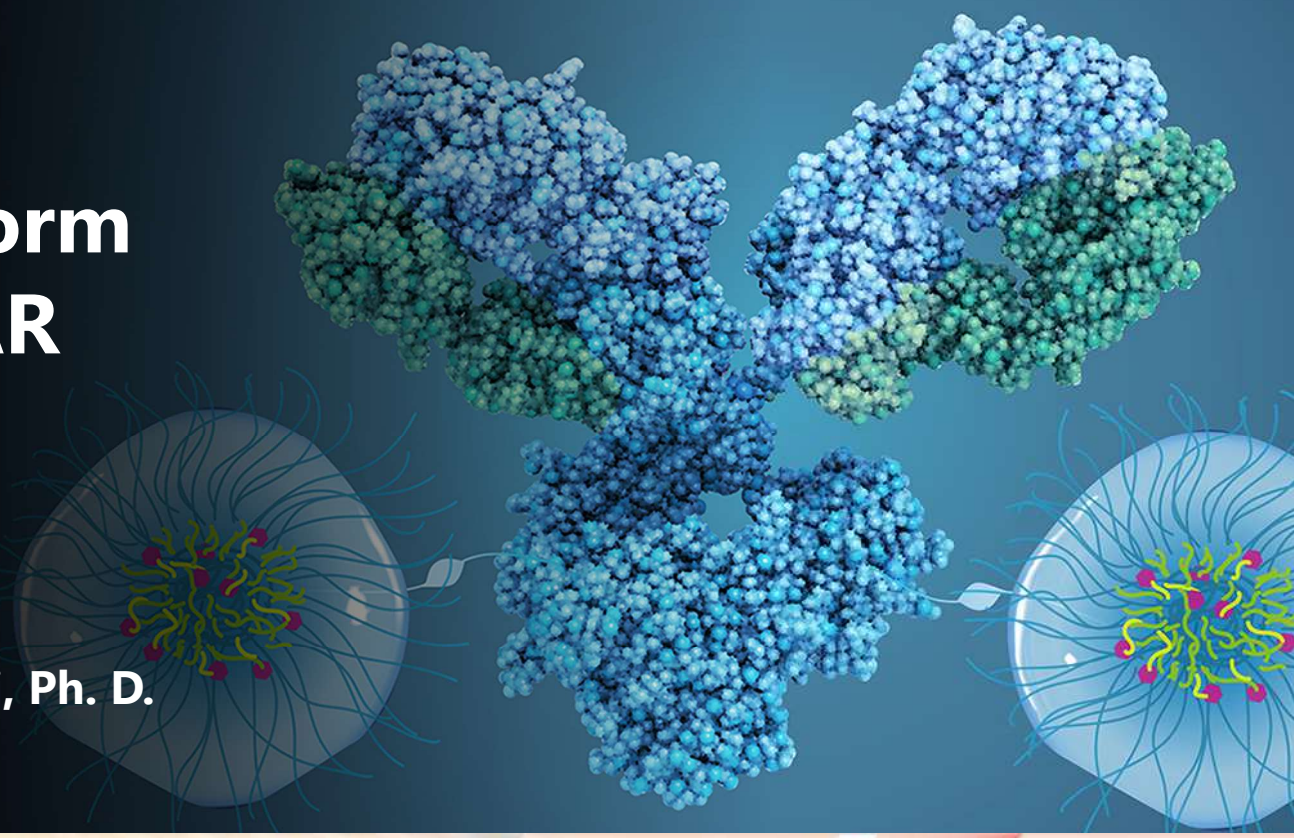
Kowa Kowa Pharmaceutical Europe AG

Antibody drug-loaded unimicelle conjugates (ADUCs): a novel platform enabling ultra-high DAR



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CRS 2025 ANNUAL MEETING & EXPOSITION

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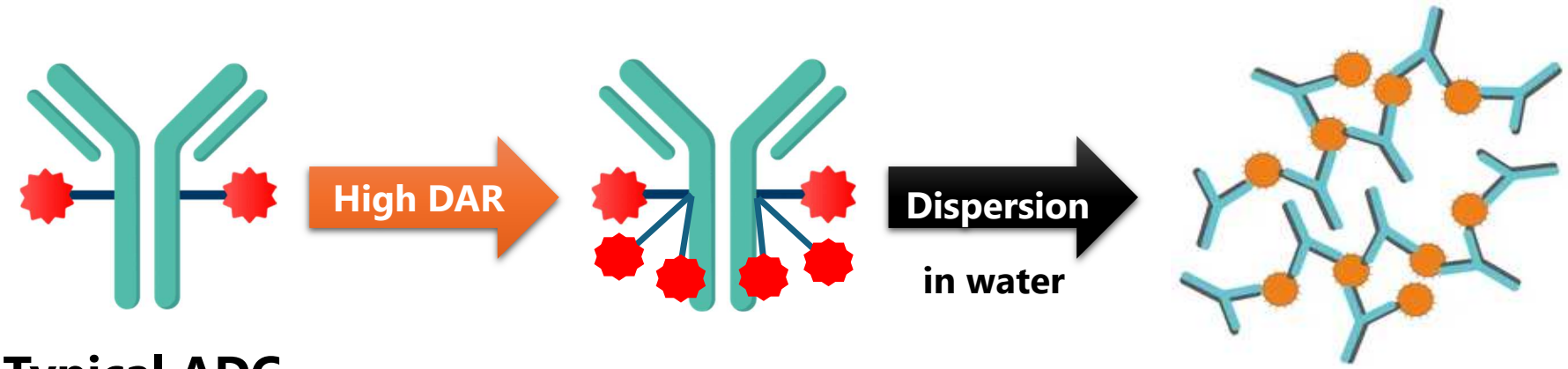
NEXT-GENERATION DELIVERY INNOVATIONS

Introduction

- Current ADCs (Antibody-drug conjugates) are limited by low drug-to-antibody ratios (DAR) due to physicochemical instabilities.

