

Platelet-Drug Conjugates Engineered *via* One-step Fusion for Cancer Treatment

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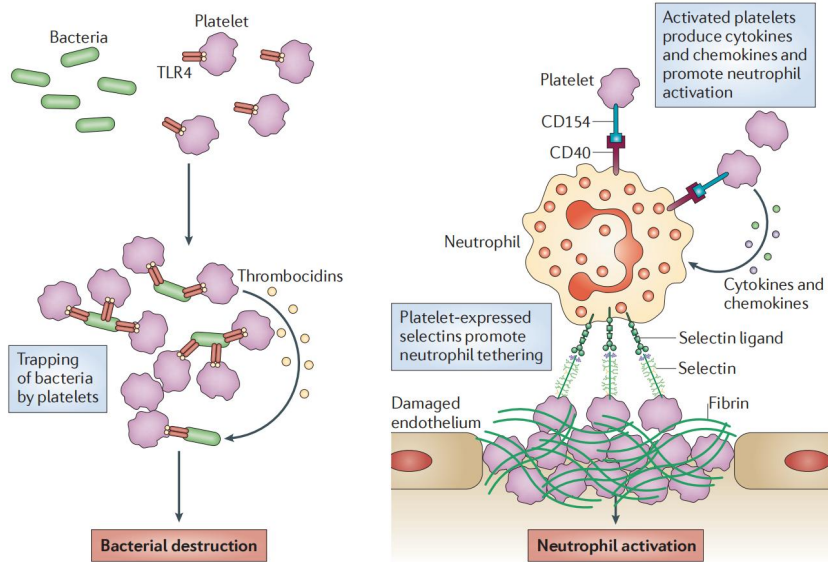
PHILADELPHIA, PA
JULY 13-18, 2025

**NEXT-GENERATION
DELIVERY INNOVATIONS**

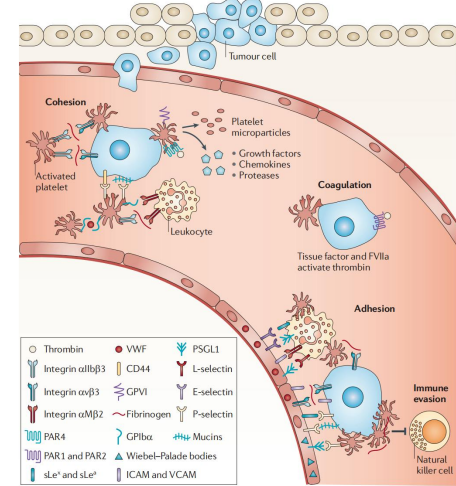
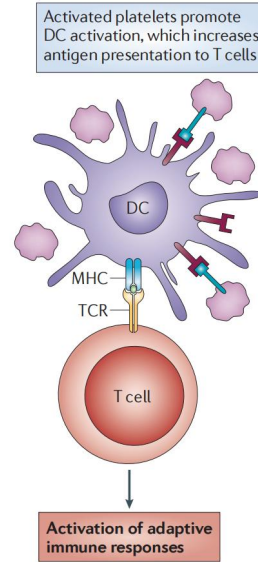
Platelets immunofunctions: beyond hemostasis

Platelets play roles in **immunity**, and **inflammation**;

They interact with immune cells, release cytokines, and **support metastasis** by shielding tumor cells.



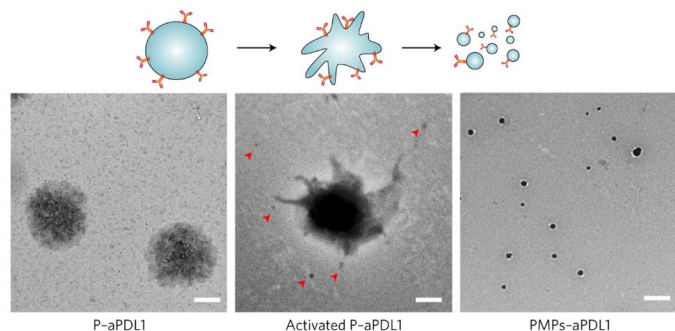
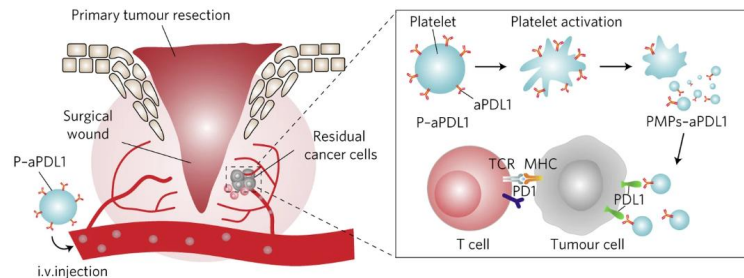
Nat. Rev. Immunol. 2011, 11, 264-274



