Nano-Metalloimmunotherapy for Cancer Eradication

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CRS 2025 ANNUAL MEETING & EXPOSITION
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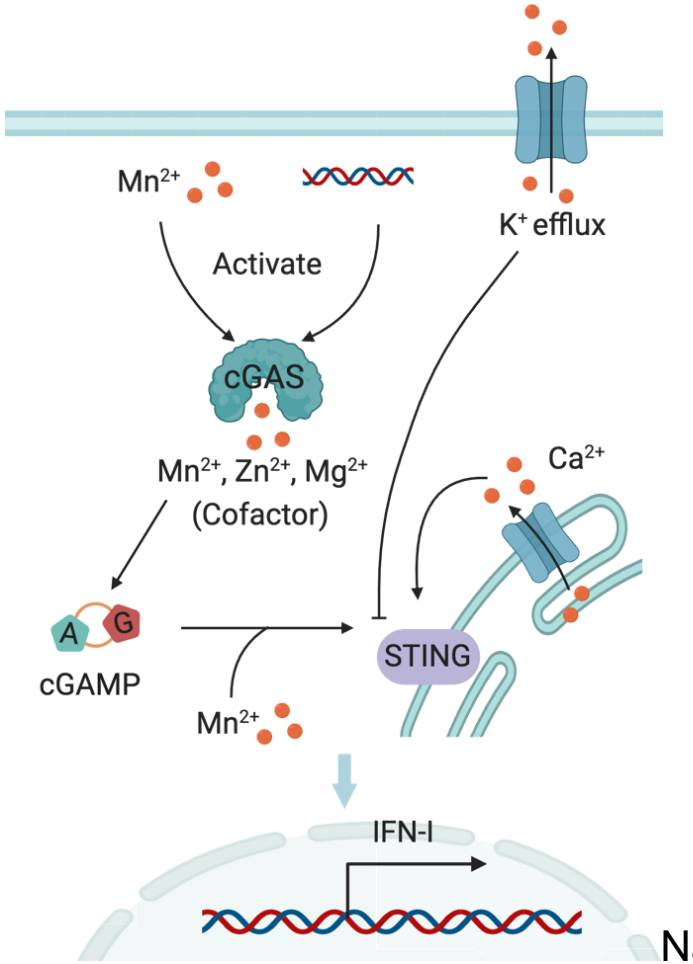
NEXT-GENERATION DELIVERY INNOVATIONS

Modulation of cGAS-STING Pathway by Nutritional Metal Ions

Metal ions in cGAS-STING signaling



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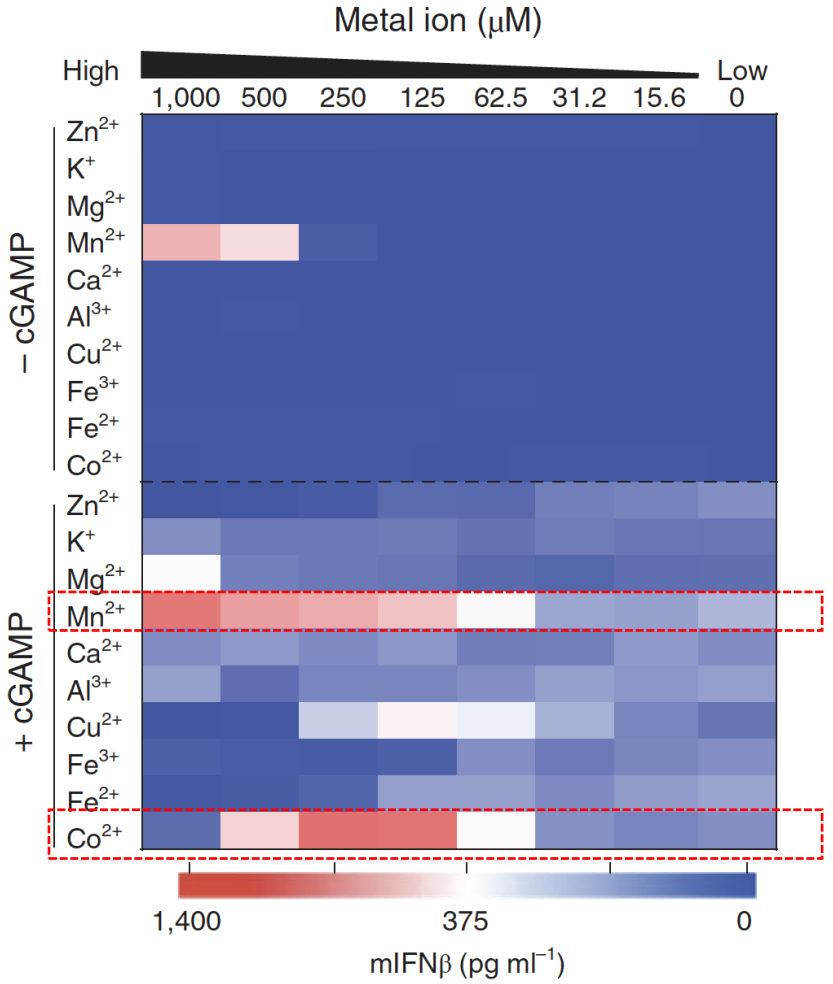
Mn^{2+} potentiates CDN STING agonist