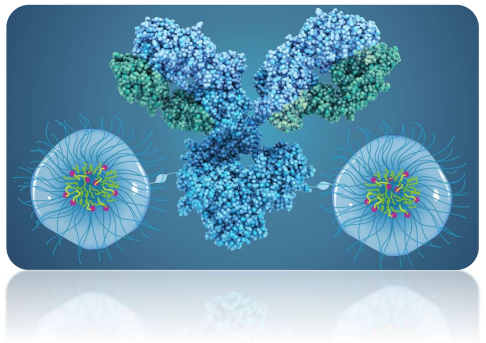


Typical ADC

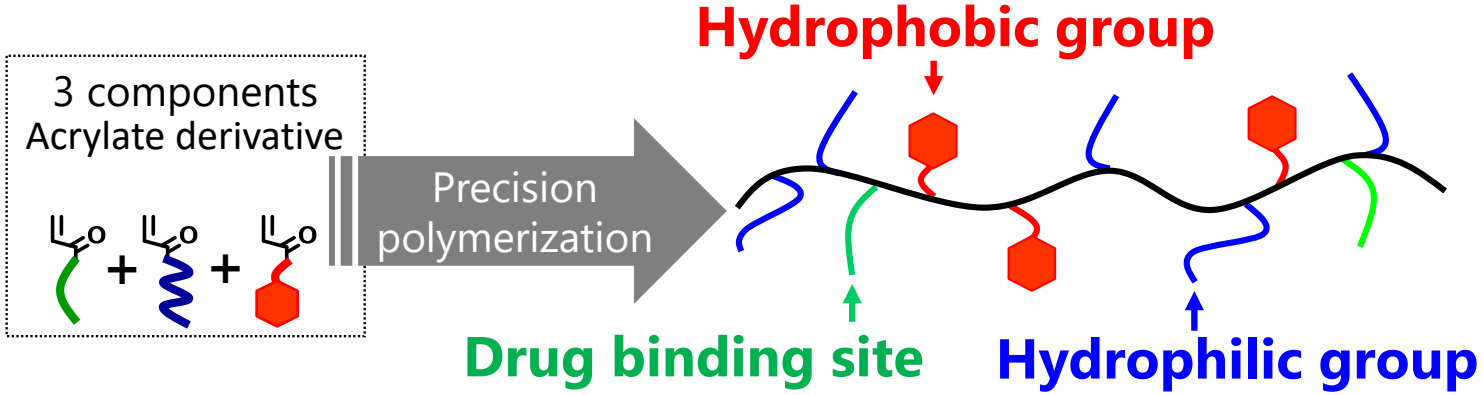
NG: Coagulation / Precipitation

Introduction

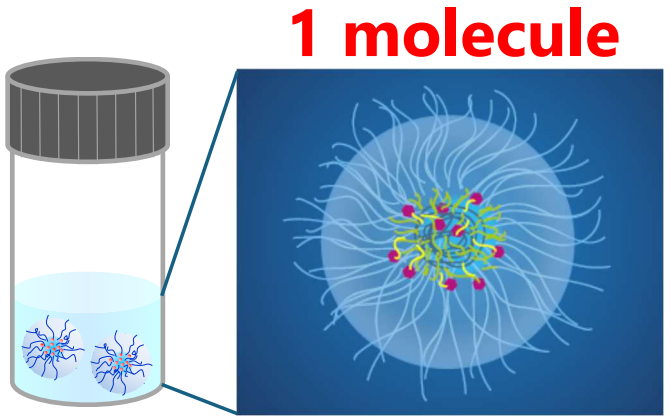
- We developed a novel platform: **Antibody-Drug-Loaded Unimicelle Conjugates (ADUCs)** using single-chain polymer nanoparticles (SCNPs).
  - Achieved an **ultra-high DAR** of approximately **40**.
  - Leveraged the amphiphilic nature of **unimicelles** for favorable physicochemical properties.
  - Demonstrated potent antitumor effects in pharmacological studies.



