

Split Bullets Loaded Nanoparticles Dually Targeting Mitochondria and Endoplasmic Reticulum for Amplified Chemo-Immunotherapy

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Poster number: 688

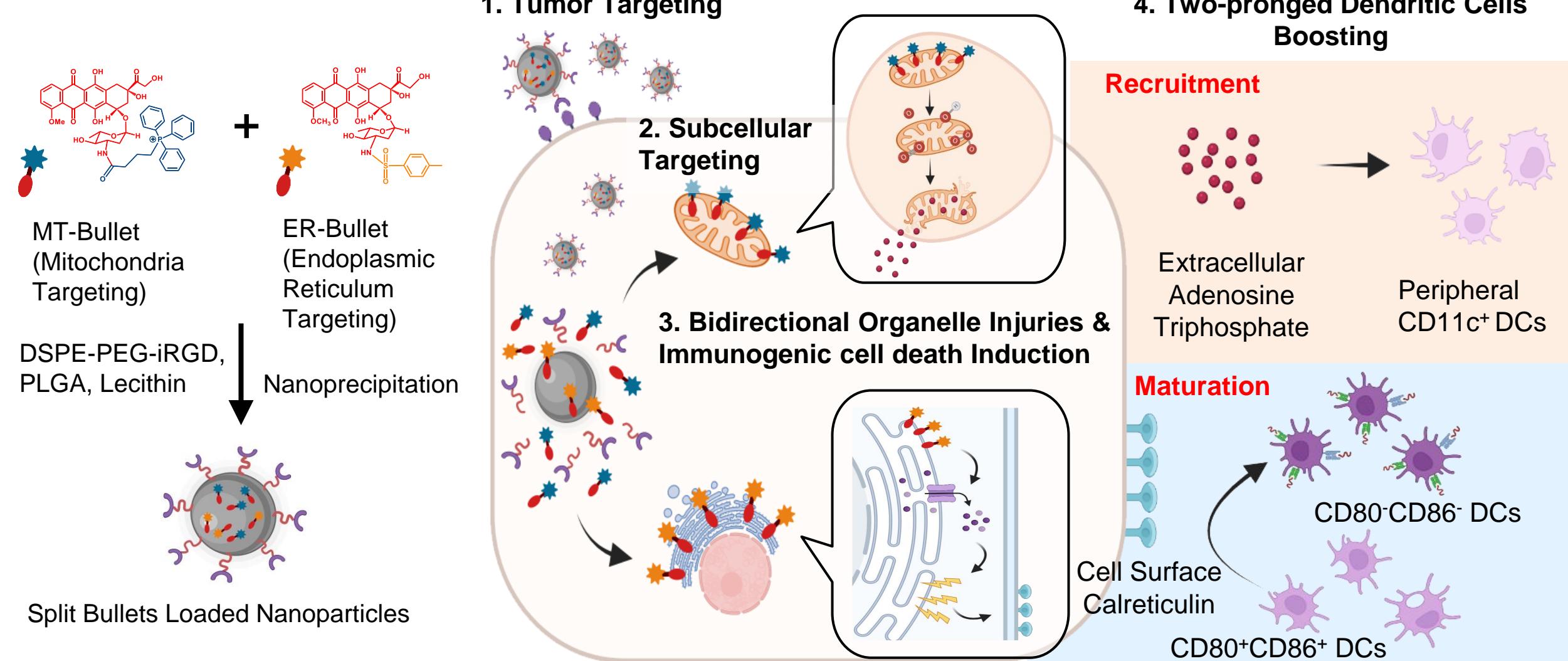
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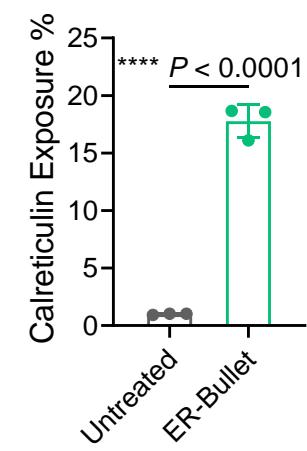
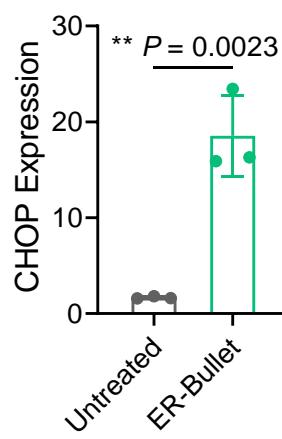
