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VIRUS-LIKE DNA, A SINGLE-AGENT POLY-FUNCTIONAL THERAPEUTIC PLATFORM THAT POTENTLY ACTIVATES ANTI-CANCER PROTECTIVE IMMUNITY

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Background Combination immune therapy has demonstrated curative potential in multi-agent pre-clinical studies and early clinical studies. We have created a single-agent combination immune therapy platform, dubbed virus-like DNA (VLD), to activate multiple anti-cancer immune signals leveraging the robust T cell responses elicited by viral infection. VLD was designed to avoid neutralizing antibody responses, immunotherapy-mediated toxicities, and extensive manufacturing cost and time. VLD comprises of a) antigen, composed of a polypeptide selected based on genomic variants to activate CD4+ and CD8+ T cells, b) a proprietary protein that activates three independent T helper 1 and cytotoxic T cell signaling pathways, and c) a proprietary dual CTLA-4/PD-1 engaging agent. We hypothesized that a rationally-designed combination of different classes of immune modulating factors will elicit tumor antigen-specific effector T cell responses and eradicate established tumors.

Methods Mice were implanted with tumor cells prior to treatment with VLD. VLD expressing immunomodulators and predicted T cell epitopes was administered intravenously to tumor-bearing mice. Tumor measurements and animal health were monitored for the ensuing 2 months, upon which, surviving animals were rechallenged with tumor cells.

Results Intravenous administration of VLD to animals with established tumors completely eradicated or significantly delayed tumors in recipient animals. Combining VLD with anti-PD-L1 far outperformed anti-PD-L1 alone which was not significantly better than untreated controls. Furthermore, rechallenge of tumor-free animals with tumor cells demonstrated complete protection 60 days after initial challenge, suggesting VLD-mediated formation of immunological memory. VLD's combination of immunomodulators uniquely activated splenic effector memory and antigen-reactive CD8+ T cells.

Conclusions These data suggest that VLD provides a scalable, modular, rapid, robust, and cost-effective means of inducing a durable anti-tumor host response by harnessing critical components of vaccines and gene therapies into one immunogene product to eradicate cancer by activating antigen-reactive T cells.

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