Polymer Design



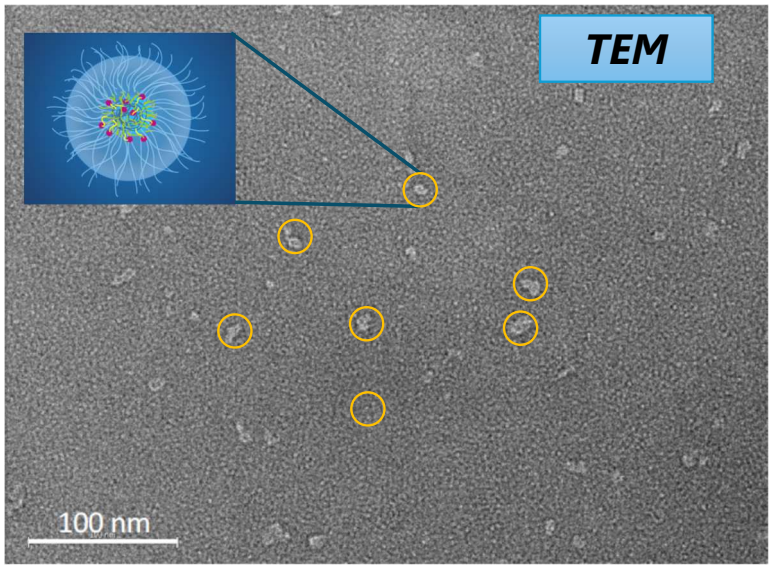
Parameter	Range
Molecular Weight	10,000～60,000
Particle diameter	5～10 nm
Drug #/particle	Approx. ~40

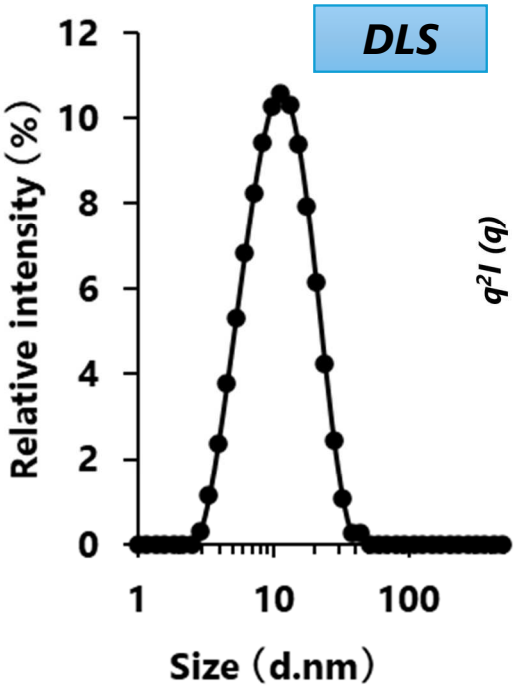


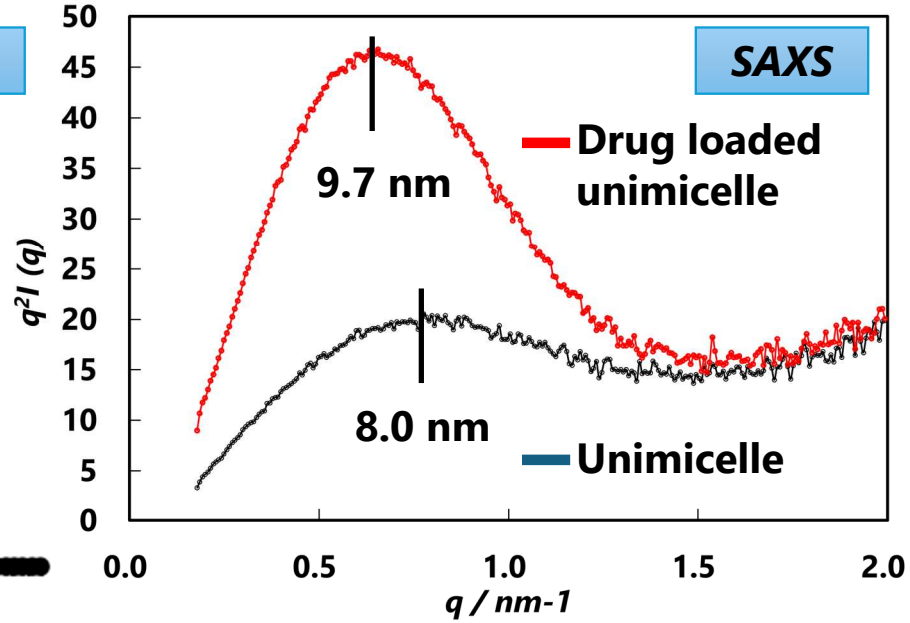
Amphiphilic unimicelle

Ultra-high drug capacity achieved with KOWA's novel unimicelle technology while maintaining favorable physicochemical properties

