Engineering cytotoxic T cells for cancer immunotherapy

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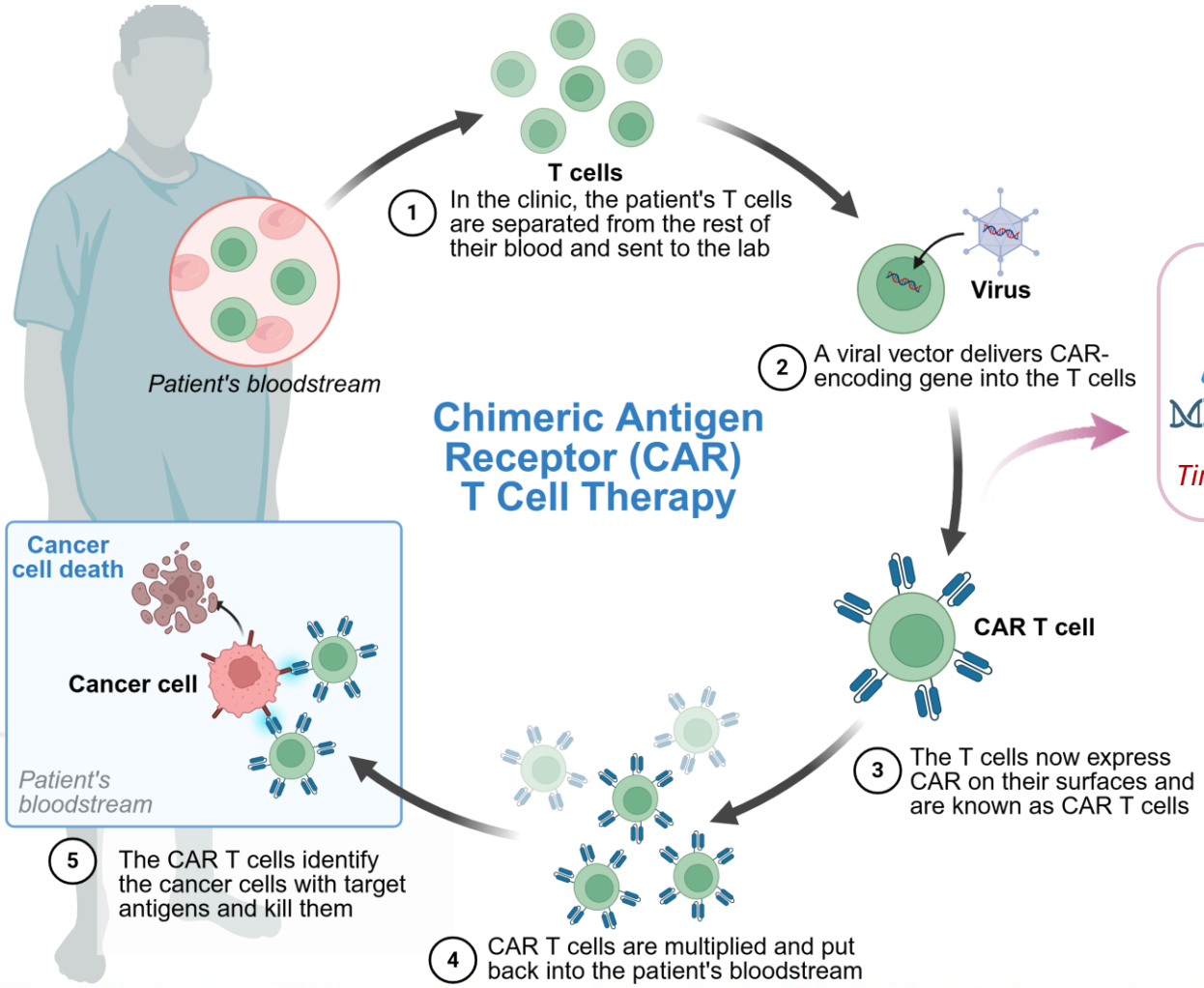
Background



