Living macrophage-based drug promotes antitumor immunotherapy

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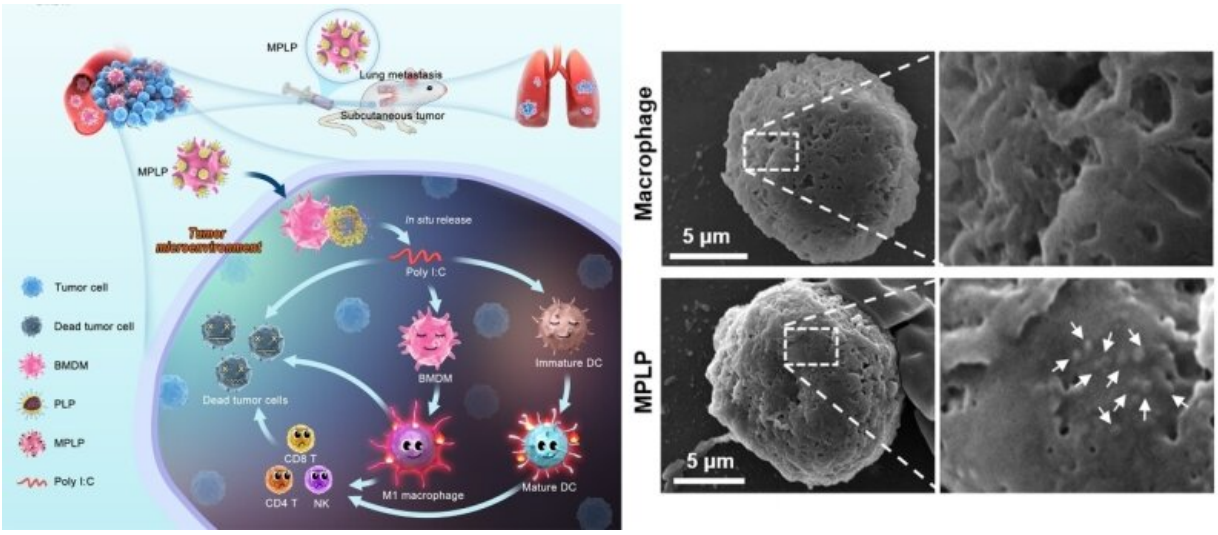

Schematic depiction of PLP NPs loaded on BMDM surface (MPLP). Credit: SIAT

Immunotherapy is one of the most promising approaches to inhibit tumor growth and metastasis by activating host immune functions. However, so far, immunotherapy still exhibits limitations of efficacy and safety, such as huge individual differences in treatment responses, difficulty to work on solid tumors, systemic immune storm and other immunotoxicity.

Therefore, the development of advanced strategies to activate in situ

tumor-specific immune response for the anticancer immunotherapy is highly desirable.

A research team led by Prof. Cai Lintao at the Shenzhen Institutes of Advanced Technology (SIAT) of the Chinese Academy of Sciences developed a "cytopharmaceutical" based on living macrophages. The study was published in *Biomaterials*, Jan. 7.

As important immune cells, macrophages not only directly kill tumor cells, but also present antigens to effector cells as antigen-presenting cells. What's more, they can also form antigen-specific immune memory, allowing the body to trigger a stronger immune response when specific antigen appear again.

In previous studies, macrophages were usually used as drug carriers and did not effectively exert their anti-tumor immunity after entering the tumor microenvironment. Therefore, it will be a promising tumor treatment strategy of using natural living macrophages as drug carriers and maintaining the anti-tumor immunity of macrophages.

In this study, Cai's group constructed Poly I: C-encapsulated poly (lactic-co-glycolic acid) nanoparticles (PLP NPs) with a slow release profile. They synthesized a biomimetic system (MPLP), which loaded PLP NPs on the surface of bone marrow-derived macrophage (BMDM) via the maleimide-thiol conjugation. This system could effectively deliver PLP, control drug release and activate the tumor-specific immune response in situ.

"PLP NPs loading does not affect the activity and function of BMDM. BMDM acts as a living cell drug vehicle and promotes the accumulation of PLP NPs in tumors, where Poly I: C is released from PLP NPs and reprograms BMDM into tumoricidal M1 macrophage," said Prof. Cai. "MPLP triggers potent antitumor immune responses in vivo and

effectively inhibits local and metastatic tumors without causing adverse pathological immune reactions."

The study offers an inspiration to facilitate clinical translation through the delivery of drugs by living immune cells for future anticancer therapy.

More information: Haimei Zhou et al. In situ Poly I:C released from living cell drug nanocarriers for macrophage-mediated antitumor immunotherapy, *Biomaterials* (2021). DOI: 10.1016/j.biomaterials.2021.120670

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