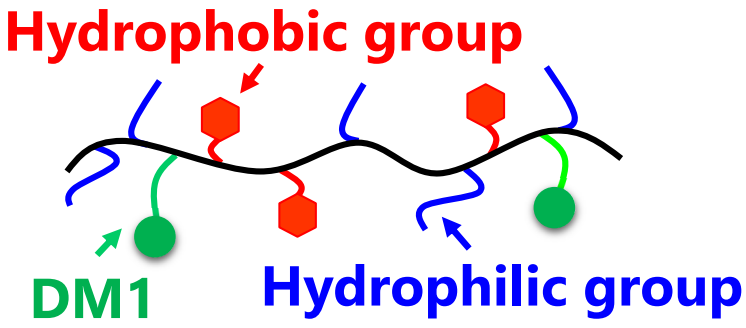
Unimicelle Characterization







MALS

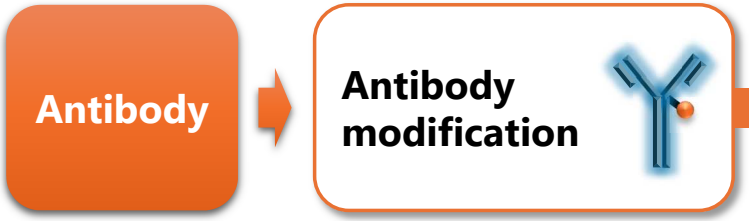


Unimicelle self-assembly in water

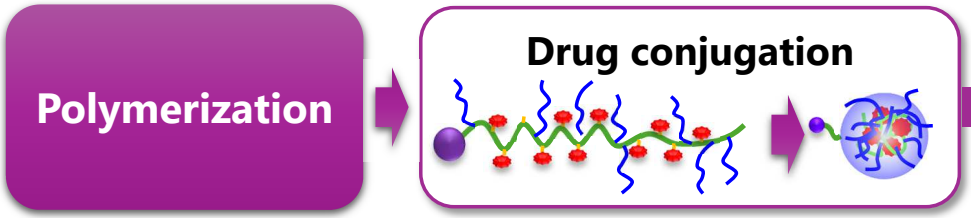
(Single molecule aggregate, 10 nm)

Antibody Drug-Loaded Unimicelle Conjugate (ADUC)

1. Preparation of functional group-modified Ab

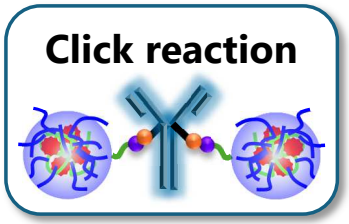


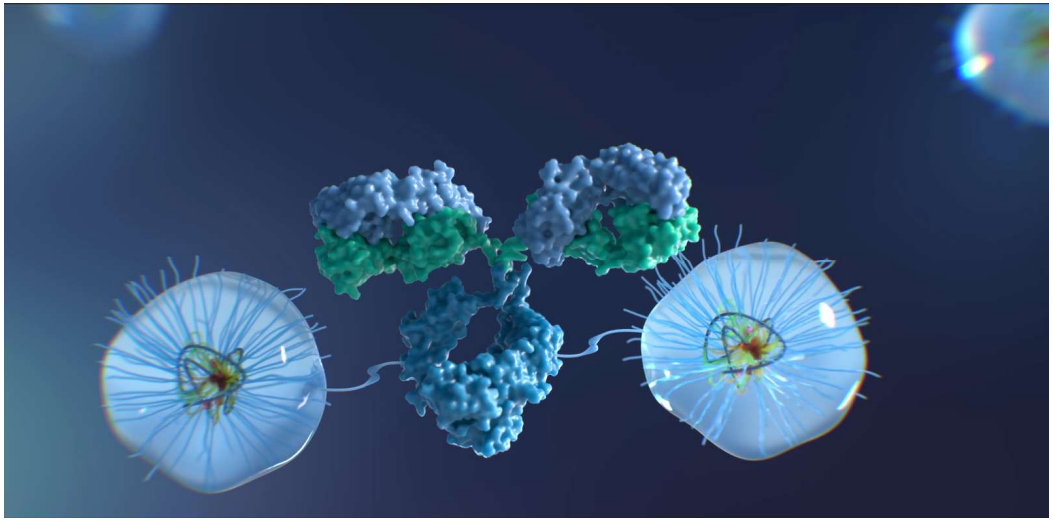
2. Polymerization and drug binding



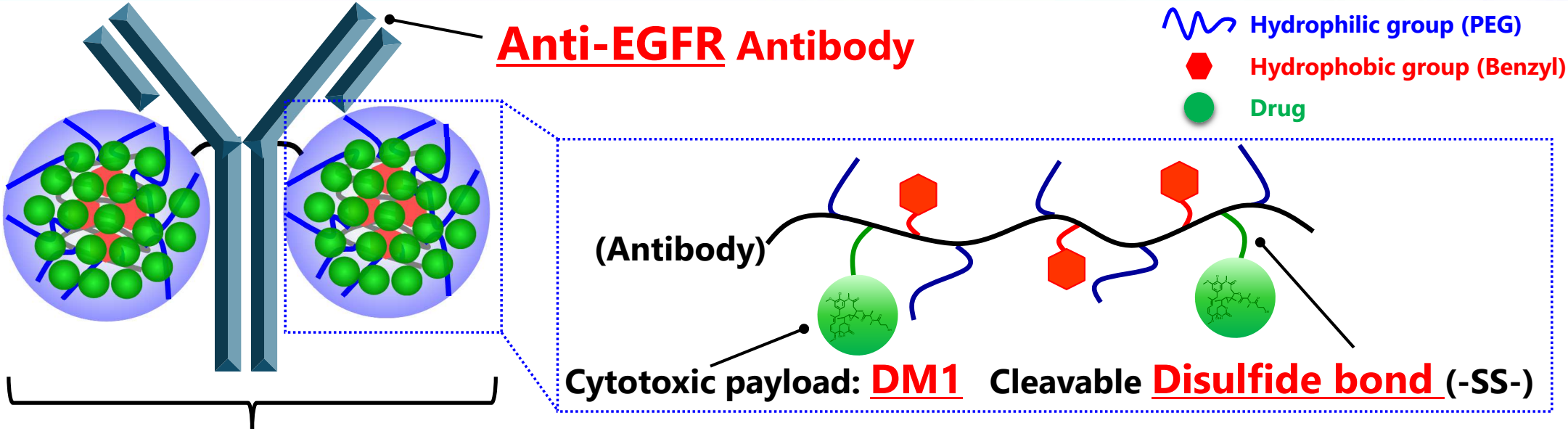
3. Conjugation and Purification

PAR（Polymer-Antibody Ratio）：ca. 2.0





K-679: Combination of Anti-EGFR Ab and DM1



Compact (Diameter: 20 nm) ➡ **Superior tumor-targeted delivery**

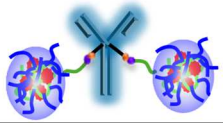
Ultra-high DAR* (>40: 20 DM1/unimicelle × 2 unimicelles/antibody) ➡ **Effectiveness**