Challanges in vivo

T cell exhaustion

Defected killing capability

Tumor barriers

Limited infiltrating T cells

Tumor microenviornment

Turning T cells to exhaustion

Challanges in vitro

Complex genetic modification

Time-consuming and high-costing

To solove abovementioned challanges

No-genetic modification

Convenient and high efficiency

Relieving T cell exhaustion

Therapeutic payload

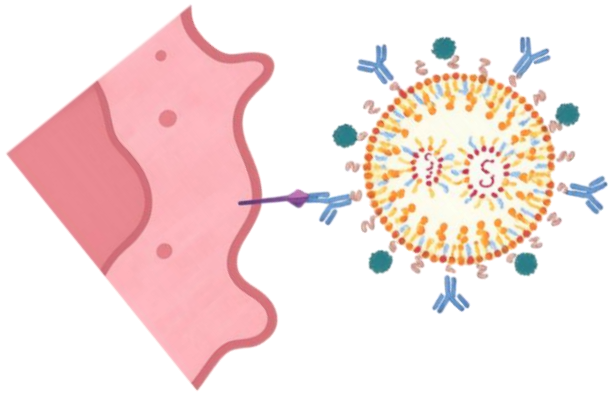
Tumor barriers

Loosening dense extracellular matrix

Tumor microenviornment

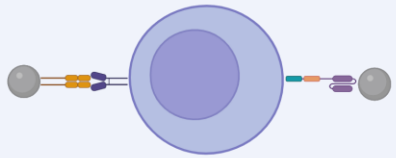
Immunoregulation

Nanoparticles Engineering CTLs



How to build the Nanoparticle Engineering CTLs

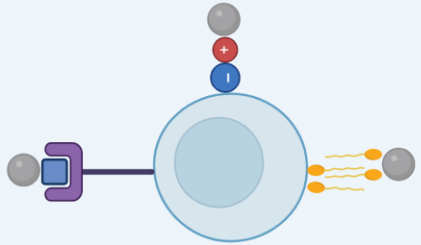
Ligand-receptor interaction



CD-mediated interaction

Gene-engineered cell marker-mediated interactions

Non-covalent interactions

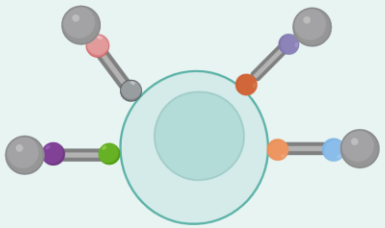


Host-guest interaction

Electrostatic interaction

Hydrophobic interaction

Covalent interactions



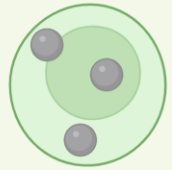
TEOS- APTES

Azido-DBCO

EDC-Sulfo/NHS

SH-Mal

Internalization

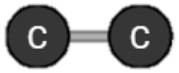


NPs can be internalized by endocytic pathways

Cheng R, Wang S. Cell-mediated nanoparticle delivery systems: towards precision nanomedicine[J]. Drug Delivery and Translational Research, 2024, 14(11): 3032-3054.

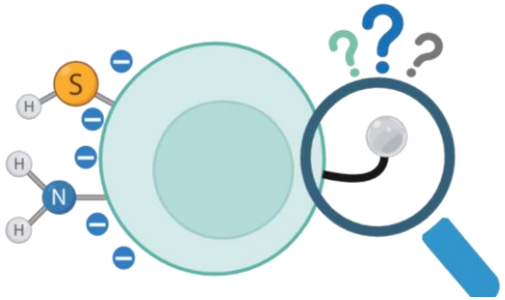
Questions and Aims

How these interaction methods influence the behaviours of nanoparticles engineering CTLs?