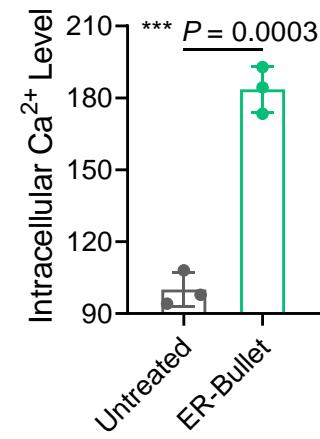
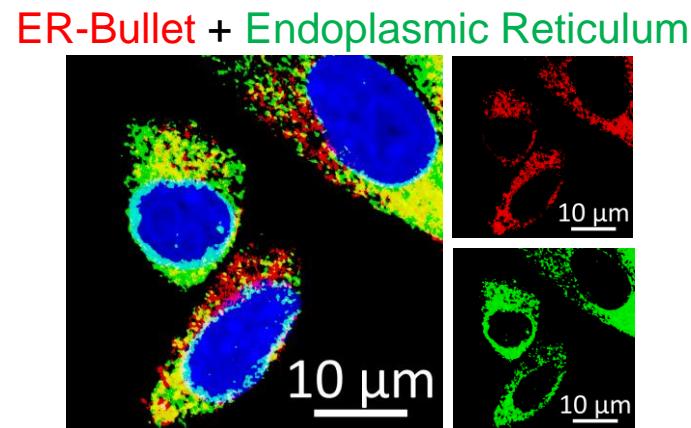
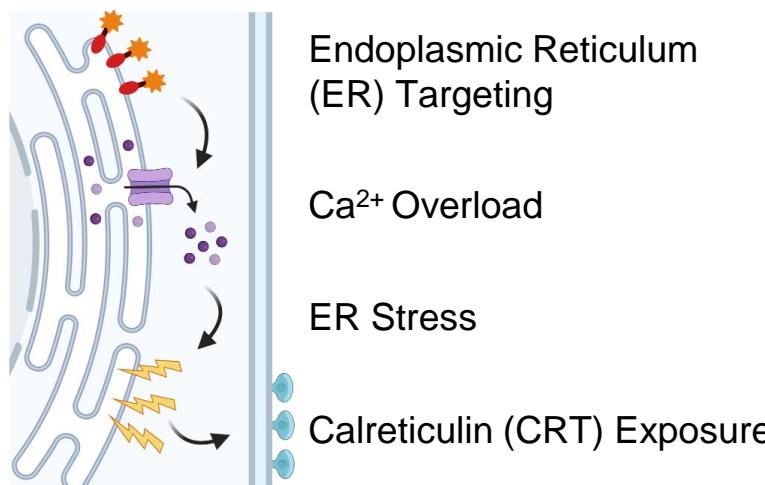
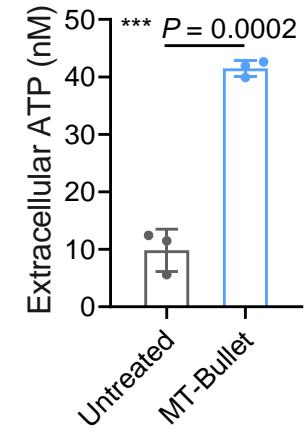
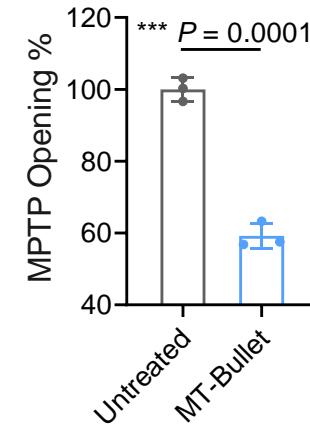
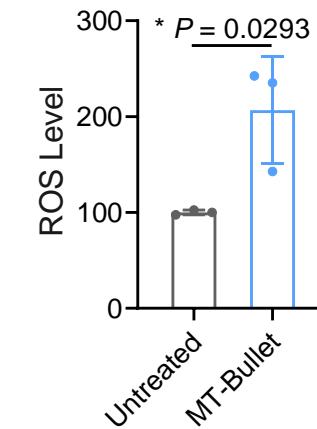
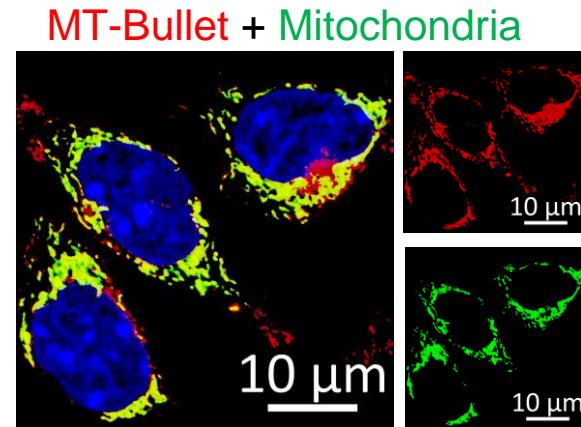
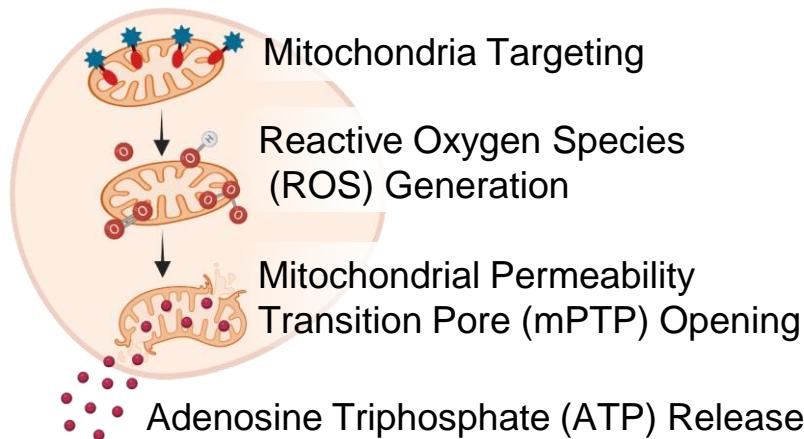
INTEGRATING
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ACROSS DISCIPLINES