ADUC: Enhanced anti-tumor effect with higher payload delivery

*DAR: Drug to antibody ratio

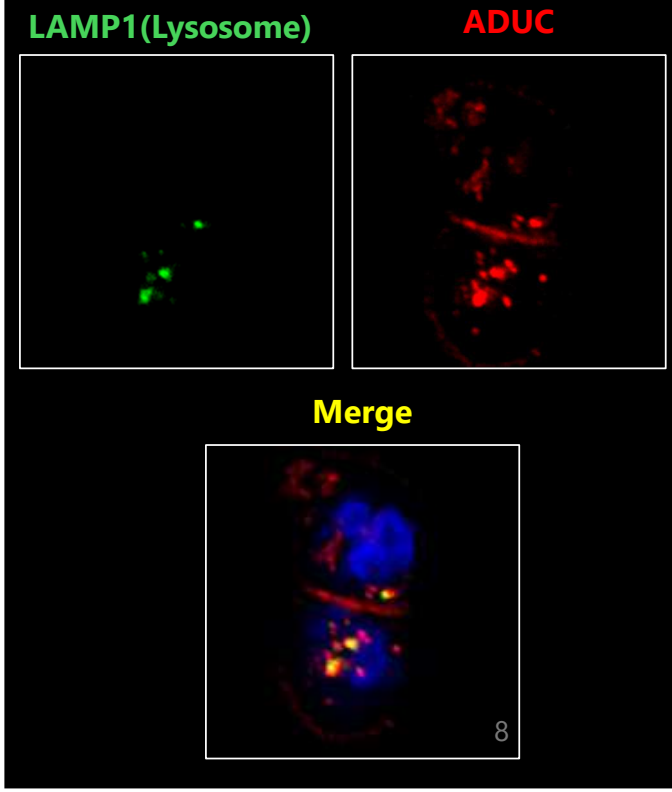
Antigen Recognition / Intracellular Uptake and Localization

EGFR binding affinity and kinetic parameter

Entry		Drug	Association Rate *k* a (1/Ms)	Dissociation Rate *k* d(1/s)	Equilibrium Dissociation Constant K_D (M)
Cetuximab		None	$0.94 \pm 0.06 \times 10^{6}$	$1.33 \pm 0.02 \times 10^{-3}$	$1.40 \pm 0.11 \times 10^{-9}$
ADUC		DAR=40	$1.10 \pm 0.04 \times 10^{6}$	$1.30 \pm 0.05 \times 10^{-3}$	$1.20 \pm 0.08 \times 10^{-9}$

ADUC showed EGFR-binding affinity comparable to Cetuximab and lysosomal internalization in EGFR-positive cancer cells

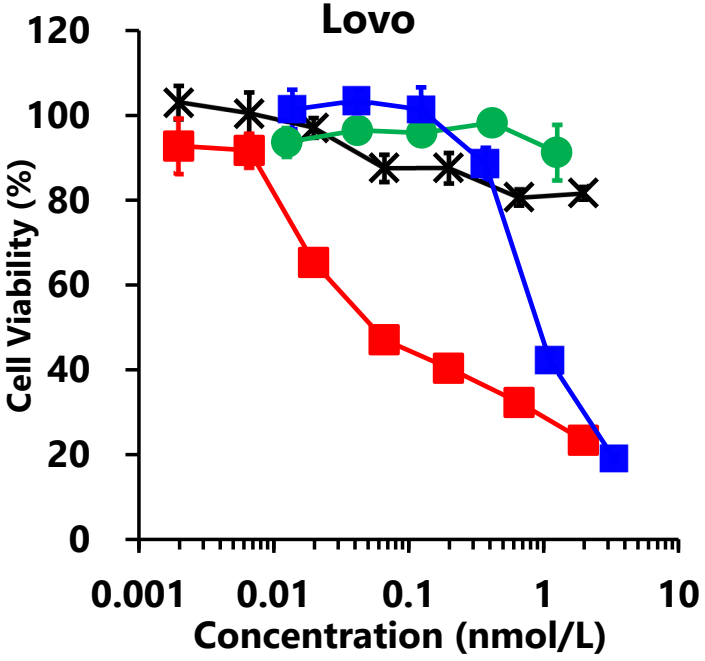
Lysosomal trafficking in EGFR-positive LoVo cells



ADUC Concept: EGFR-dependent Cell Killing Effect (*in vitro*)