Covalent interactions

Electrostatic interactions



Evaluate

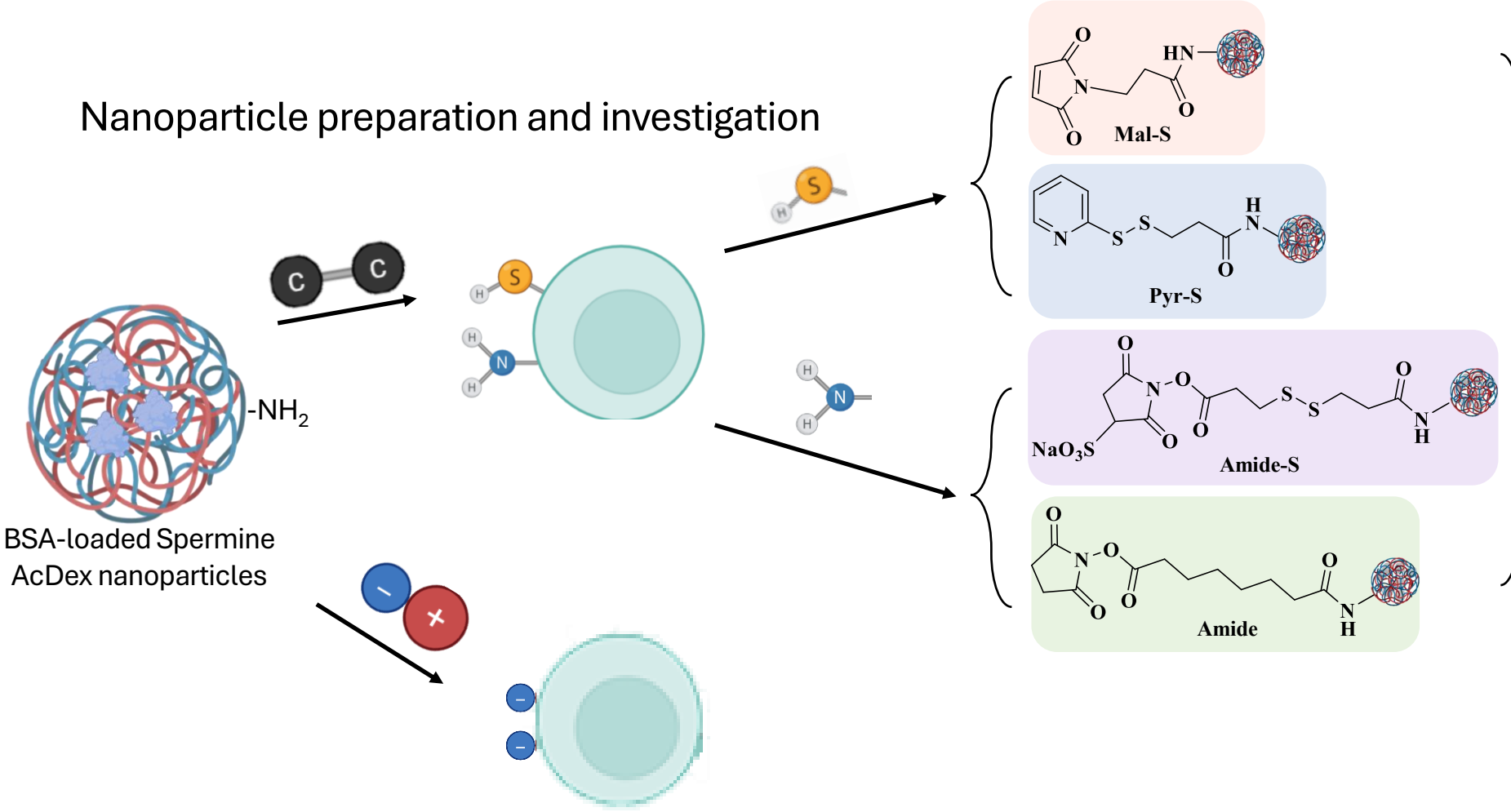
Stability

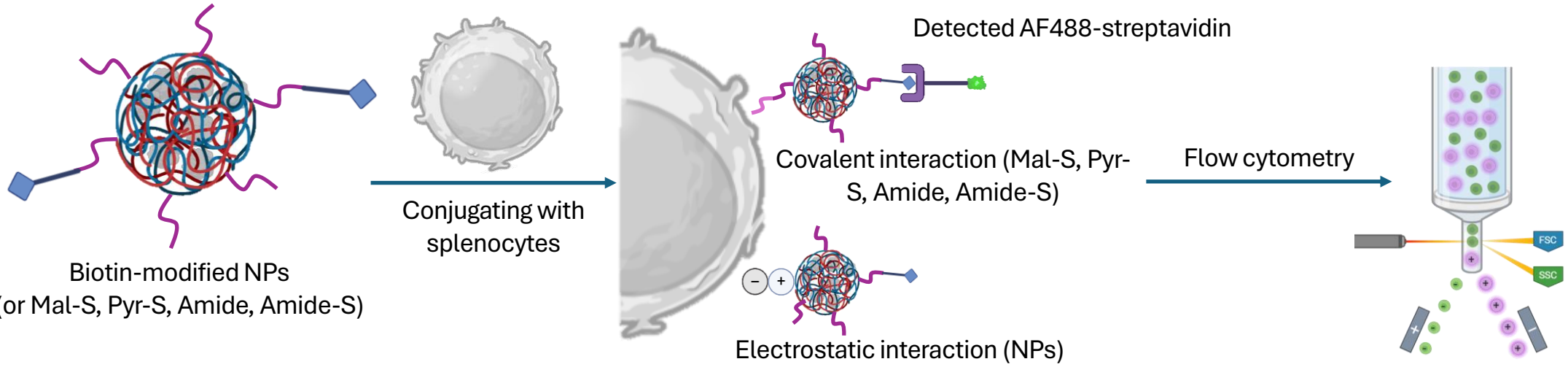
Conjugation efficiency

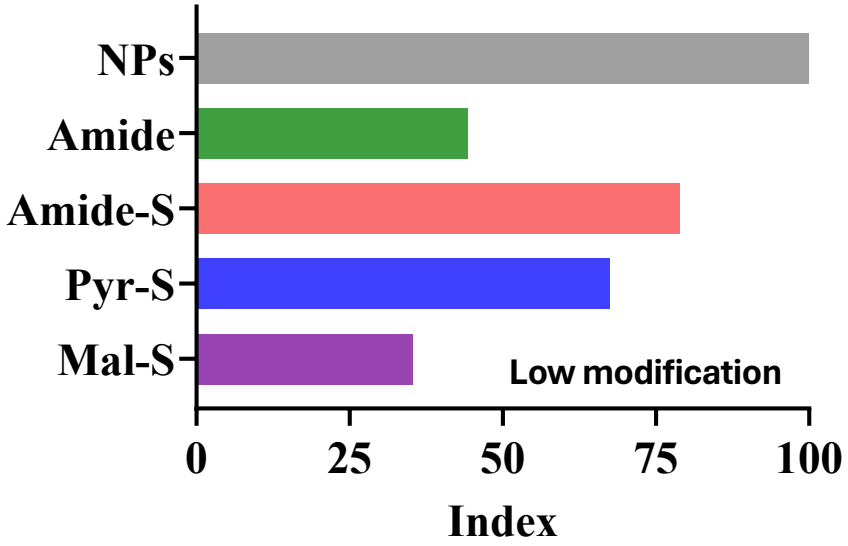
Su Y, Cheng R, Du B, et al. The impact of conjugation strategies and linker density on the performance of the Spermine-AcDex nanoparticle–splenocyte conjugate[J]. RSC Chemical Biology, 2025, 6(10): 1546-1554.