Nat. Rev. Cancer. 2011, 11, 123-134

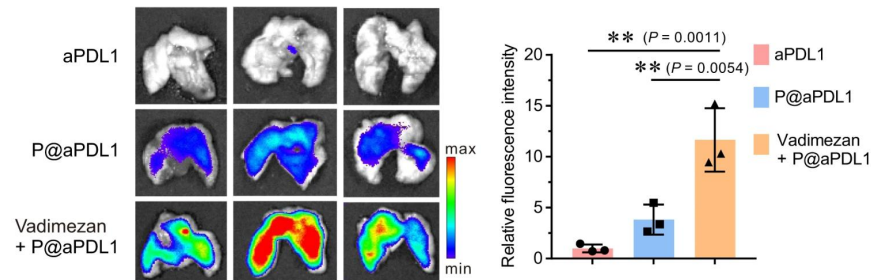
Platelet for targeted drug delivery

- Release of microparticles (PMPs) after activation



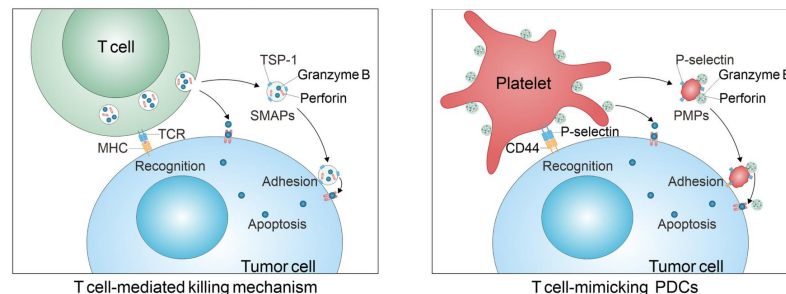
Nat. Biomed. Eng. 2017, 1, 0017

- Targeting tumor metastases and bleeding sites



Nat. Commun. 2021, 12, 2773

- Tumor cell affinity via P-selectin-CD44 interaction



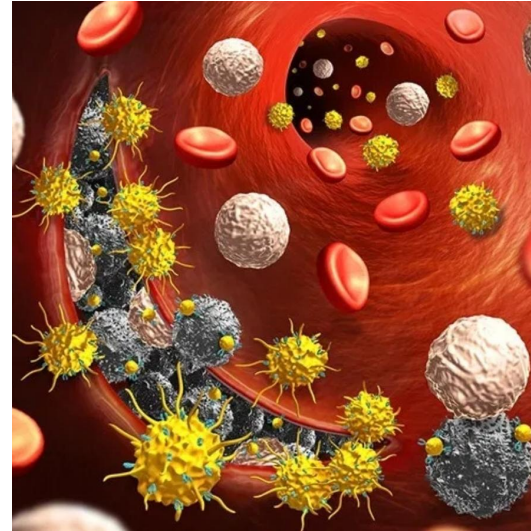
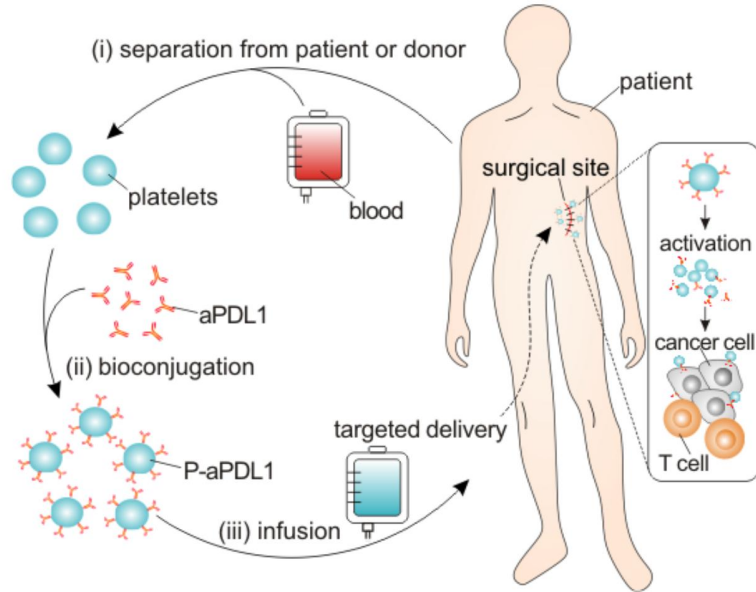
T cell-mediated killing mechanism