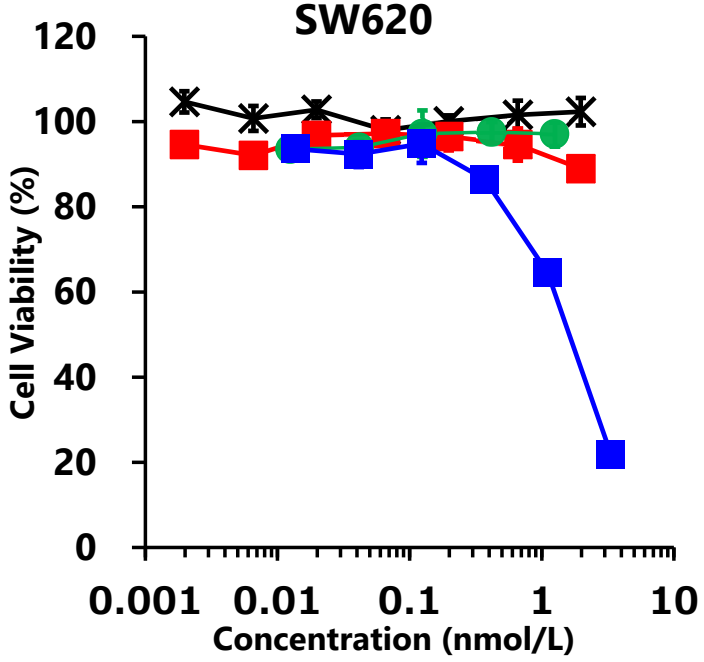
EGFR positive

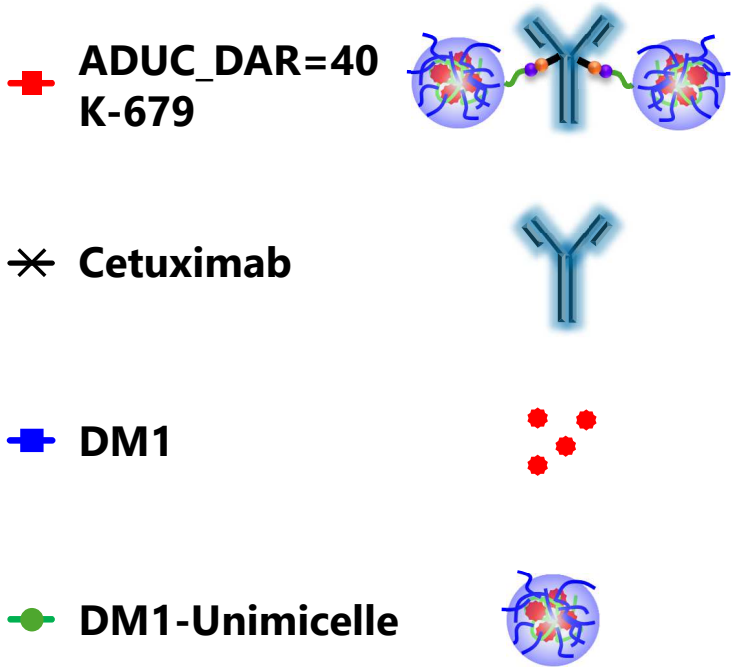
Human colon cancer cell line
Lovo



EGFR negative

Human colon cancer cell line
SW620



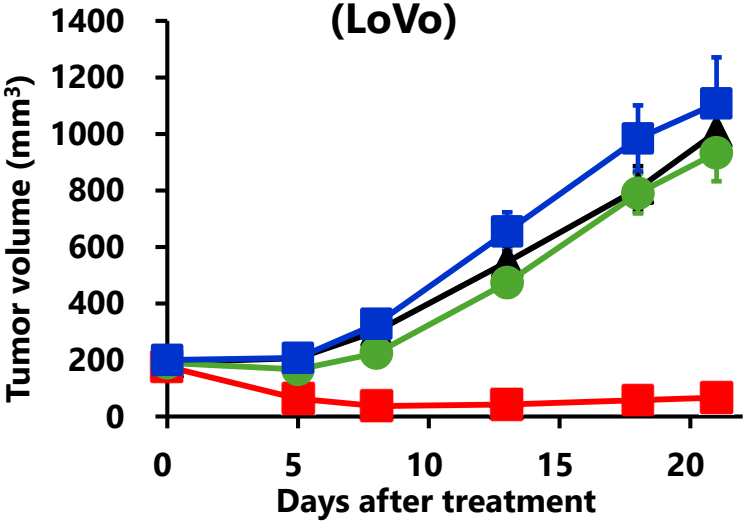


ADUC showed cell killing effect at lower concentration than DM1 or Cetuximab

ADUC Concept: EGFR-dependent Anti-tumor Effect (Mice, *in vivo*)

EGFR-positive

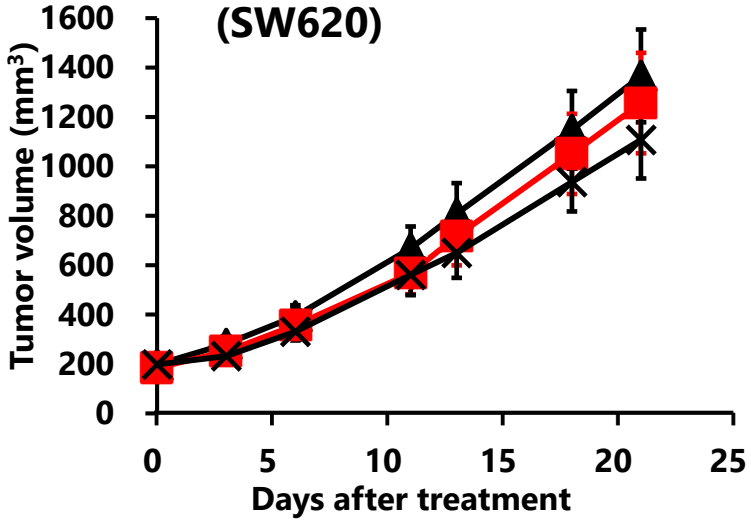
Human colon cancer cell line (LoVo)



n = 10, Mean ± S.E.

