Circumvention of biological barriers for improved therapeutic delivery

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Successful accumulation of therapeutics specifically at diseased sites is mainly limited by biological barriers to therapeutic transportation, which includes the nonspecific uptake of drug carriers in mononuclear phagocyte system (MPS). Hence, it is critical to develop therapeutic delivery systems that can specifically act on diseased cells. In this presentation, strategies that can circumvent biological barriers will be demonstrated for improved therapeutic delivery. We will illustrate a versatile approach for the engineering of polymer nanoparticles (NPs) with tunable physicochemical properties (e.g., size, components, stiffness, surface chemistry) via the replication of metal-organic frameworks. Specifically, stealth poly(ethylene glycol) (PEG) NPs are prepared and can avoid the secretion of anti-PEG antibodies. The presence of anti-PEG IgM and IgG does not significantly accelerate the blood clearance of PEG NPs, indicating the inhibition of accelerated blood clearance effect for PEG NPs. Functionalization of the PEG NPs with HA affords PEG NPs that retain their stealth properties against macrophages, and when loaded with the anticancer drug doxorubicin, effectively target CD44-expressed cancer cells and inhibit tumor growth. In addition, hydrogels in combination with NPs, which are used to encapsulate therapeutics (e.g., drugs, enzymes, antibodies, adjuvants), are used as postsurgical drug carriers at the tumour sites for combinational chemo-immunotherapy. The demonstrated strategies highlight the advances of the designed therapeutic carriers in cancer therapy.

References:

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