

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

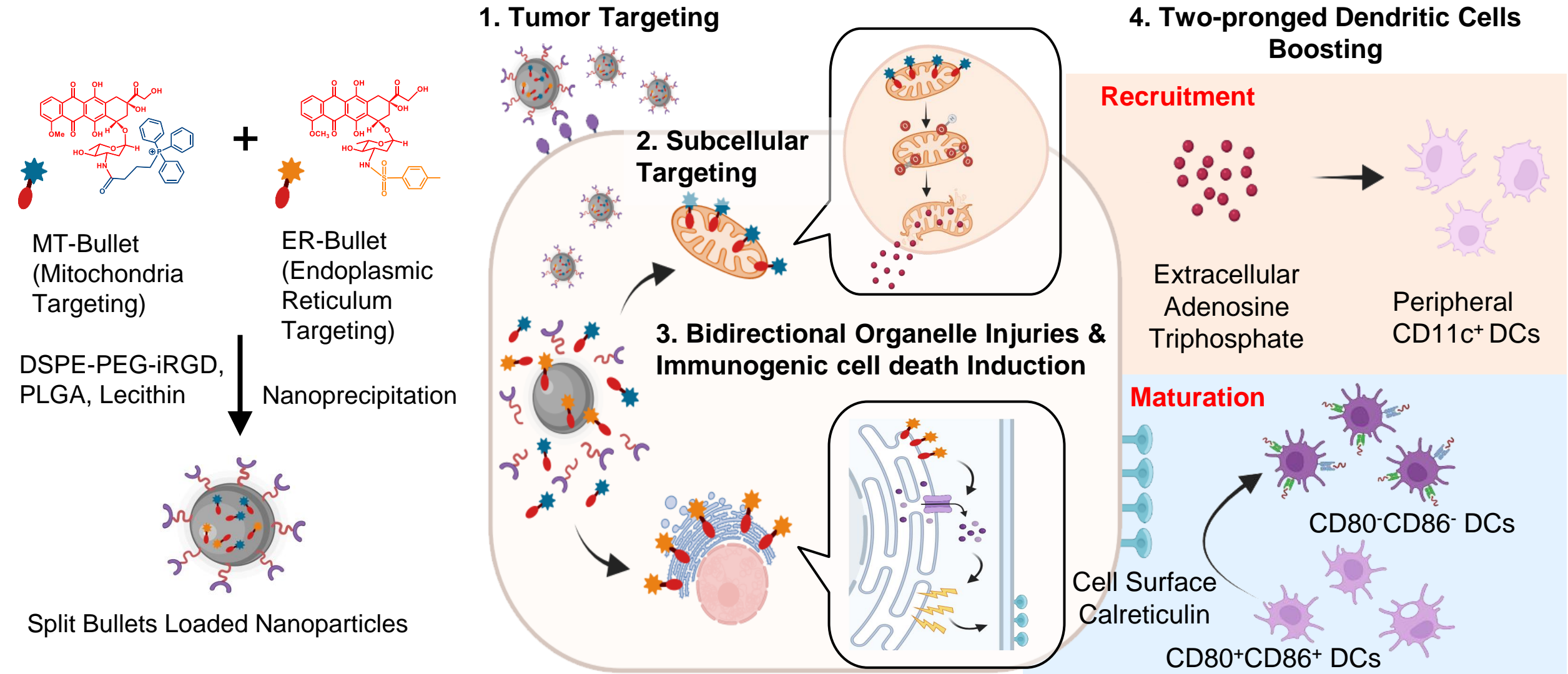
Chendong Liu

Poster number: 688

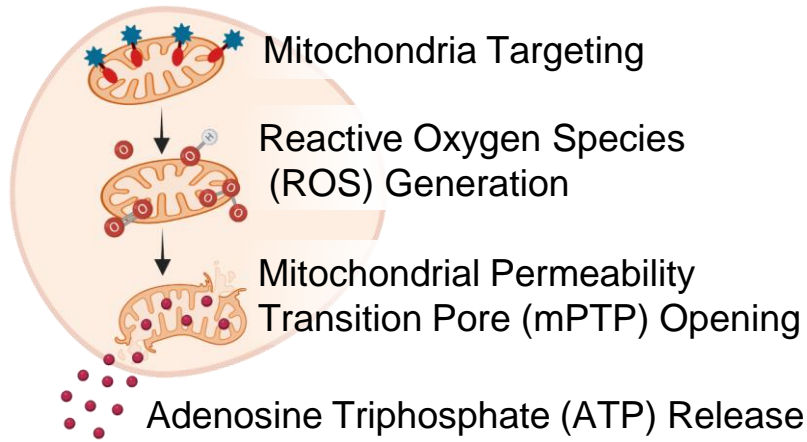
*PhD Candidate,
West China School of Pharmacy,
Sichuan University*