EGFR-negative

Human colorectal adenocarcinoma (SW620)

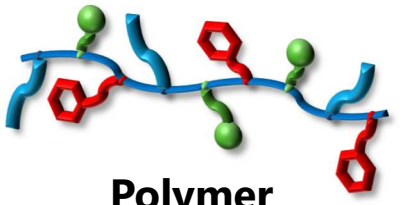


n = 10, Mean ± S.E.

- Vehicle
- ADUC_DAR=40, K-679 (0.48 mg antibody/kg, 0.1 mg DM1/kg)
- Cetuximab (0.48/kg) + DM1-micelle (0.1 mg DM1/kg)
- DM1 (0.1 mg/kg)
- Cetuximab (10 mg/kg)

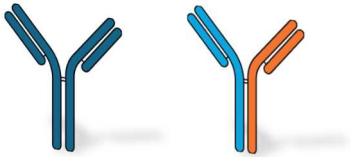
ADUC showed EGFR-specific anti-tumor activity

Future Works

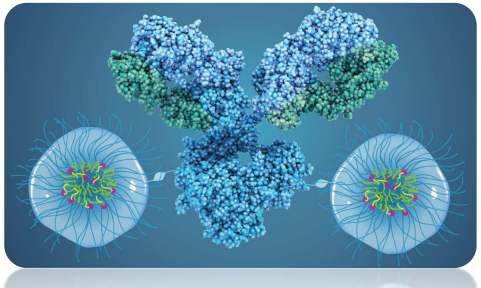


Polymer
(Unimicelle)

Drug binding site



Antibody



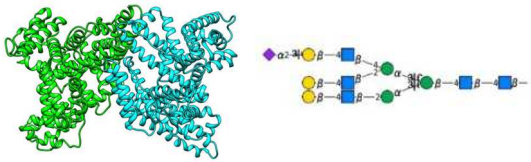
ADUC

Therapeutic agent

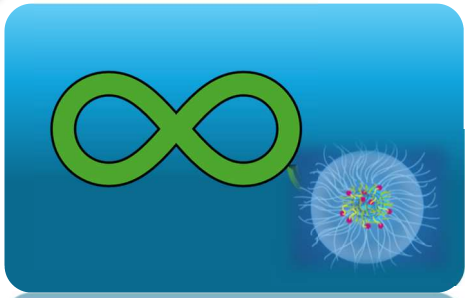
Imaging agent

Antibody Fragments

Affibody
(Ab mimetics)



Peptide, Sugar chain



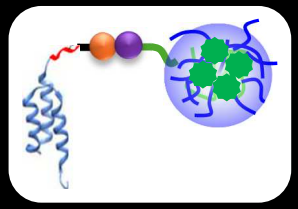
“X”DUC

Conclusion

- Innovative ADUC platform enables highly effective anticancer treatment with precise targeted drug delivery and ultra-high DAR.
- Allows combination of multiple targeting agents and payloads.
- Demonstrates versatility of the ADUC platform technology.
- Stands out as an expandable modality with broad applications.
- Supports potential in various therapeutic areas.