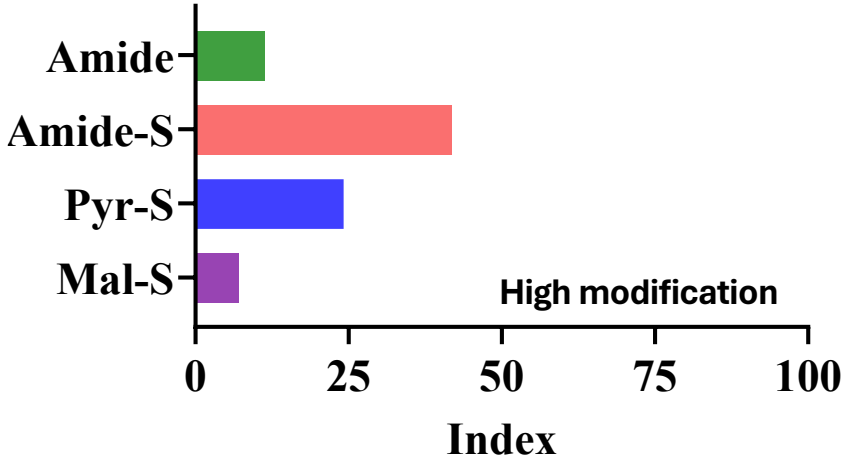
Methods and Results

Nanoparticle preparation and investigation



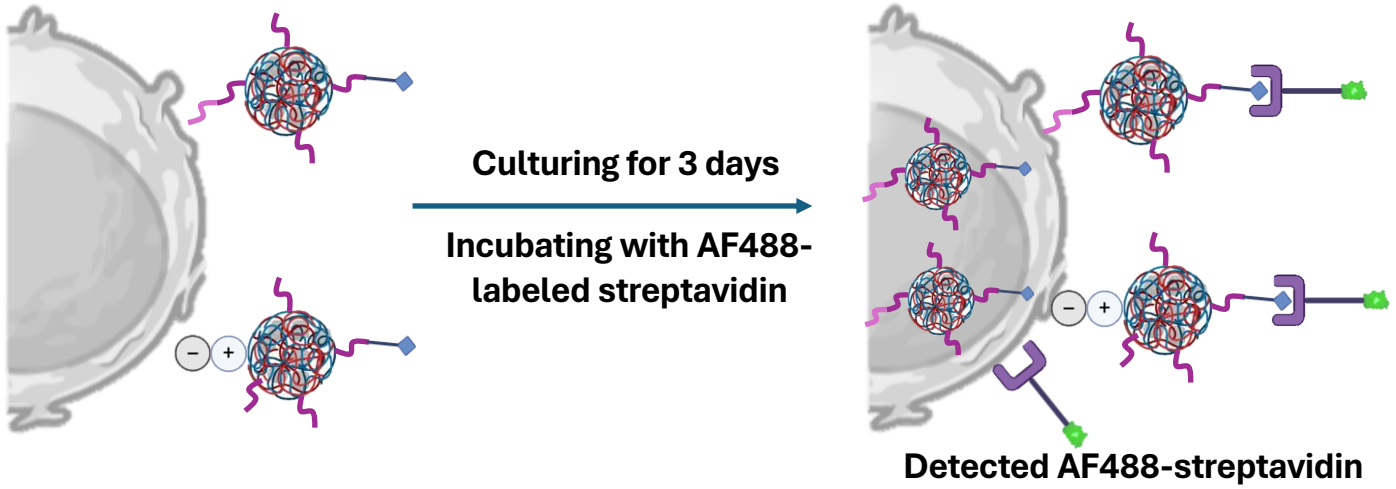






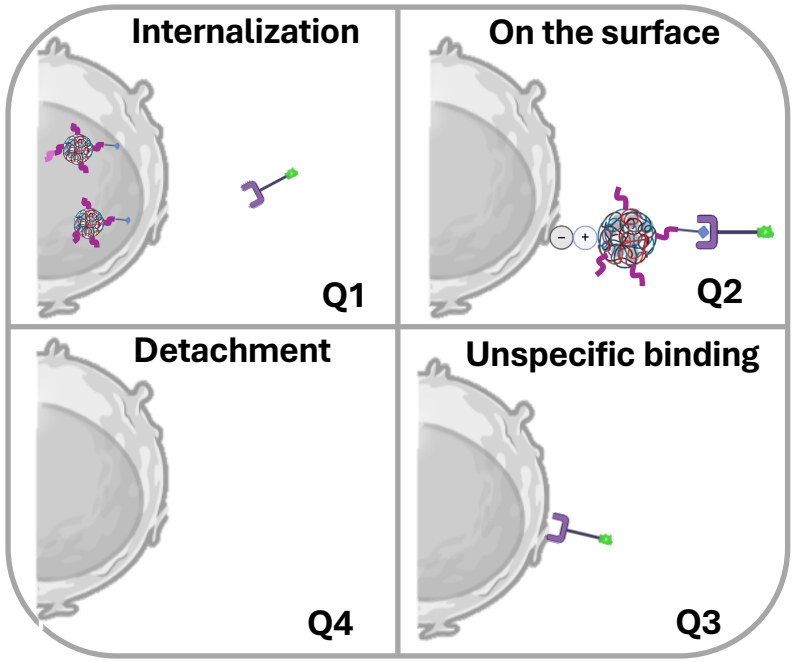
Conjugation efficiency

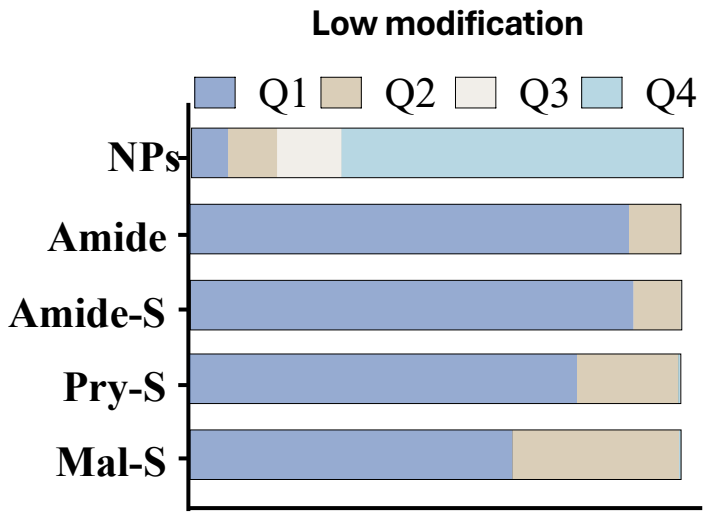
- NPs showed the highest conjugation efficiency
- Low modification groups exhibited higher conjugation efficiency than that of high modification groups

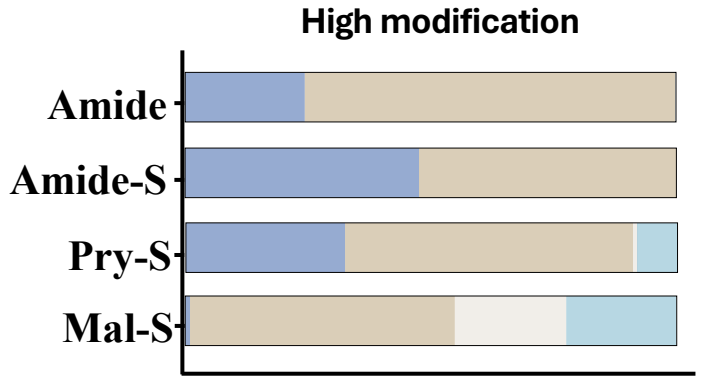


Stability

- NPs showed the lowest surficial stability
- High modification groups exhibited higher surficial stability than that of low modification groups
- Different degrees of modification could regulate the cell-nanoparticle interactions







Conclusion

- Electrostatic interaction could engineer the cells most efficiently, but less nanoparticle surface-stable
- Hybrid interaction (Covalent and electrostatic interactions appear at the same time) leads to a higher possibility of internalization compared to the pure covalent interaction.
- Covalent interaction leads to a higher nanoparticle surface-stable compared to the electrostatic and hybrid interactions.

Acknowledgement

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Shiqi Wang Lab

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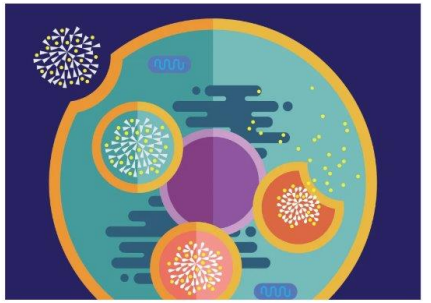

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