Nanoparticle-mediated intratumoral platelet deletion improves drug penetration and accumulation in tumors by augmenting EPR effect

Supported by the National Distinguished Young Scientist Program and National Natural Science Foundation of China, the research group led by Prof. Nie GuangJun (聂广军) from the National Center for Nanoscience and Technology of Chinadevelops a new strategy to specifically destabilize tumor vasculature and increase its leakage, which is crucial for nanomedicine application for cancer therapy. This creative study was published in *Nature Biomedical Engineering* (2017, 8: 667—679).

Platelets are shown to be loyal guardians of tumor vessels, where they protect vascular integrity and prevent tumor hemorrhage by secreting granule contents and/or directly adhering to neutrophil-induced vascular breaches. With these findings in mind, the authors hypothesized that targeting platelets may represent an effective method to destabilize tumor vasculature and consequently augment the enhanced penetration and retention (EPR) effect, which is essential for promoting nanoparticle extravasation in tumor tissue. To test this hypothesis, they constructed a hybrid nanoparticle comprising lipid and polymer loaded with chemotherapeutic drug doxorubicin and R300, an antiplatelet antibody. The nanoparticles were coated with a shell layer composed of matrix metalloproteinase 2 (MMP2)-cleavable peptides, conferring the particles an active targeting ability to tumors. In various tumor-bearing mouse models, these nanoparticles selectively deleted intratumoral platelets after intravenous administration and increased the size of fenestrations of tumor vasculatures, consequently enhancing doxorubicin accumulation in tumors.

These researchers have successfully developed a nanoparticle-based strategy for increasing EPR effect of tumor vessels, and believe that this drug delivery platform may benefit not only nanomedicines, but all drugs in general. This study is potentially applicable for various combinations therapies (such as chemotherapy, gene therapy and immunotherapy). Further preclinical and clinical developments are urgently needed.

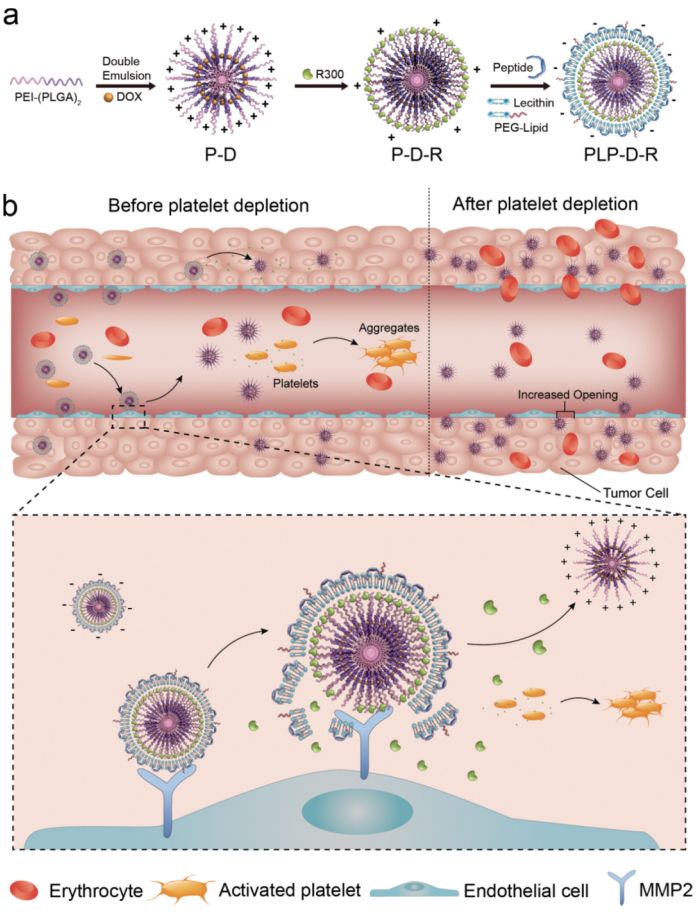

Figure Design features and proposed mechanism of nanoparticles in tumor blood vessels *in vivo*.