MAG-based Glycopolymers for Enhanced Immune Cell Activation

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Sugar chains play critical roles in biological processes such as cell signalling and molecular recognition. Pathogen recognition by C-type lectin receptors (CLRs) expressed by DCs is important not only for antigen presentation, but also for the induction of appropriate adaptive immune responses.[1] Indeed, CLR-binding carbohydrates are potential therapeutic reagents for cancer immunotherapy. And the lectins on macrophage surfaces are able to induce intracellular killing mechanisms when bound to their specific glycan ligands.[2] Synthetic polymers with pendent carbohydrate moieties widely called 'glycopolymers'[3] have attracted much attention in intensive research and biological engineering due to advancements of polymerization techniques and their ability of mimicking biological functions in recognition processes. Herein reversible addition-fragmentation chain transfer (RAFT) polymerization of N-3,4-dihydroxybenzenethyl methacrylamide (DMA) and 2-(methacrylamido) glucopyranose (MAG) is employed to fabricate multivalent glycopolymer under sunlight irradiation using 2-cyanoprop-2-yl-α-dithionaphthalate (CPDN) as iniferter agent, and the polymer is further utilized to design "pathogen-mimetic" glycoadjuvant recognized by both CLRs and Toll-like receptors (TLRs) that can enhance the adjuvant activity as "infected signals" in vitro. Furthermore, a new chem-bio strategy was developed to modify the surface glycocalyx of cancer cells by combining HaloTag protein (HTP) fusion technique with RAFT polymerization. Using this approach, synthetic well-defined glycopolymers containing MAG units were introduced and stably presented on the cell surface via the stable covalent binding of chloroalkane-terminated polymers with membrane-bound HTP. The glycopolymer-engineered HeLa cells with HTP anchors increased expression of M1-sepcific marker CD86, and upregulated secretion of pro-inflammatory cytokines (IL-12p70, TNF-α and NO), promoting M1 polarization of macrophages and also promoted the maturation of dendritic cells, demonstrating the strong potential of MAG in cancer immunotherapy.

References

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