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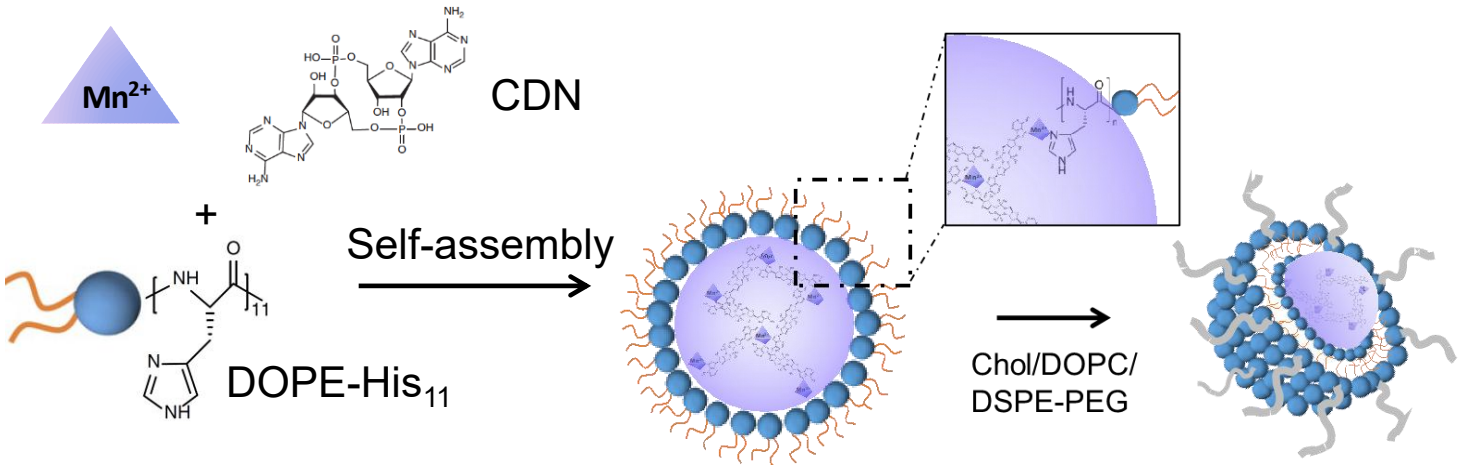
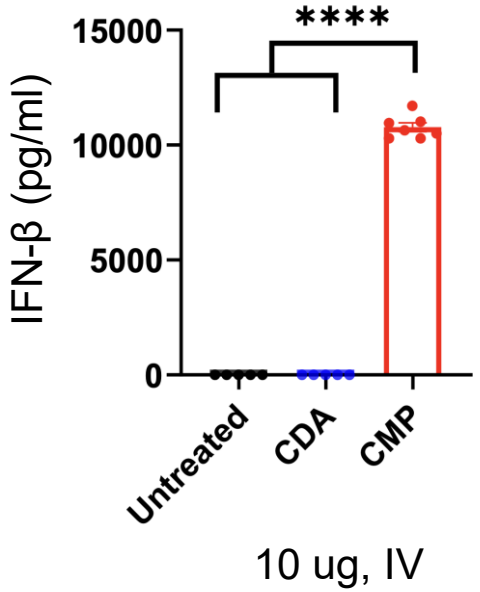
Mn^{2+} Assemble CDN into a Novel Lipid Nanoparticle Formulation