Concept

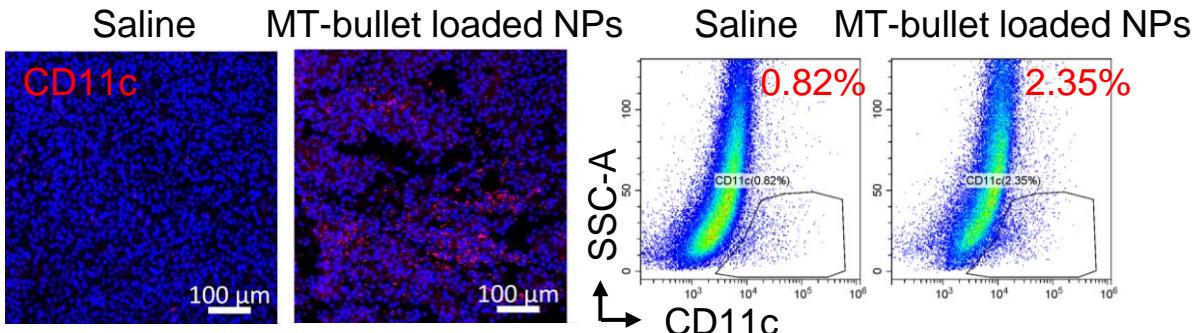


From Organelle Injuries to Immunogenic Cell Death

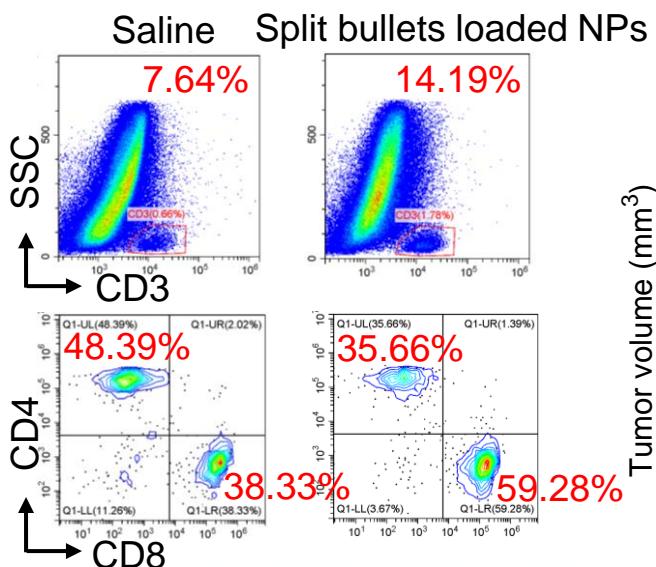


Delivering Subcellular-Targeted Bullets to Resuscitate DCs

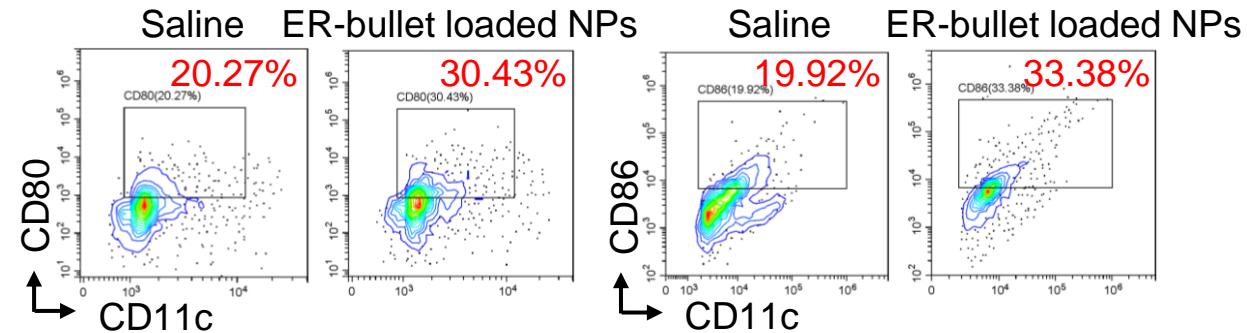
Nanoparticles loading with Mitochondria-targeted bullets recruited peripheral dendritic cells into tumor



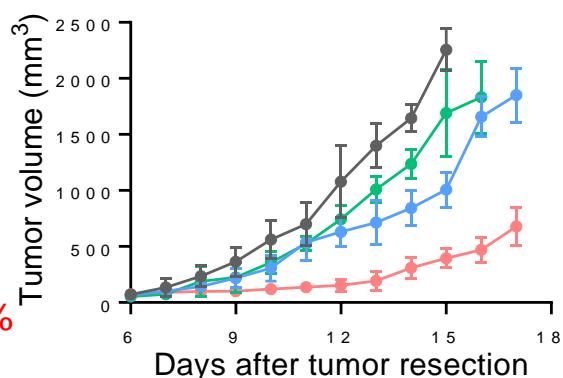
Split bullets loaded nanoparticles elicited robust anti-tumor immunity



Nanoparticles loading with endoplasmic reticulum-targeted bullets matured intra-tumoral dendritic cells



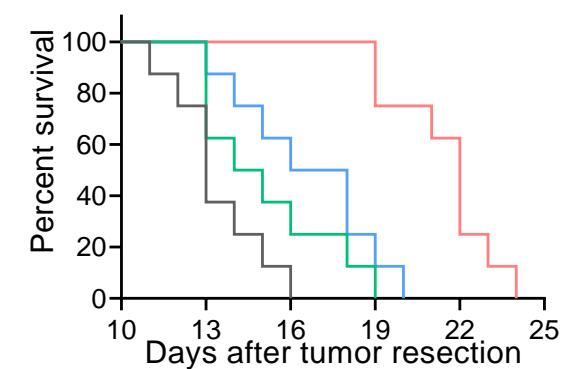
- Saline (G1)
- MT-bullet loaded NPs (G2)
- ER-bullet loaded NPs (G3)
- Split bullets loaded NPs (G4)



** $P = 0.0083$

*** $P = 0.0005$

**** $P < 0.0001$



Conclusions & outlook

- Redirecting chemotherapeutics to mitochondria and endoplasmic reticulum can improve their ability of inducing immunogenic cell death.
- Mitochondria targeting chemotherapeutics and endoplasmic reticulum targeting chemotherapeutics exerted distinct effects on tumor immunity: i) MT-bullet recruits peripheral DCs into tumor sites, due to its capability to trigger adenosine triphosphate release from tumor cells; ii) ER-bullet activates tumor infiltrating DCs, which is attributed to its ability to evoke calreticulin exposure on tumor cells.
- Split bullet loaded nanoparticles that dually targeting mitochondria and endoplasmic reticulum would improve the tropism and reactivity of DCs to tumor-specific antigen in a complementary way for amplifying tumor immunotherapy.
- Other subcellular structures, such as Golgi apparatus, lysosomes, and cytoskeleton, might also have signal molecules/pathways that are targetable for tumor immunotherapy.
- Subcellular targeting drug delivery is a promising technology to address problems in immunology.
- Dual-organelle targeting and even multi-organelle targeting are the future in subcellular drug delivery.



Acknowledgements



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Huang's Lab YYDS!