T cell-mimicking PDCs

Matter 2023, 6, 2340-2355

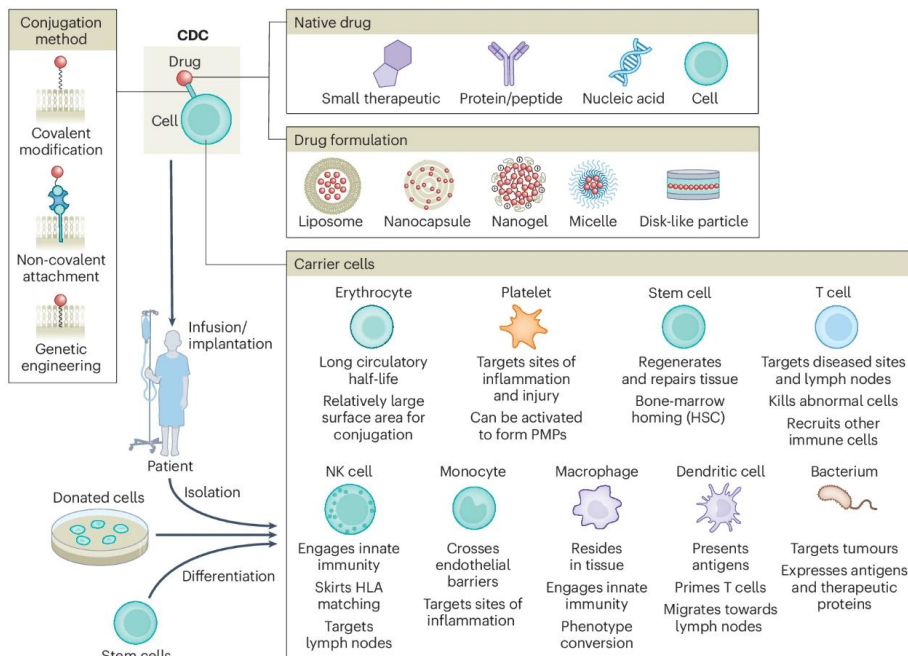
Platelet-driving immunotherapies

- One single plateletpheresis procedure yields up to 4×10^{11} platelets, providing an **abundant and clinically accessible** source for large-scale transfusion.



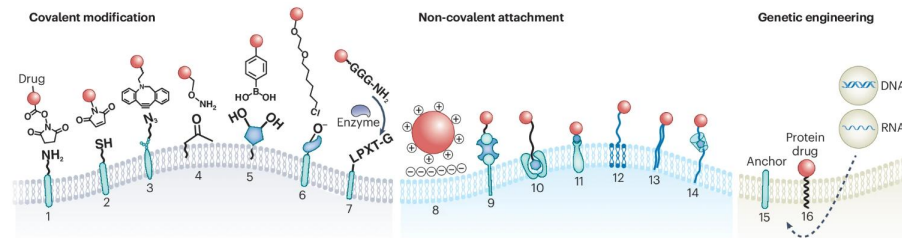
Common cell–drug conjugates (CDCs)