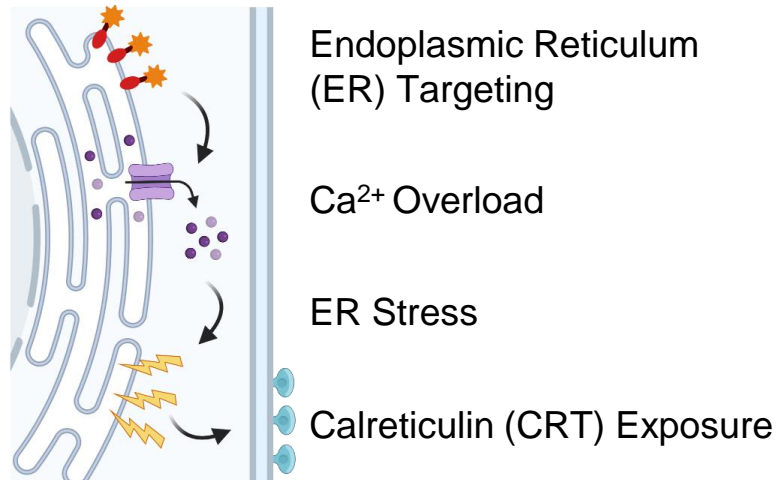
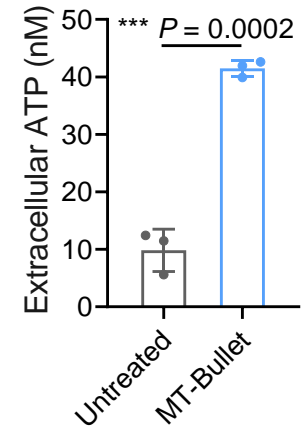
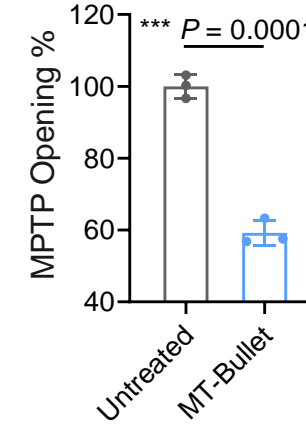
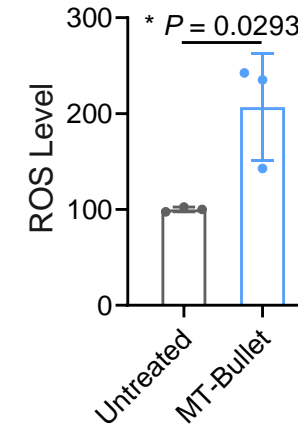
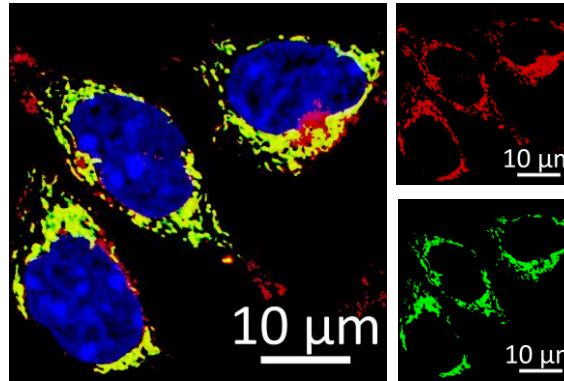
Concept



