TME-Modulating Bionanomedicine to Improve CAR T-Cell Infiltration and Potency in Solid Tumors

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Chimeric Antigen Receptor (CAR) T-cell therapy is facing significant challenges in treating solid tumors.[1] One of the main challenges is immunosuppressive Tumor Microenvironment (TME), which has been extensively characterized as hostile for CAR T-cells. The project aims to develop novel nanoparticles (NPs) to administer immunomodulatory drugs to the tumor site in a safer, more controlled manner that could enhance their therapeutic potential and reduce toxicity. [2,3]

Our hypothesis is that stimuli-sensitive polymeric nanomaterials can be modified with functional groups and tumor-targeting peptides, making them selectively accumulate in the tumor area for a prolonged period and normalize the cellular and vascular microenvironments in solid tumors while actively attracting immune cells, which will greatly augment both the infiltration and potency of CAR T-cells at the tumor site. [4,5] To date, we have successfully designed and synthesized a functional biomaterial. By conjugating drugs/cytokines and incorporating enzyme-responsive linkers to form a prodrug system, we have preliminarily demonstrated its blocking capability and cytokine efficacy upon linker cleavage. Further optimization of key parameters and functional enhancements are underway, after which the system will be subjected to in vivo characterization.

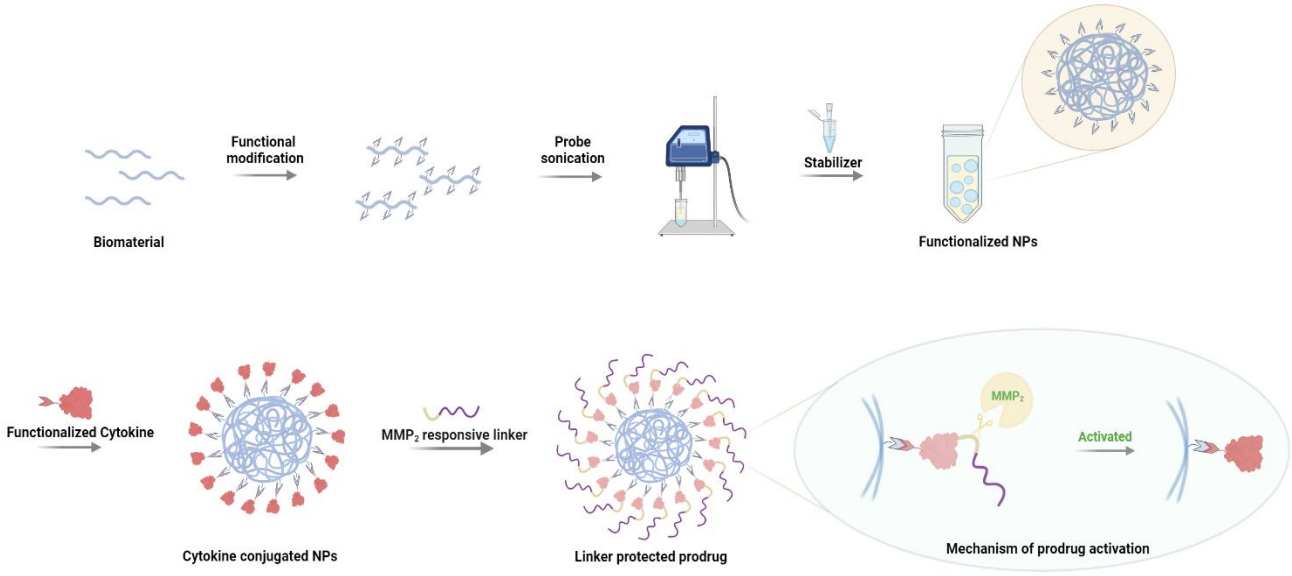

Figure 1: Design and mechanism of functional prodrug-based targeted cytokine delivery.

References:

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[4] Yu, Gaoyu, et al. "Recent Advancements in Biomaterials for Chimeric Antigen Receptor T Cell Immunotherapy." *Biomaterials Research* 28 (**2024**).
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