Nano-Gel-Nano vaccines for immune modulation to treat cancers

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Cancer immunotherapies have low response rates due to immunosuppressive tumor microenvironments (TMEs)[1]. To alter unfavorable TMEs, supplementing tumor-associated antigens and stimulating the immune cells in the target sites are indispensable in eliciting antitumoral immune responses[2]. Herein, we propose a localized and multi-target nano-gel-nano system that 1) can load both chemicals and adjuvants by simple mixing, 2) transform from solution to gel after injection for local and long-term existence, 3) release the nanocomplexes from the hydrogel which deliver drugs to cancer and immune cells via active and passive targeting, respectively, over a long term. The polymer for the nano-gel-nano system was synthesized. Isoleucine ethyl ester, amino ethyl methacrylate, and amino polyethylene glycol (AMPEG) were added slowly to poly(dichlorophosphazene) in dry tetrahydrofuran including trimethylamine. And RC peptides were conjugated in dimethylformamide. The polymer formed nano-sized complexes with drugs via ionic interaction at low temperatures. The polymer/drug solution showed temperature-dependent sol-gel transition and released nano complexes from the hydrogel was also. Besides, the maintenance of hydrogel after injection was observed for 3 weeks with drugs. After administration of the nano-gel-nano system to tumor-bearing mice, whether local immunogenic responses in primary tumors could elicit systemic therapeutic effects on distant tumors was checked. Regressed secondary tumor formation was observed in the experimental group and it was related to increased memory T cells. It suggested therapeutic efficacy of the system induces long-lasting immune responses by maintaining the activity of memory T cells against tumors. We developed the nano-gel-nano system for effective *in situ* cancer vaccines for extended periods with a single intratumoral administration and it could be applied to various cancers as a patient-specific therapy

References

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