TAM) observed in the tumor microenvironment (TME), we optimized an albumin nano-platform with mannose as the targeting moiety. Through this optimization, we developed the macrophage-targeted probe, Mannosylated Alb (Man-Alb), particularly designed for in vivo lung imaging. The probe, Man (6)-Alb, was engineered with six mannose molecules to achieve an optimized blood circulation time. Thus, MSA could be a promising monitoring tool that can provide additional information regarding the degree of metastatic disease, which is instructive for the early diagnosis of metastasis and therapeutic interventions[4].

In this study, using the finely controlled albumin nanoplatform, three sugars were introduced on surface of nanolatform having same glycation level, and the bio-distribution was confirmed by PET image in the body while maintaining all other conditions. Using Galactosyl- or Mannosyl-, we made a platform that is completely ingested into different types of cells in the liver in-vivo, and also evaluated the ability to target GLUT for detecting cancer using albumin that has been strictly introduced with glucosylated albumin. We evaluated in vivo kinetics through image-based analysis at the cellular level and examined the differential uptake tendencies within tumor regions of cancer models. Furthermore, these findings were validated through nuclear medicine imaging-based macro-scale evaluations, fluorescence-based micro-scale assessments and spatial transcriptomics.

References:

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