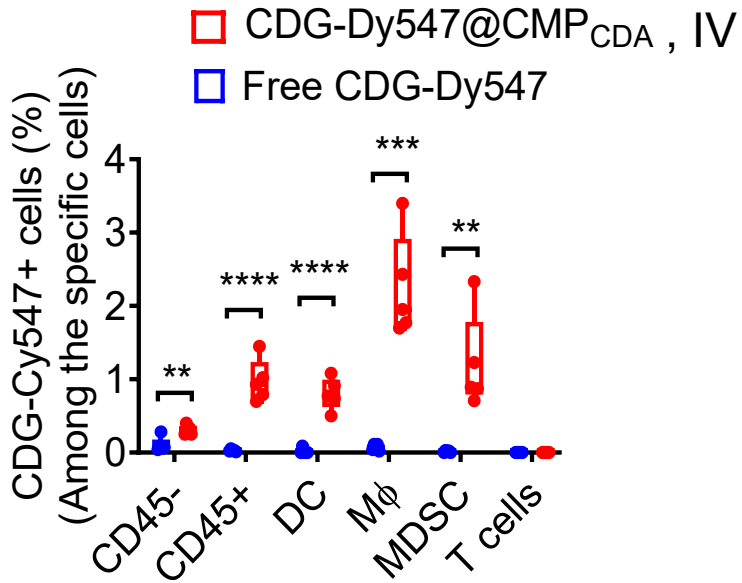
CDN-Mn Particle (CMP)

- High encapsulation
- Enhanced stability by coordination
- Effective endosomal escape