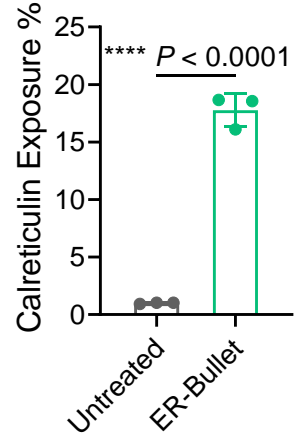
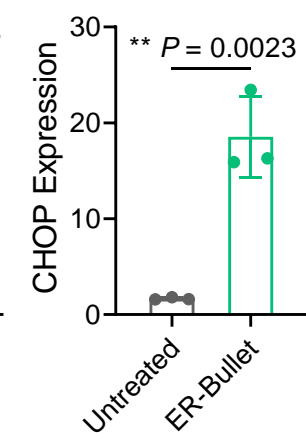
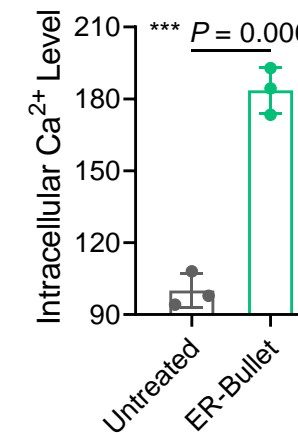
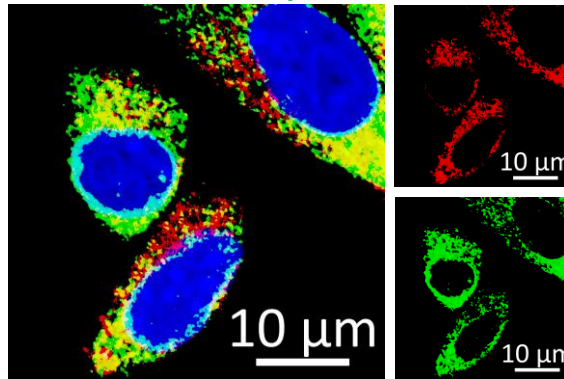
From Organelle Injuries to Immunogenic Cell Death