Cell carriers



Nat. Biomed. Eng. 2024, 8, 1347-1365

Strategies for CDCs production

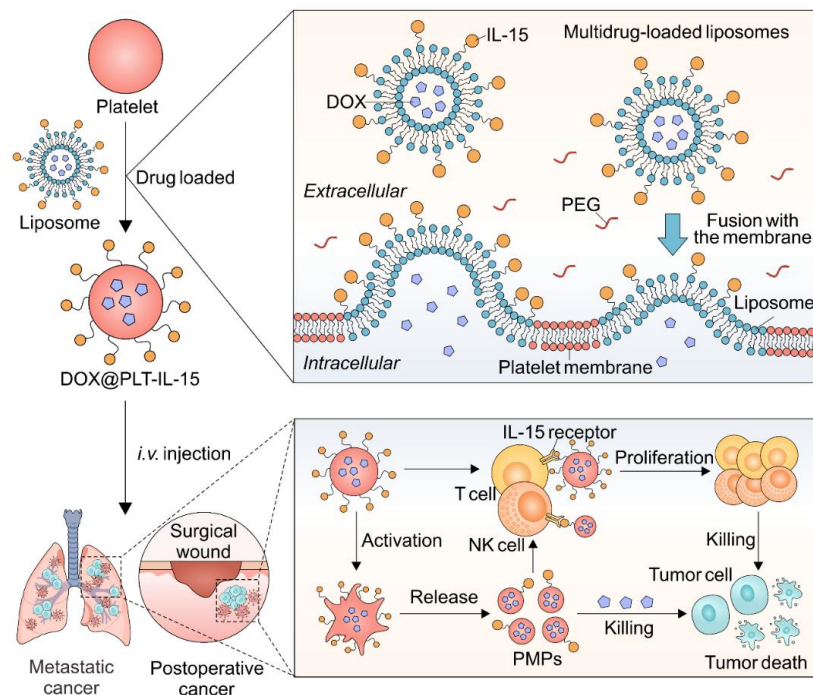


Challenges:

- Time-consuming process;
- Membrane protein changes;
- Compromised function;
- Limited genetic engineering.

Need for faster, safer, and more efficient production

Scheme

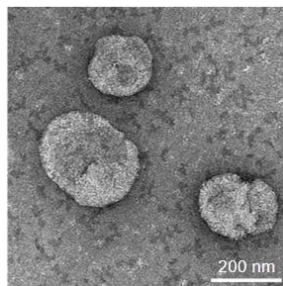
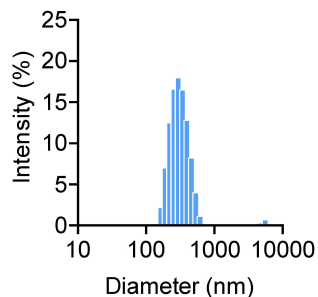
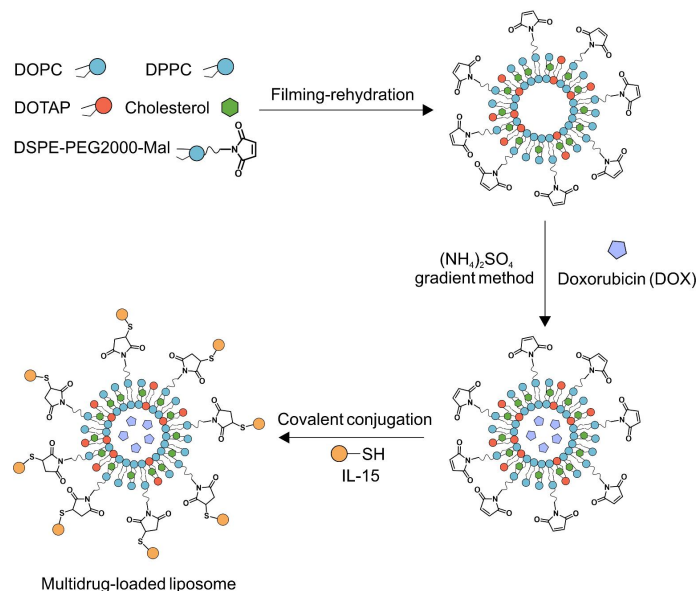


- One-step fusion strategy enabled efficient co-loading of **doxorubicin (DOX)** and **IL-15** into platelets **within minutes**.
- Engineered platelets retained innate targeting to **metastases** and **surgical wounds**.
- Platelet-drug conjugates (PDCs) suppressed **lung metastasis** and **tumor recurrence**.