Systemic IFN-I Response

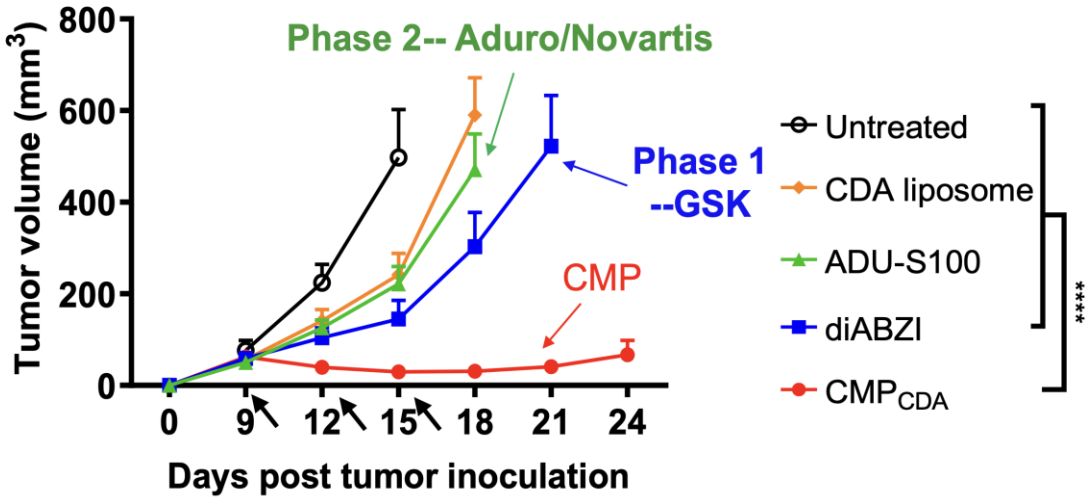


Myeloid-Selective Distribution

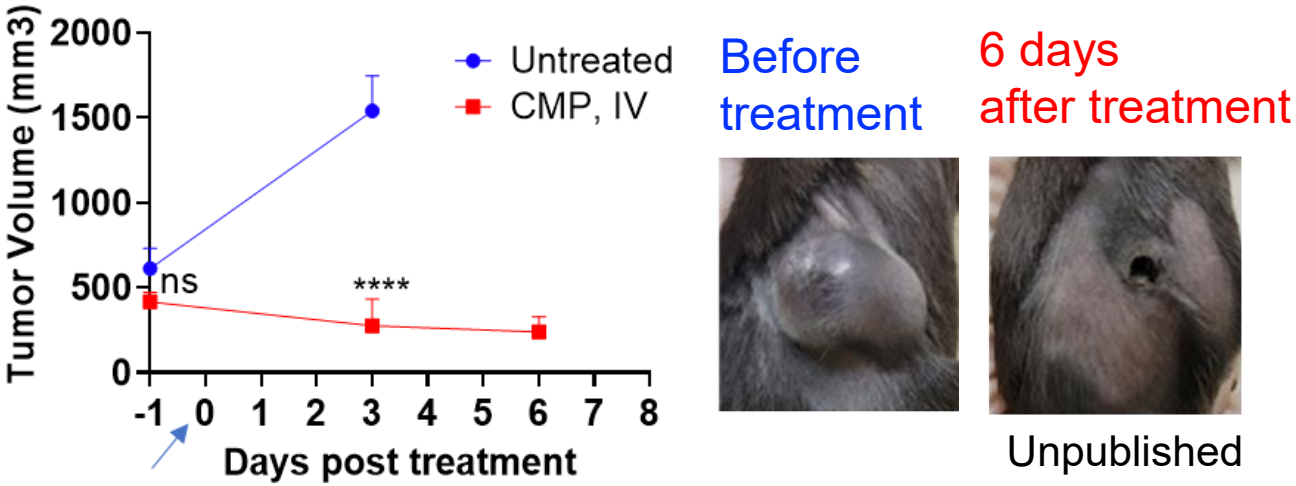


Robust Immunotherapeutic Effect of CMP in Advanced Tumors

Established B16F10 Melanoma



Terminal-Stage B16F10 Melanoma



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"Best-in-Class" Therapeutic Potential

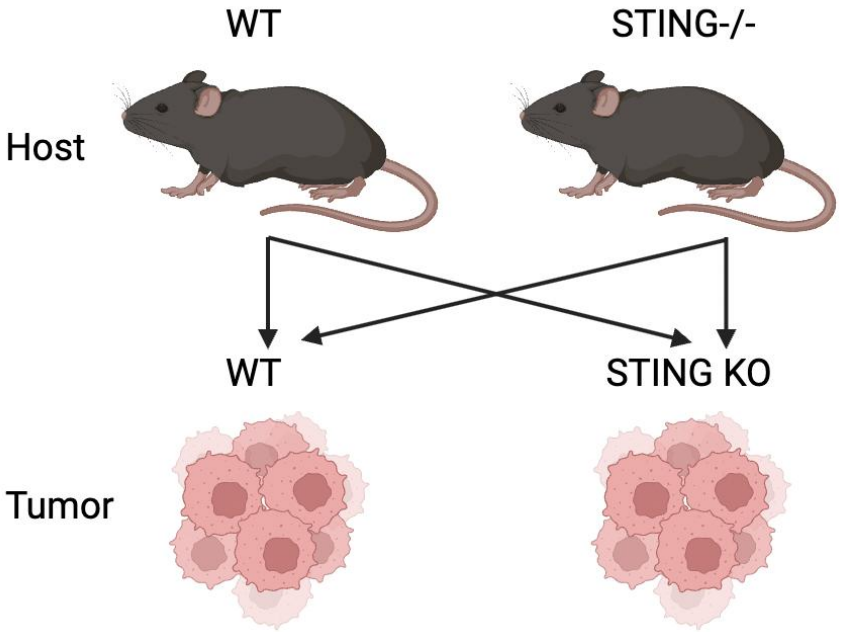
Equal dose of STING agonists, IV

Eradicate terminal-stage B16F10 tumors (1cm in diameter, 3 days before humane endpoint)

