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Intelligent nanoparticles for combination photo-immunotherapy of cancer

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Photo-immunotherapy (PIT) has emerged as a promising clinical modality for cancer therapy due to its ability to initiate an antitumor immune response. However, PIT is severely impaired by tumor cell immunosuppression of host T-cell antitumor activity through the programmed cell death 1 ligand (PD-L1) and programmed cell death receptor 1 (PD-1) (PD-L1/PD-1) immune checkpoint pathway. In this study we demonstrate that PIT can be augmented by PD-L1 knockdown (KD) in tumor cells. We rationally designed a versatile micelleplex by integrating an acid-activatable cationic micelle, photosensitizer (PS) and small interfering RNA (siRNA). The micelleplex was inert at physiological pH conditions and activated only upon internalization in the acidic endocytic vesicles of tumor cells for fluorescence imaging and PIT. The combination of PIT and PD-L1 KD showed significantly enhanced efficacy to inhibit tumor growth and distant metastasis in a B16-F10 melanoma xenograft tumor model. These results suggest that acid-activatable micelleplexes utilizing PDT-induced cancer immunotherapy are more effective when combined with siRNA-mediated PD-L1 blockade.

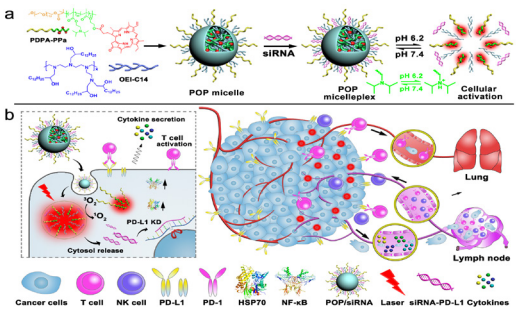

Figure-1: Schematic illustration of POP–PD-L1 micelleplex mediated photo-dynamic cancer immunotherapy.

Biography

Yaping Li has received his PhD degree in Fudan University in 2001. He has devoted himself in drug targeted delivery based on nanotechnology, mainly involved in reversing MDR and improving pharmacological efficacy of antitumor agents, designing and constructing new non-viral vector for gene delivery. He has published over 150 scientific papers in *Nat Medicine, Adv Mater, ACS Nano, Adv Funct Mater, Small, Biomaterials, Nanomedicine NBM, J Control Release*, etc. He is the Chief Scientist of National Basic Research Program of China in Nanoscience and Nanotechnology (2009), Vice Chairman of Pharmaceutics Society of Shanghai Pharmacy Association, Member of Council, Shanghai Pharmaceutical Association and Member of Branch of China in the International Controlled Release Association (CRS).

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