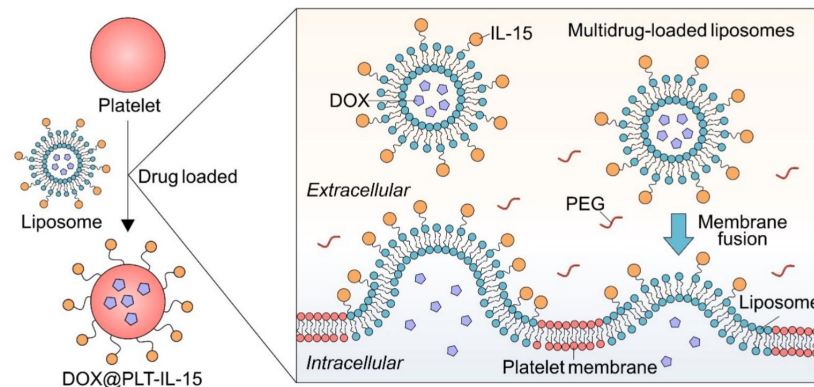
Zhengjie Zhao, Yinxian Yang, Sheng Tao,..., Zhen Gu*, Jicheng Yu*. *Angew. Chem. Int. Ed.* 2024, 23, 844–853

Preparation of liposomes for multidrug loading in platelets

Step 1: Preparation of liposomes with bilateral cargos



Step 2: Liposome-platelet fusion mediated by PEG

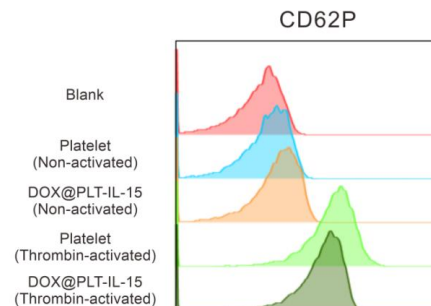
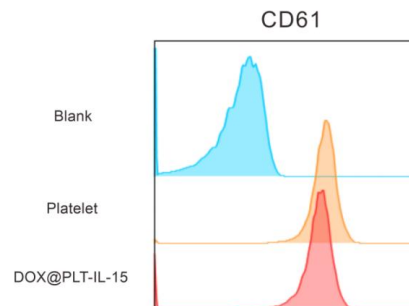
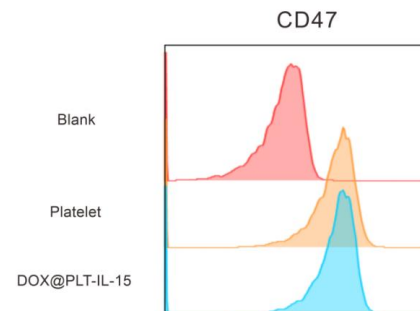
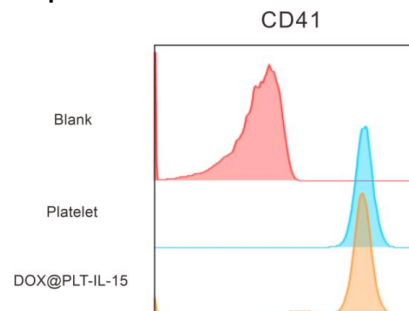
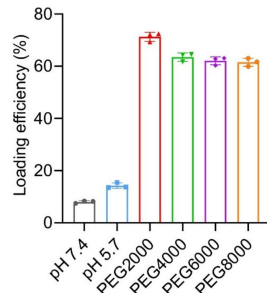
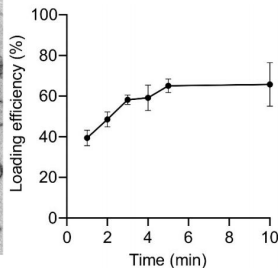
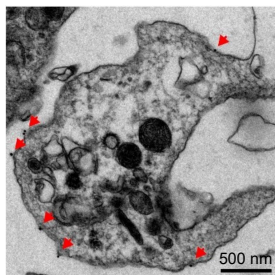
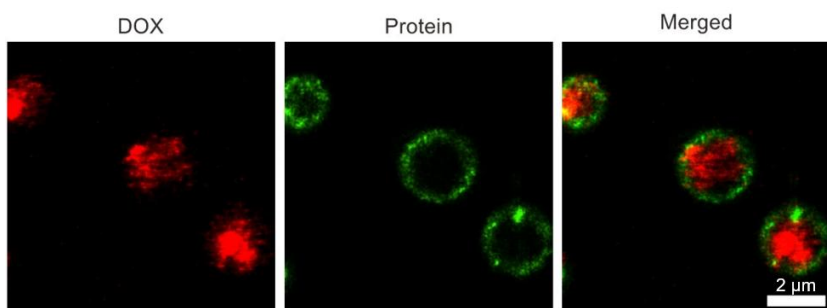


Advantages:

- Dual loading on **membrane and cytoplasm**;
- High loading efficiency;
- Low platelet activation risk;
- Simple and time-saving process.