10 ug CMP, IV

Response of CMP is Independent of STING in Cancer Cells

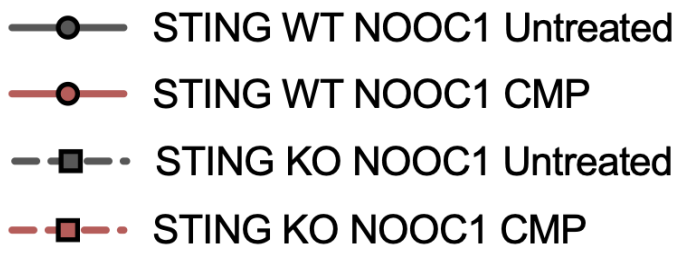
Xingwu Zhou

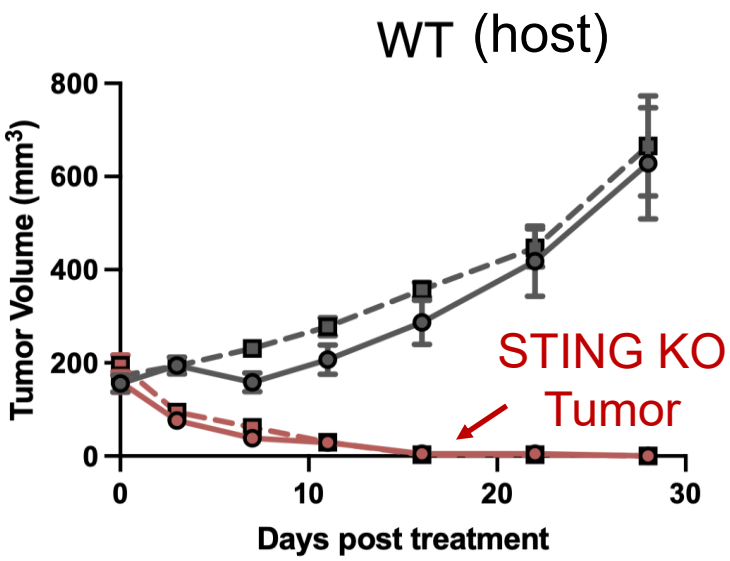


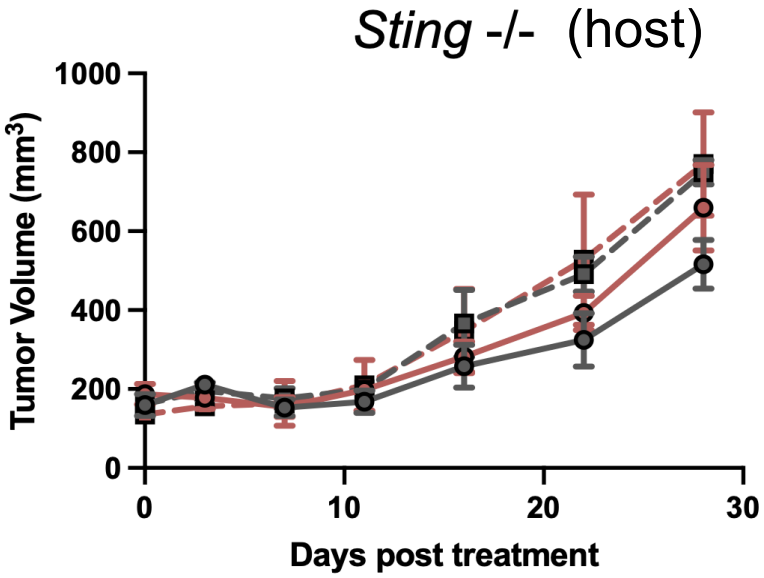
WT
Sting-/-

15 x 10^5 STING WT NOOC1 or STING KO NOOC1 (s.c.)

10 μg CMP (i.v.)







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CMP Inhibit Established VX2 Squamous Cell Carcinoma in Rabbits

