Selective Intracellular Delivery of Antibodies in Cancer Cells with Nanocarrier Responding to Endo/lysosome Hyperacidification

poster# **545**

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Endosomal barrier and selective escape

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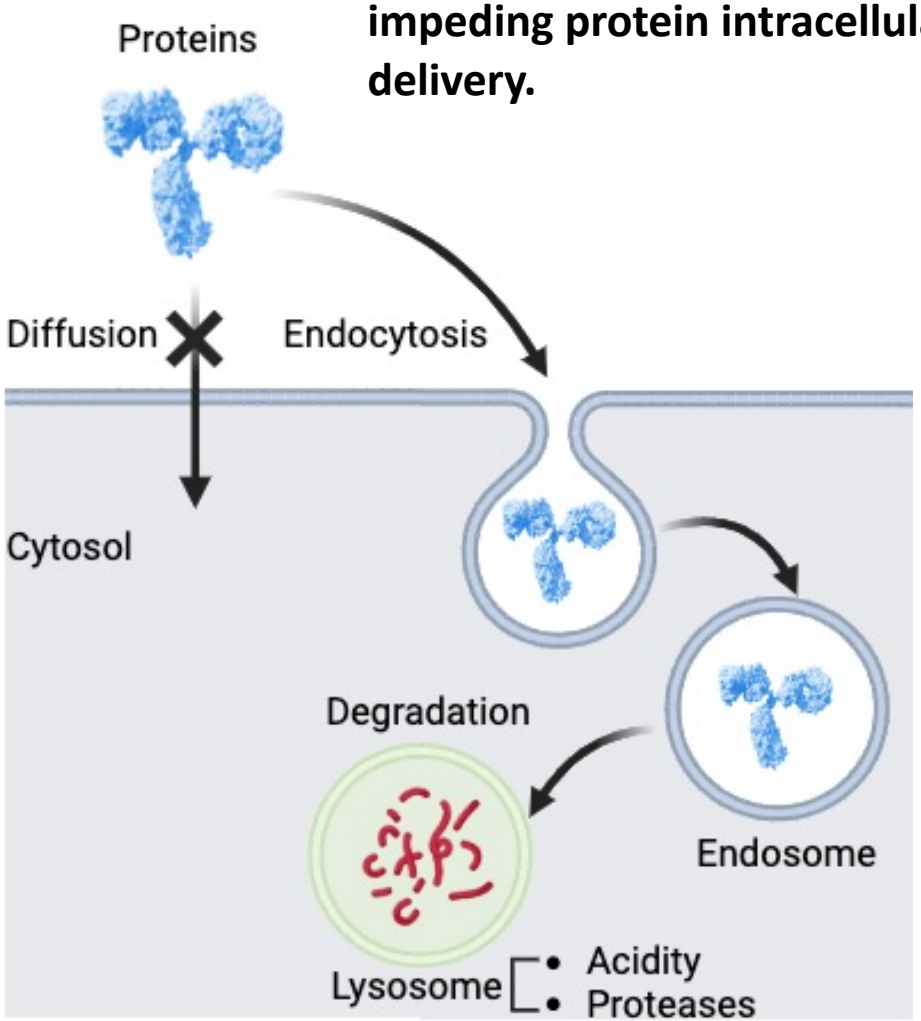
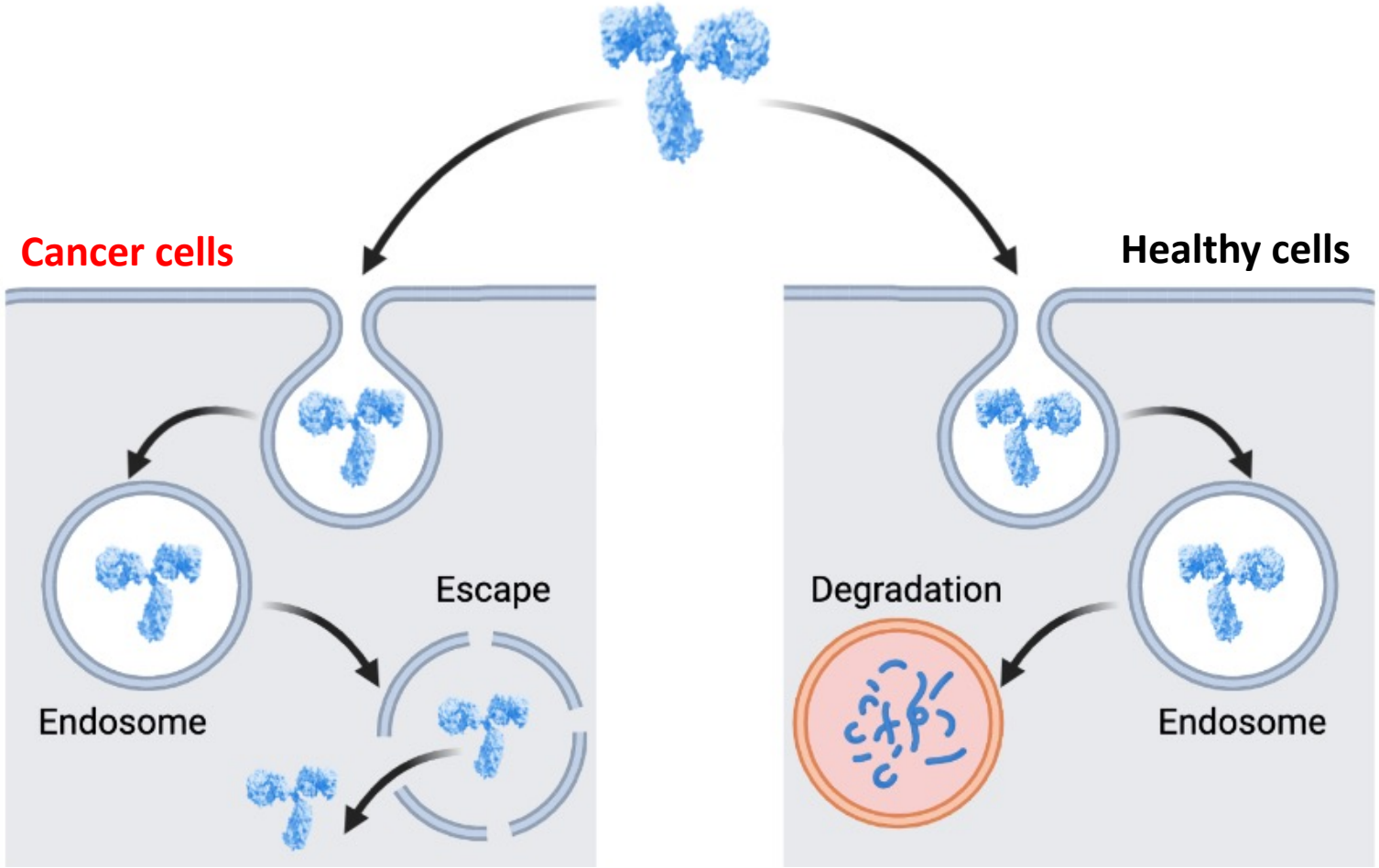
- **Endosome system is a barrier impeding protein intracellular delivery.**