Characterization of drug-loaded platelets

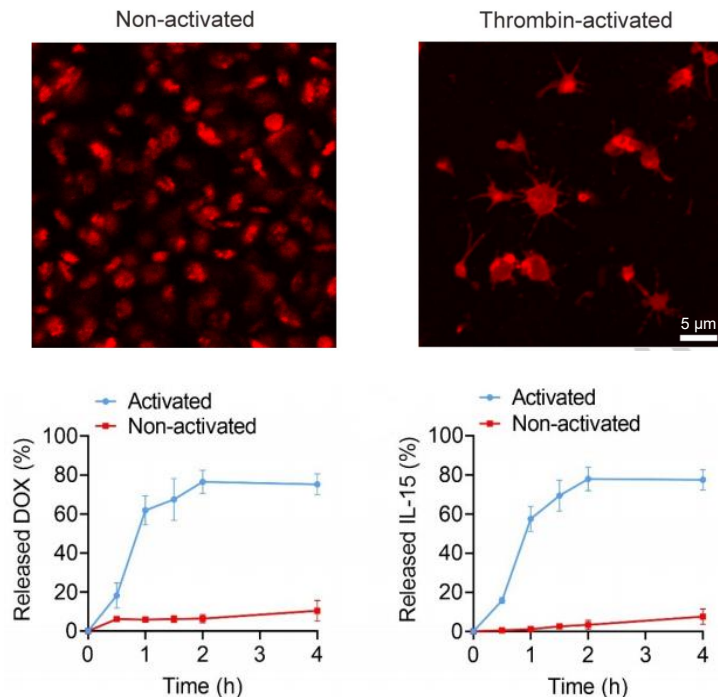
- Rapid drug loading (≤ 5 min) with preserved normal platelet markers



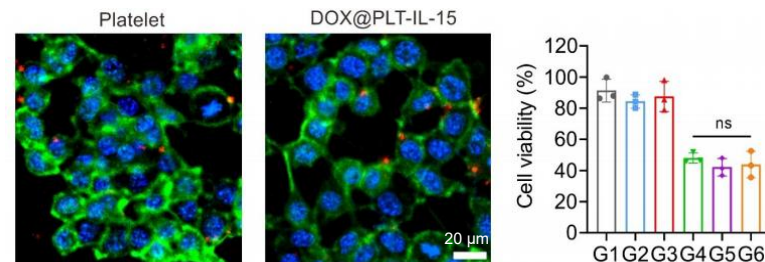
Loading capacity: 40 μ g DOX & 1.98 μ g IL-15 per 10^8 platelets

In vitro functional evaluation of drug-loaded platelets

- Thrombin-triggered stimulation & drug release

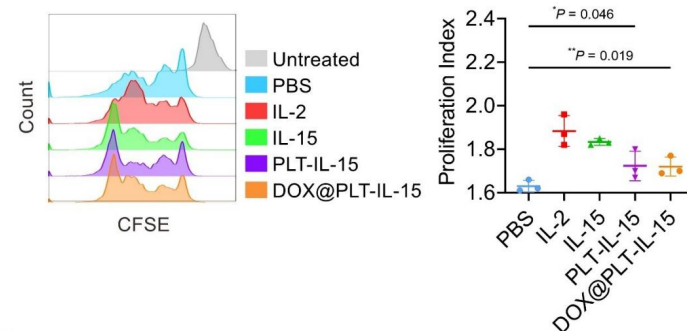


- B16F10 cell targeting and cytotoxicity



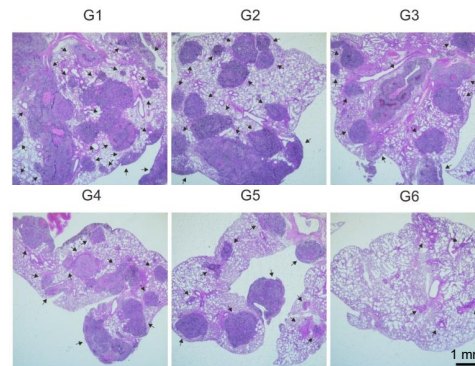
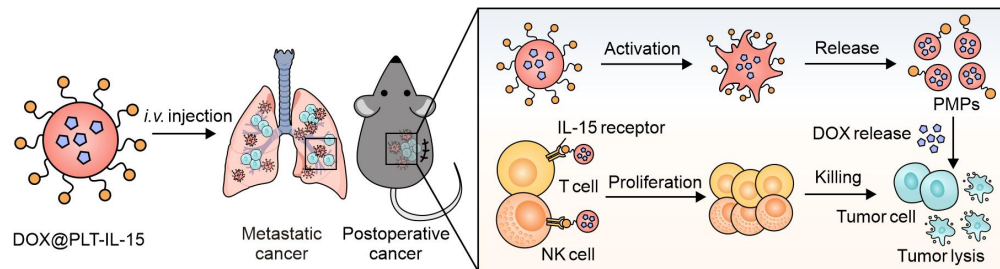
Transwell with 3 μm pores

