



COLLEGE OF PHARMACY
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Pharmaceutical Sciences Seminar

Wednesday, March 3, 2021
Join Zoom Meeting
<https://umich.zoom.us/j/99990087574>
4:00-5:00 pm

“Developing New STING-activating Cancer Immunotherapy”

Presented by:

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Abstract: Immunotherapy is advancing cancer treatment on multiple fronts. However, the current response rate for cancer immunotherapies against solid tumors is limited to 15-30%. Activation of the STING pathway has been proven as a new remarkably effective cancer immunotherapy in numerous preclinical studies but the development has been impeded by the poor drug-like properties of conventional cyclic dinucleotide (CDN) STING agonists. We have discovered specific nutritional metal ions augment STING agonist activity, wherein Mn^{2+} promoted a 12- to 77-fold potentiation effect across the prevalent human STING haplotypes. Notably, Mn^{2+} coordinated with CDN STING agonists to self-assemble into a nanoparticle (CDN- Mn^{2+} particle, CMP) that effectively delivered STING agonists to immune cells. CMP administered either by local intratumoral or systemic intravenous injection initiated robust anti-tumor immunity, achieving best-in-class therapeutic efficacy with minute doses of STING agonists in multiple murine tumor models. Meanwhile, we have conducted high-throughput screening (HTS) of microbial metabolites for discovery of the next-generation non-nucleotide STING agonists. Highly enriched innate immune stimulation activities were found in the microbial extracts and 28 STING-activating strains were identified, some of which show comparable potency as the gold standard STING agonist in insensitive human haplotypes. Further chemical profiling and isolation are undergoing. Overall, we have developed a highly effective STING agonist delivery system and a new strategy for STING agonist discovery, paving the path for the next generation of effective STING-activating cancer immunotherapy.

STING: Stimulator of IFN genes

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