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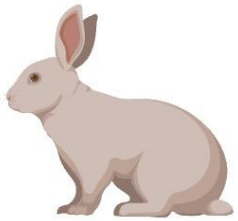
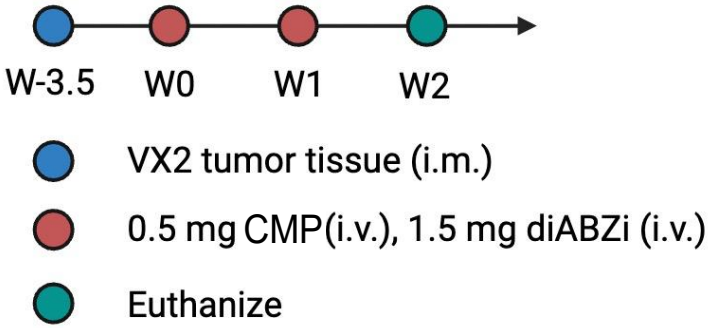
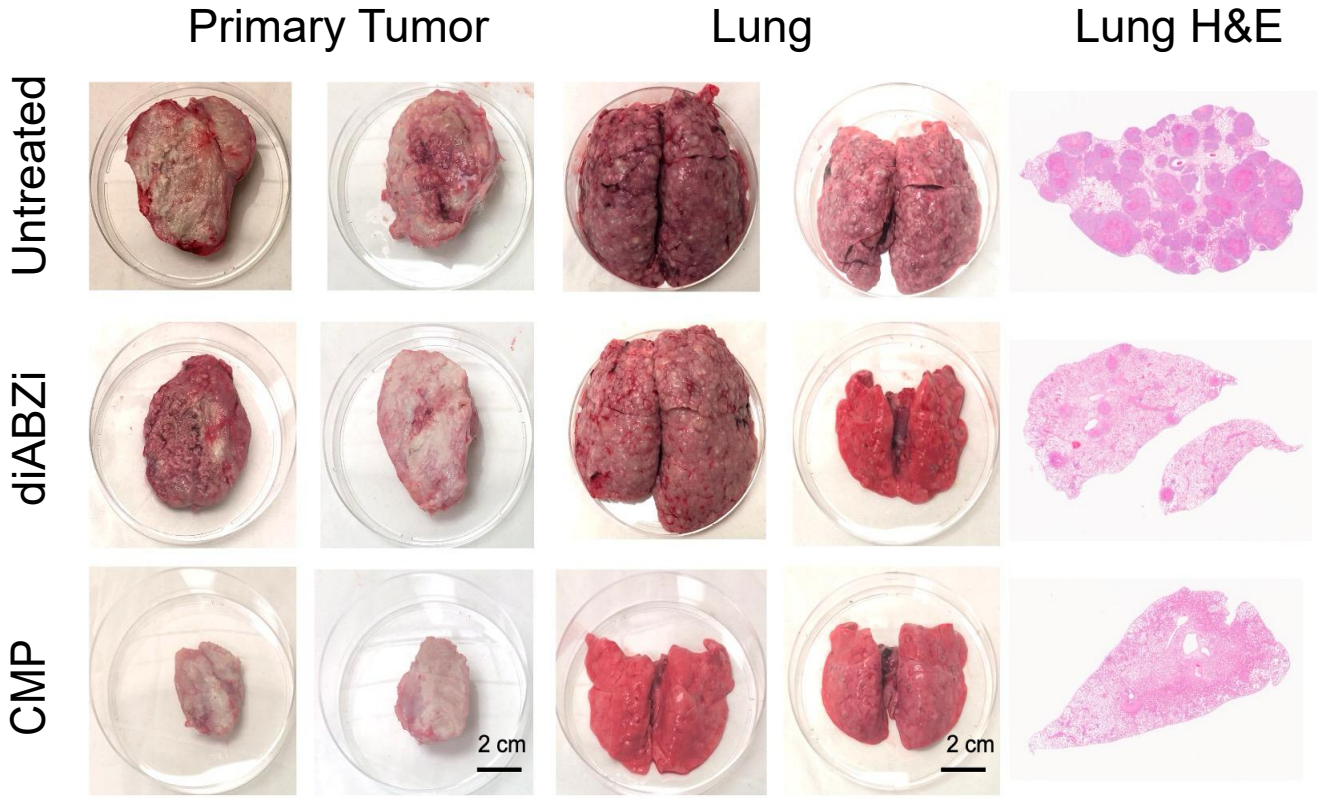
Inhibit established rabbit tumor and metastasis (~200x of mice body weight)



New Zealand white rabbit





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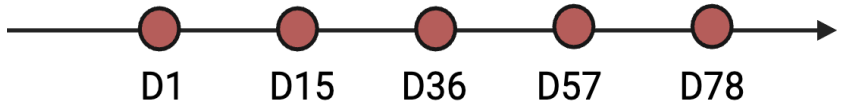
Therapeutic Response and Safety after CMP Repeated Dosing