- **Controlling on the endosomal escape can enable selective cargo delivery.**



√ Successful delivery

× Failed delivery

A novel "internal targeting" methodology

Endosome hyperacidification in cancer cells

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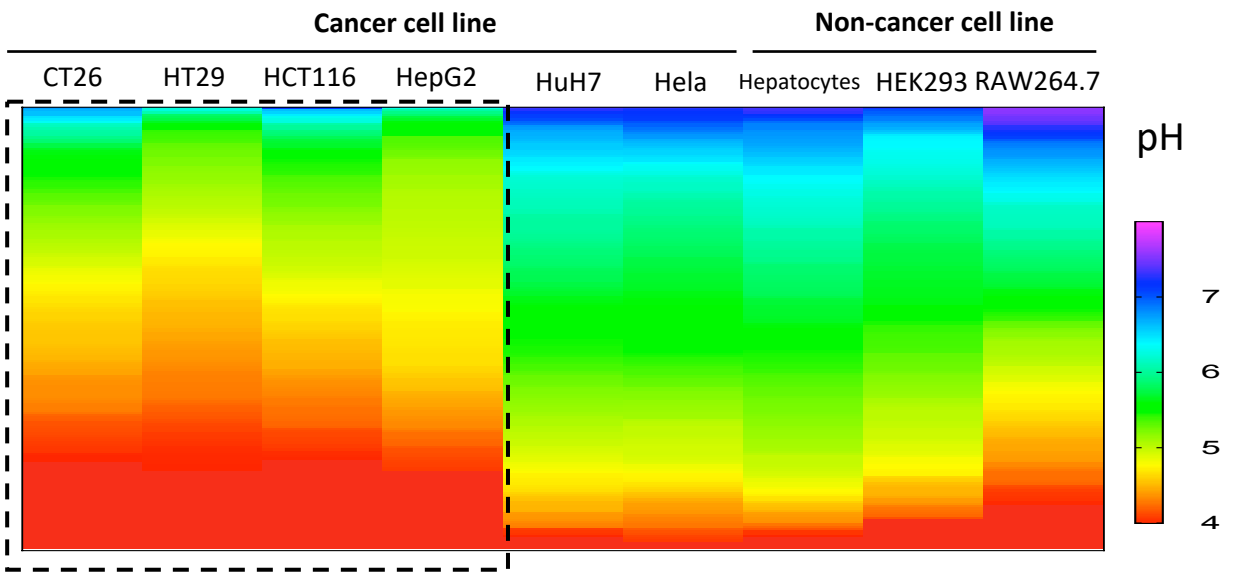
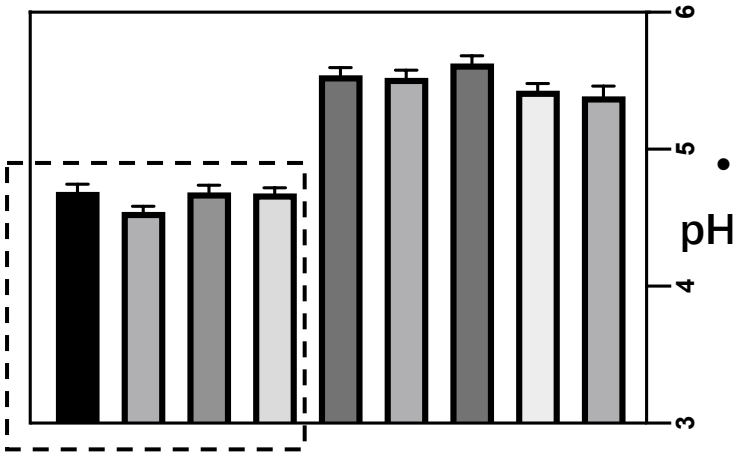
Endosome pH distribution in different cells



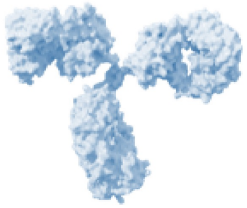
Average endosome pH



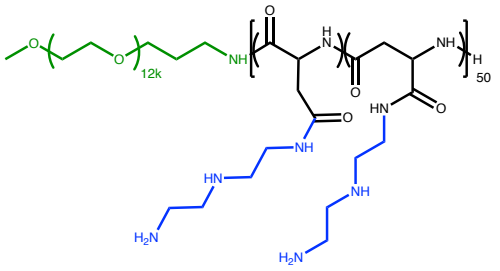
- Some cancer cells have significantly hyperacidified endosomes (pH < 5.0)

pH-sensitive nanocarriers loading antibodies

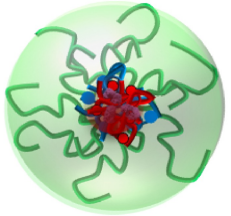
PEG-pLL(CAA)
pH-sensitive structural component