- Enhancement of CD8⁺ T cell expansion

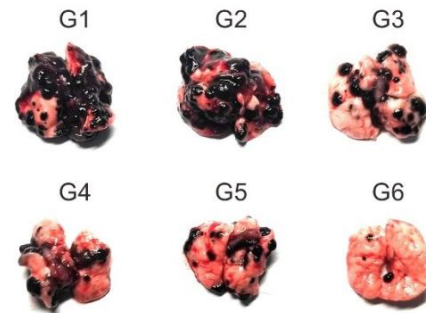
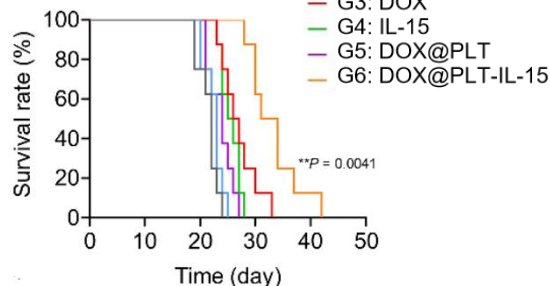
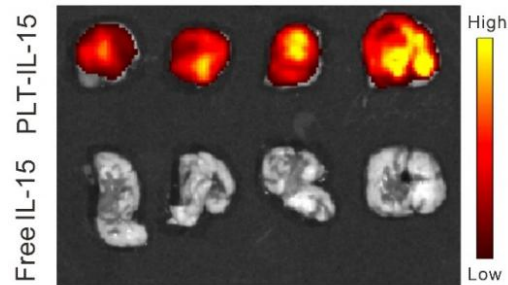


Treatment of tumor metastases in murine lungs

- Multidrug-loaded platelets (DOX@PLT-IL-15) significantly inhibited **metastatic melanoma progression**