Xingwu Zhou

NHP



Pre-bleed

D1: CMP 0.003 mg/kg

D15: CMP 0.01 mg/kg

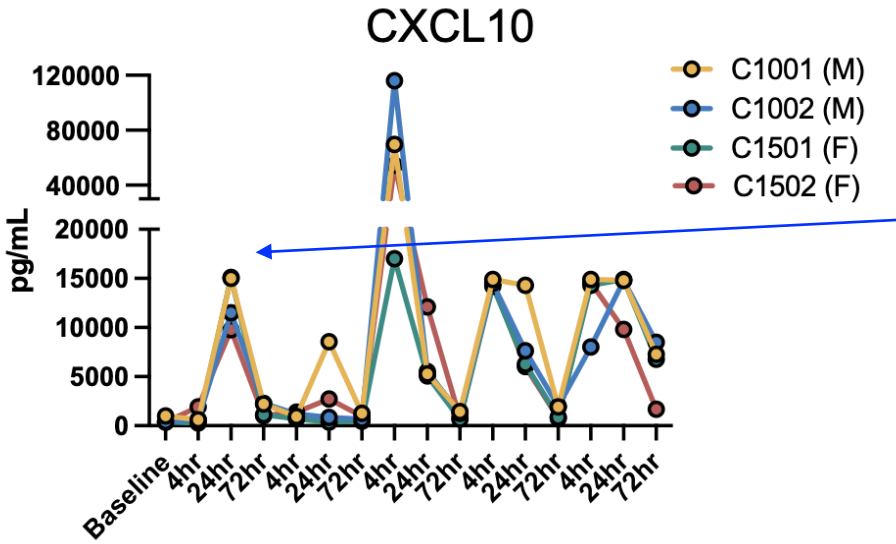
D36: CMP 0.03 mg/kg

D57: CMP 0.1 mg/kg

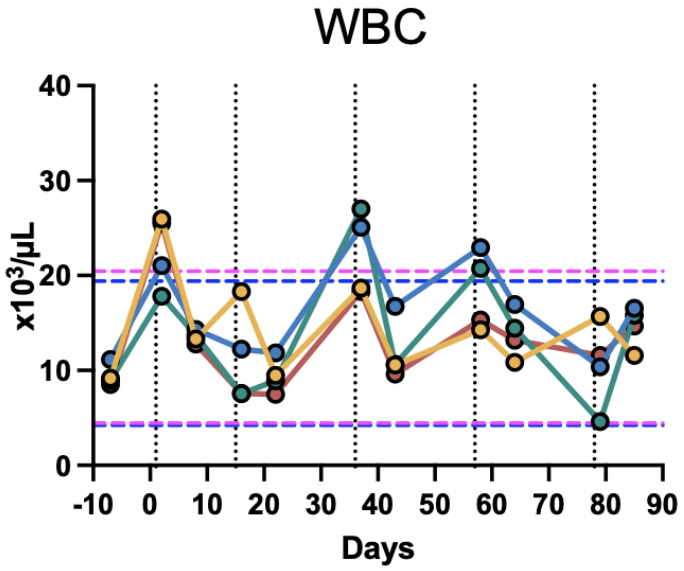
D78: CMP 0.3 mg/kg

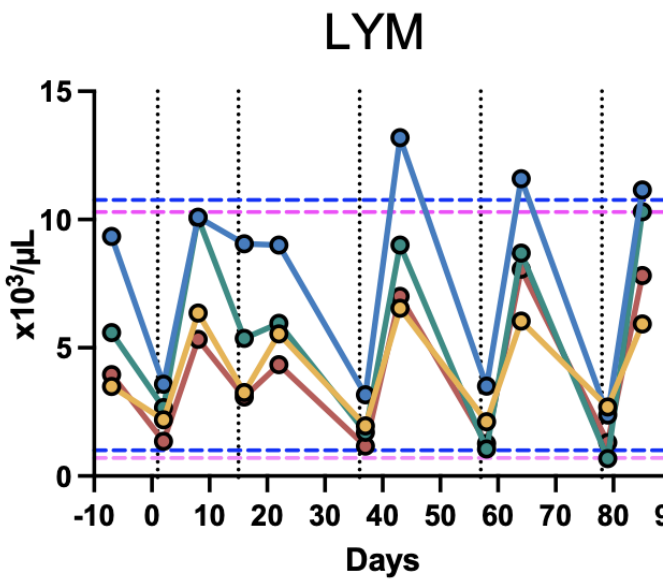
Dose escalation

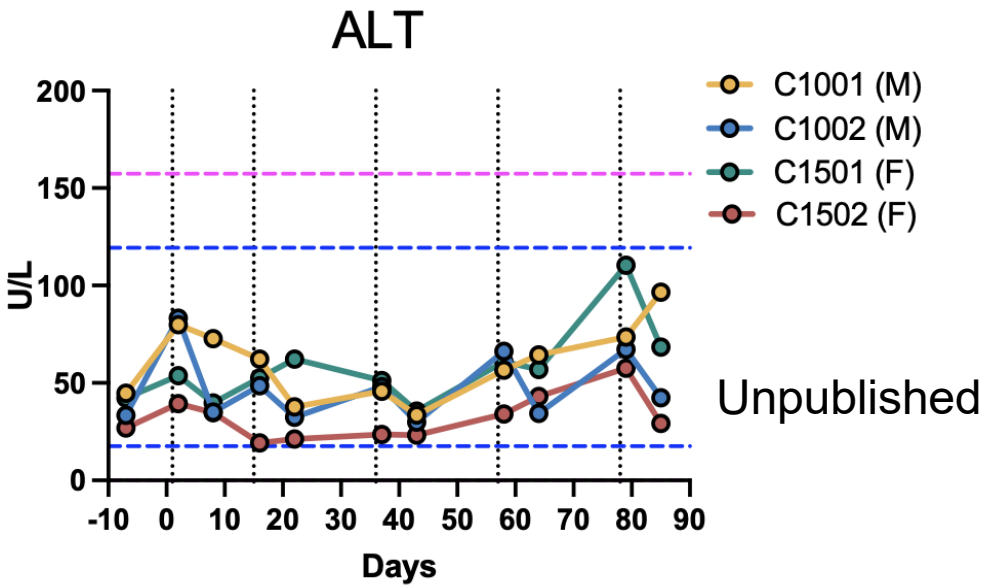
Therapeutic Window: 0.003-0.3mg/kg



IFN response at as low as 0.003 mg/kg







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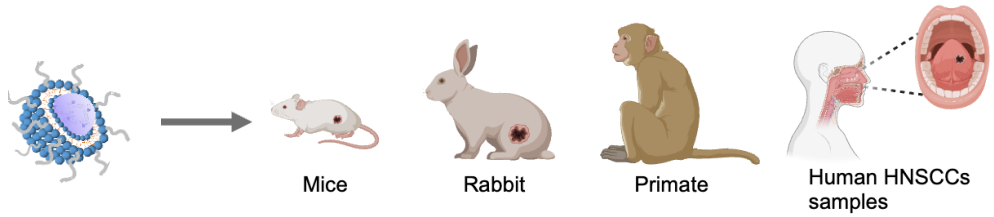
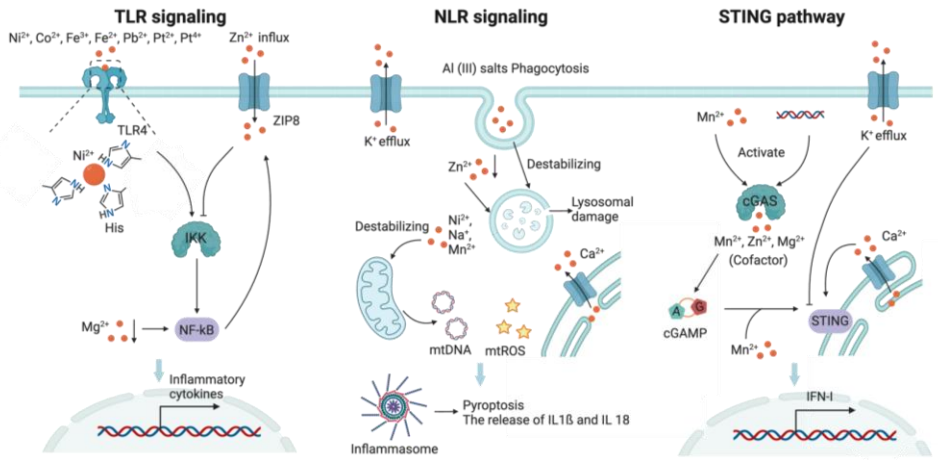
Summary



- Metal ions in immune process are potentially a new class of immune therapeutic targets