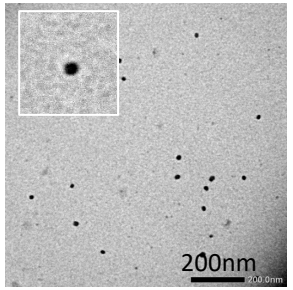
Antibody

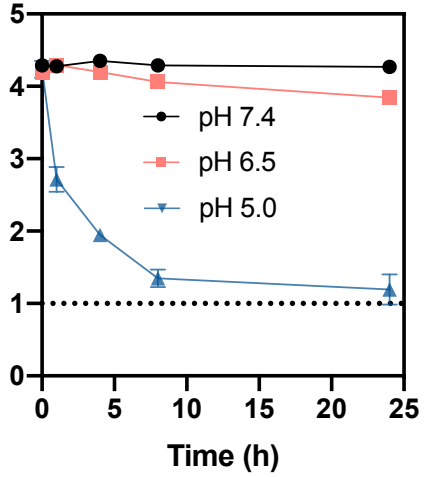


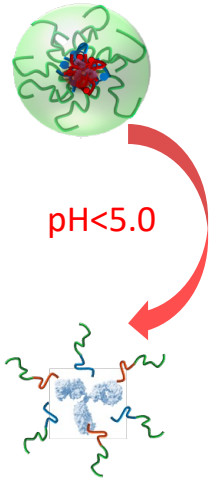
PEG-pAsp(DET)
Endosomal escape component



pH-sensitive Nanocarrier







Selective endosomal escape by pH-sensitive system

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Endosomal escape in different cells

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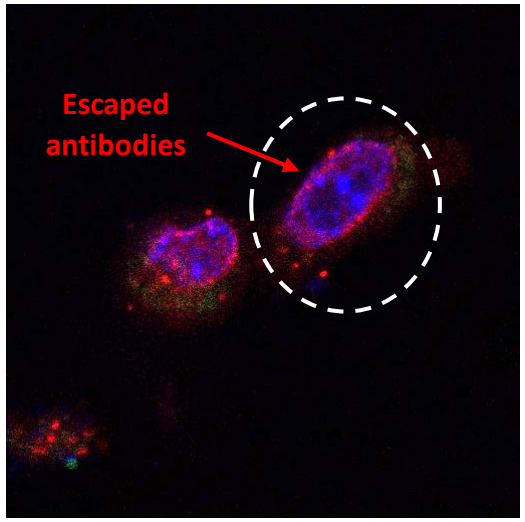
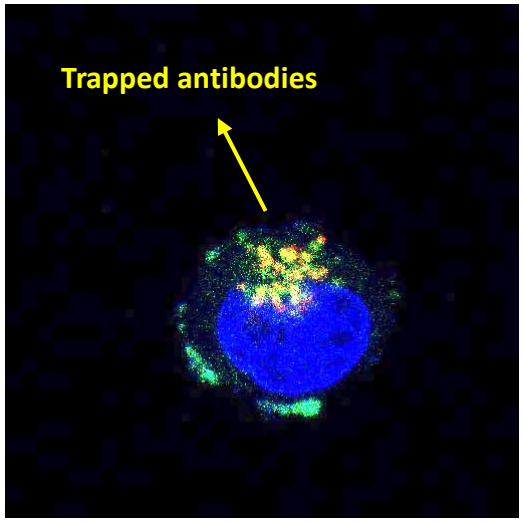
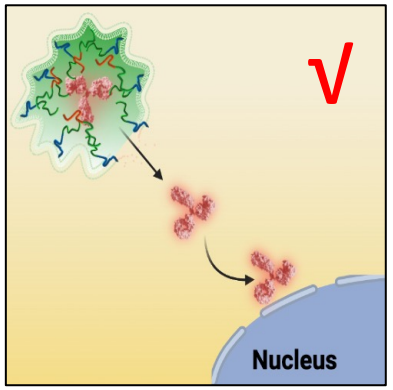