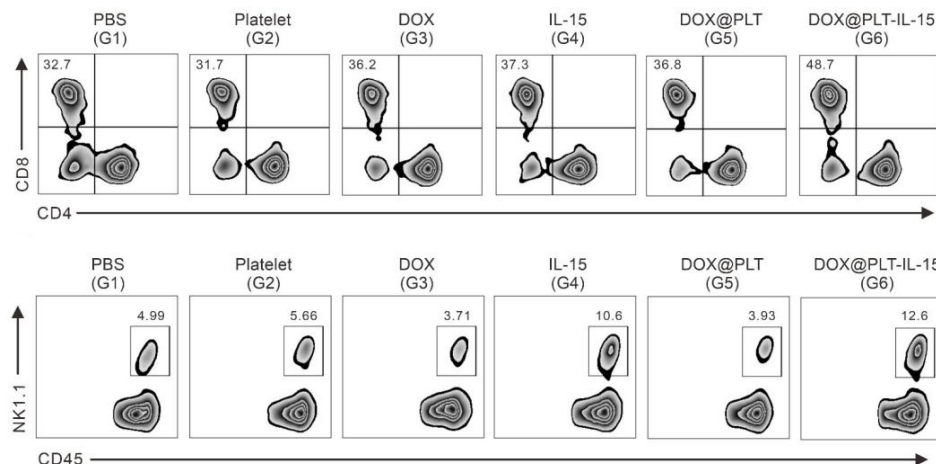


Metastatic lesions in the lungs

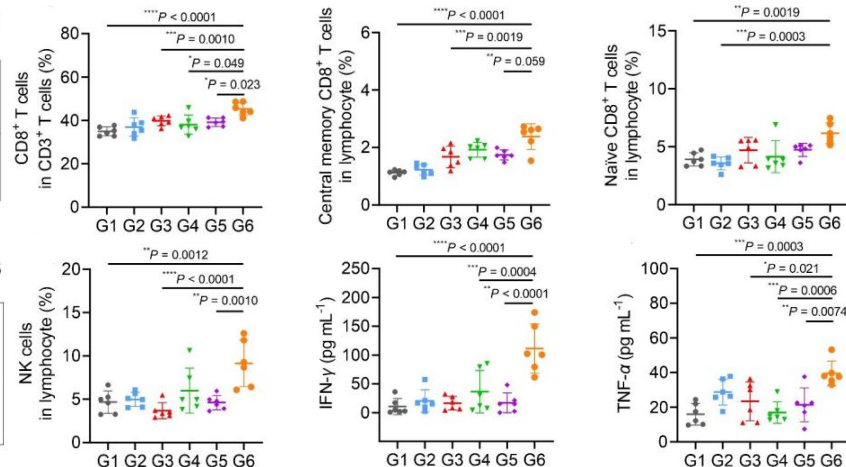


Immunostimulatory effects of drug-loaded platelets

- DOX@PLT-IL-15 triggered an anti-tumor immune response in B16F10-luc metastatic tumor model.



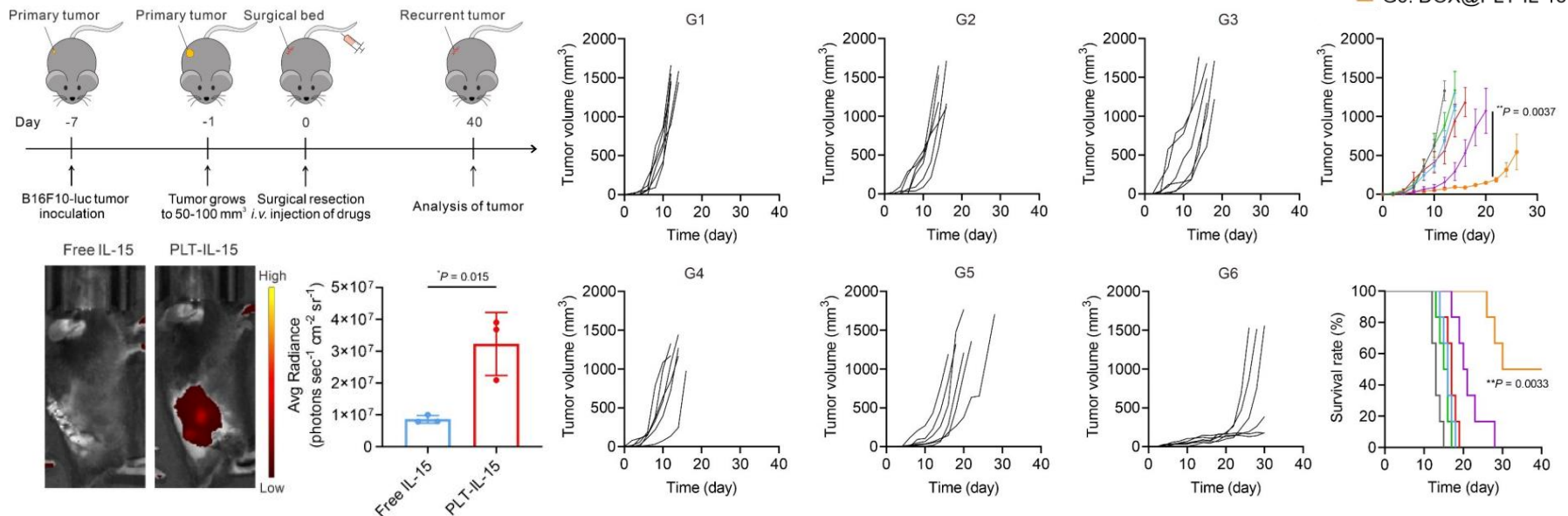
Analysis of circulating NK and CD8⁺T cells



Spleen-resident memory T cells & circulating antitumor cytokine levels

Treatment of postoperative tumors in mice

- DOX@PLT-IL-15 selectively accumulated at **surgical tumor bleeding sites** and markedly inhibited **postoperative tumor recurrence**.

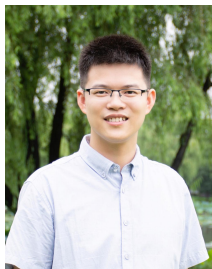


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Thank you!
Welcome to Hangzhou, China!