MT-Bullet + Mitochondria

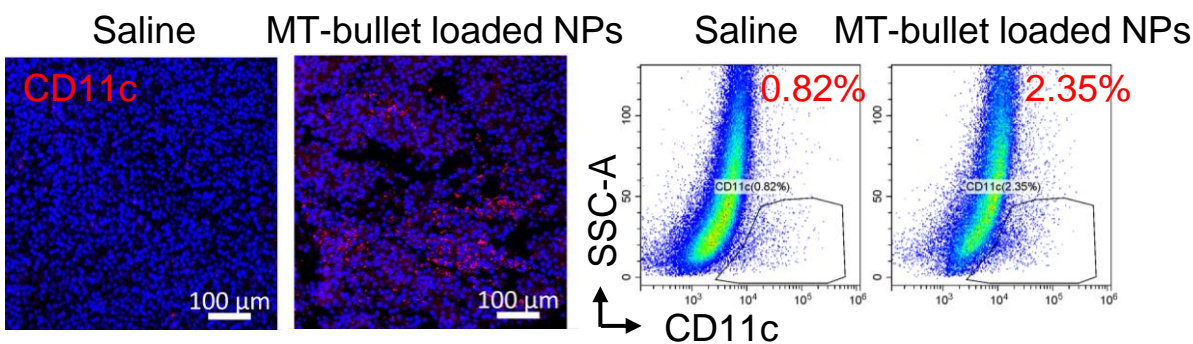


ER-Bullet + Endoplasmic Reticulum

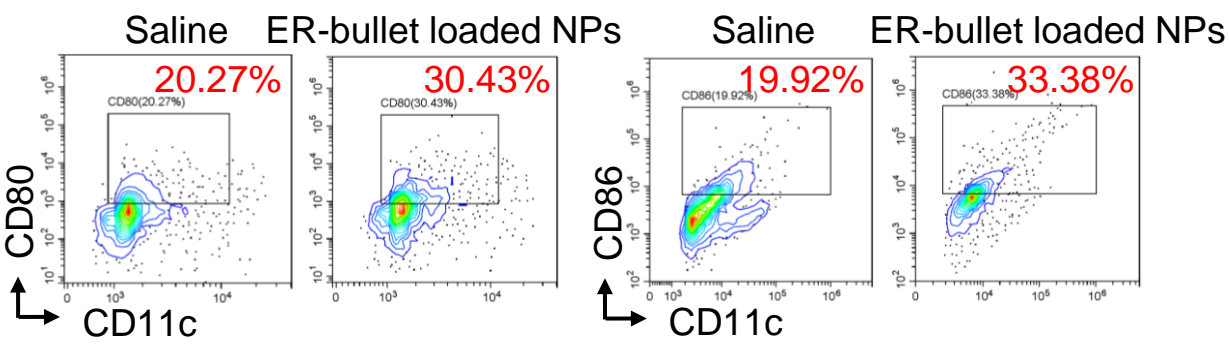


Delivering Subcellular-Targeted Bullets to Resuscitate DCs

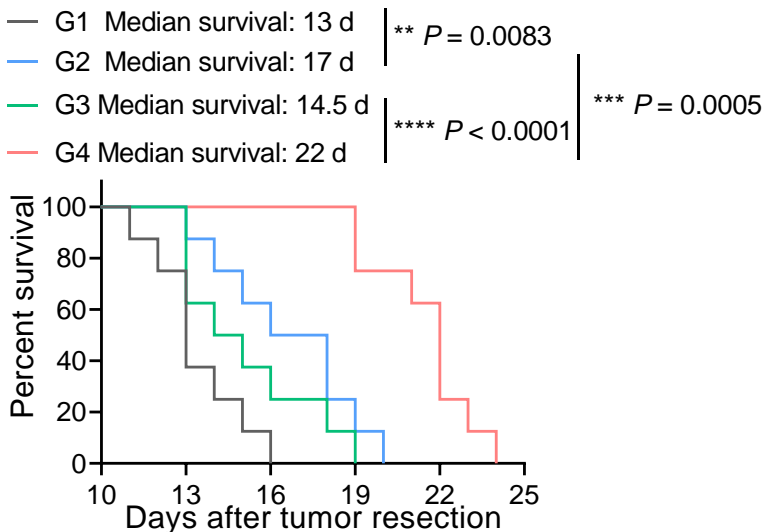
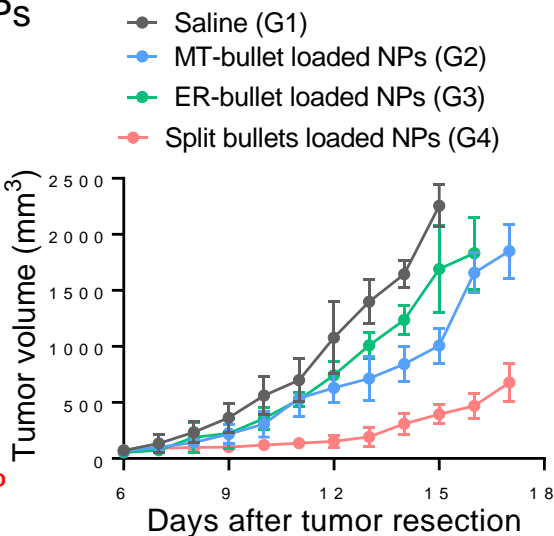
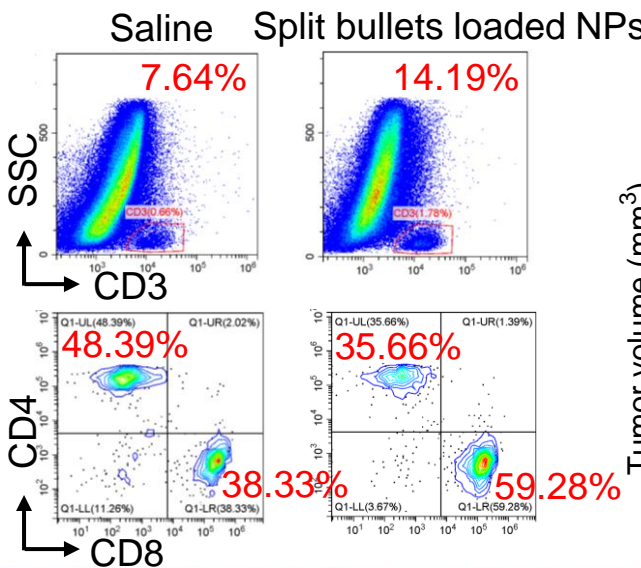
Nanoparticles loading with Mitochondria-targeted bullets **recruited** peripheral dendritic cells into tumor



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



Split bullets loaded nanoparticles elicited robust anti-tumor immunity



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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