- A novel lipid nanoparticle, CMP, was design for co-delivery of Mn^{2+} and CDN STING agonist
- CMP induced robust STING activation after IV injection and exerted remarkable anti-tumor efficacy in advanced tumor models.
- CMP demonstrated good response and safety profile in NHPs, with a therapeutic index of ~100.

Perspective for metalloimmunotherapy

New therapeutic targets



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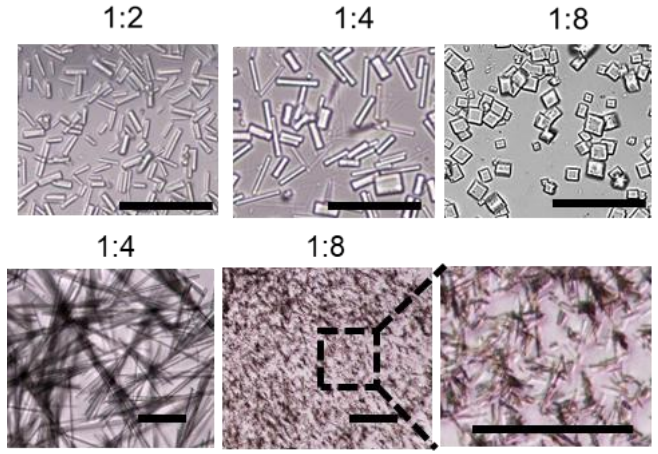
New formulation mechanisms



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FRANKEL INNOVATION INITIATIVE

DRUG DISCOVERY

SAROS THERAPEUTICS

Thanks for your attention!