Appendix

Anti-HER2 Affibody Micelles: Cellular Uptake and Cytotoxicity Evaluation

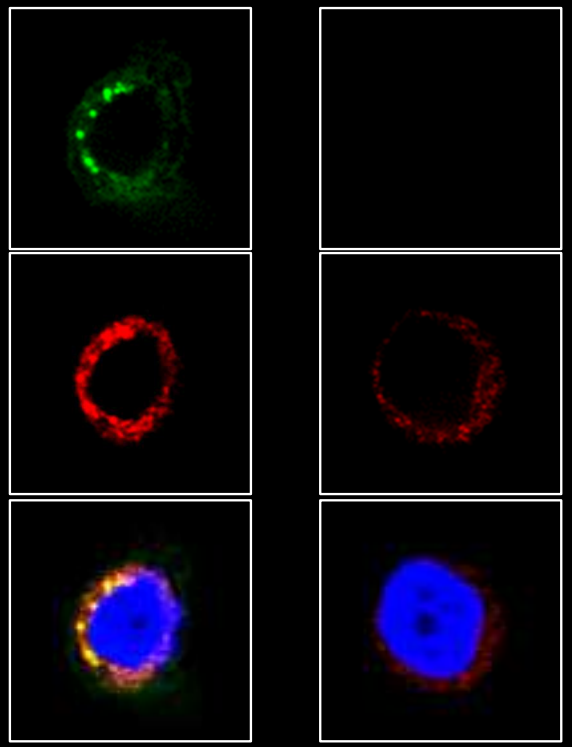


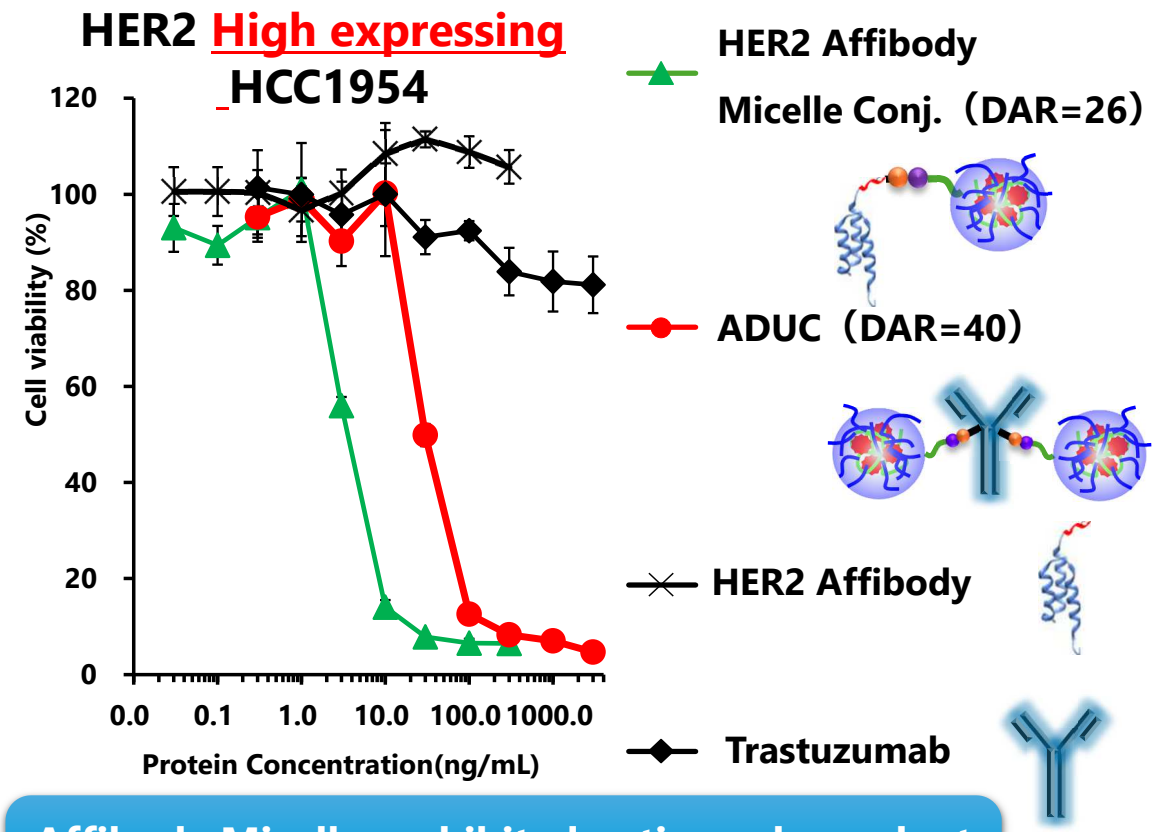
Fluorescently Labeled Unimicelle (TAMRA)

Transferrin (Alexa 647) (As Early Endosome Marker)

DAPI

Merge



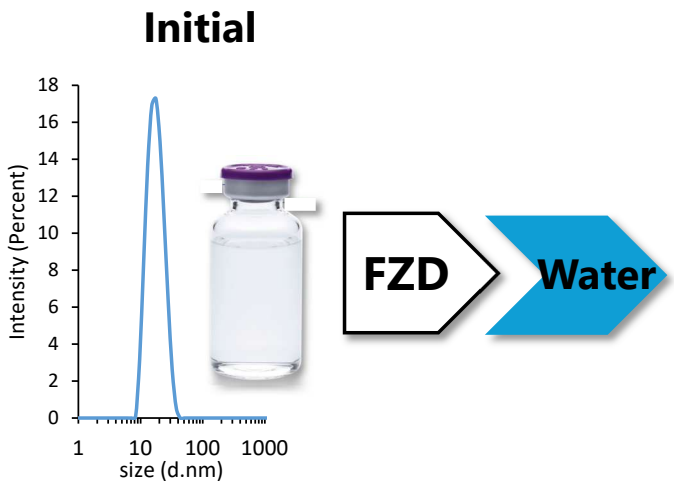


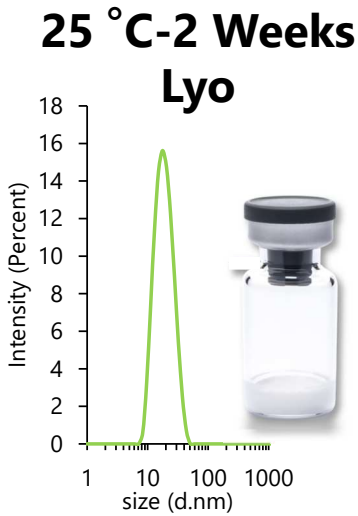
Affibody Micelles exhibited antigen-dependent cell growth inhibition similar to ADUC

Physical property: Stability in solution and Lyo form

Formulation	
ADUC（μg）	200
Trehalose （μg）	200
Polysorbate 80（μg）	6

Liquid	Initial	2W	4W	3M	6M
4°C	18 nm (0.17)	18 nm (0.19)	19 nm (0.14)	18 nm (0.17)	19 nm (0.20)
25°C		20 nm (0.25)	18 nm (0.26)		





Storage condition	Solution	Lyo
	Initial	25 °C-2 weeks
Average diameter	17 nm	18 nm
PDI	0.20	0.16