Hepatocytes



Hoechst/ Lysotracker/ anti-nuclear pore complex (NPC)

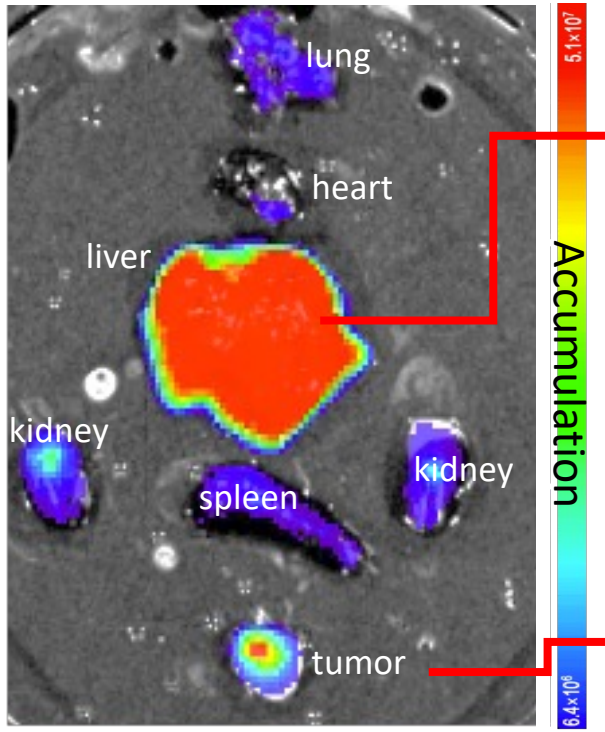


Successful escape

Failed escape

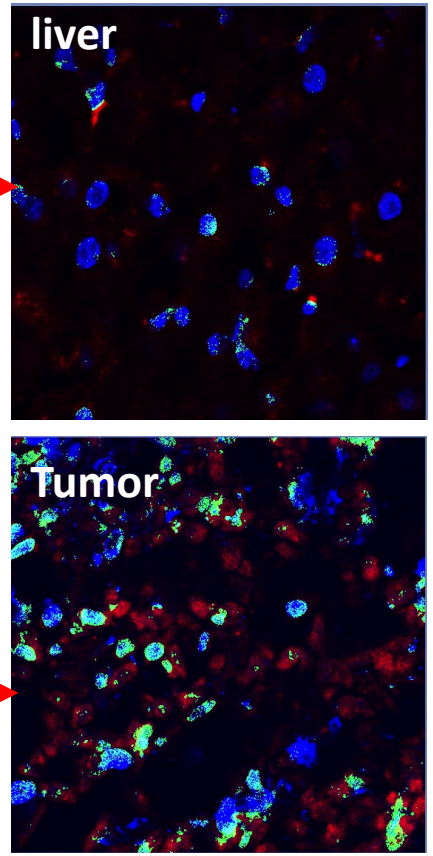
In vivo selective endosomal escape

(by intravenous injection)



anti-NPC biodistribution

Subcellular distribution of anti-NPC in tissues



× failed delivery

√ successful delivery

Hoechst/ anti-NPC/ co-localization (binding to antigen)

- Targeting delivery of antibodies to cancerous intracellular spaces is achieved.

Conclusion and acknowledgements

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- Certain cancer cells show endosome hyperacidification.
- pH-sensitive nanocarriers can conduct selective endosomal escape among different cells.
- Selective endosomal escape leads to cancer-specific intracellular delivery of biomacromolecules.

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