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STINGel: Controlled Release of a Cyclic Dinucleotide for Enhanced Cancer Immunotherapy

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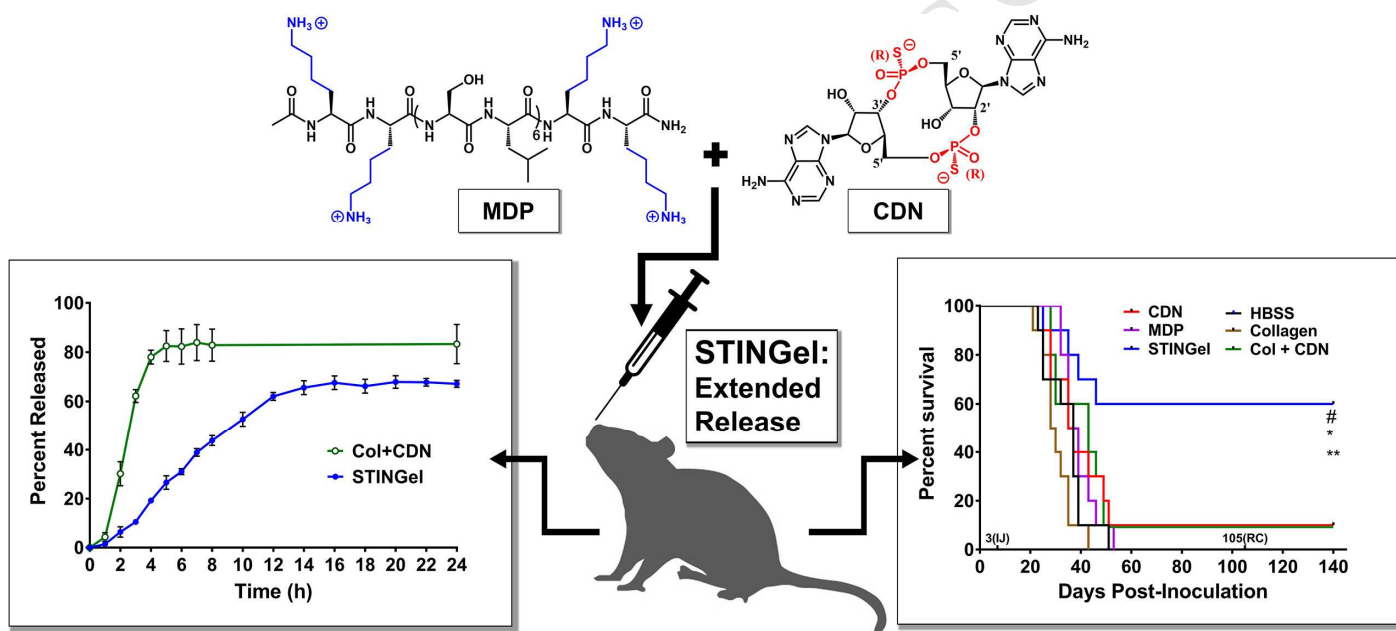
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Graphical Abstract**Abstract**

Recent advancements in the field of immunotherapy have yielded encouraging results for the treatment of advanced cancers. Cyclic dinucleotides (CDNs) are a powerful new class of immunotherapy drugs known as STING (Stimulator of Interferon Genes) agonists, currently in clinical trials. However, previous studies of CDNs in murine cancer models have required multiple injections, and improve survival only in relatively nonaggressive tumor models. Therefore, we sought to improve the efficacy of CDN immunotherapy by developing a novel biomaterial we call “STINGel.” STINGel is an injectable peptide hydrogel that localizes and provides controlled release of CDN delivery, showing an 8-fold slower release rate compared to a standard collagen hydrogel. The carrier hydrogel is a positively charged, MultiDomain Peptide (MDP) which self-assembles to form a nanofibrous matrix and is easily delivered by syringe. The highly localized delivery of CDN from this nanostructured biomaterial affects the local histological response in a subcutaneous model, and dramatically improves overall survival in a challenging murine model of head and neck cancer compared to CDN alone or CDN delivered from a collagen hydrogel. This study demonstrates the feasibility of biomaterial-based immunotherapy platforms like STINGel as strategies for increasing the efficacy of CDN immunotherapies.

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