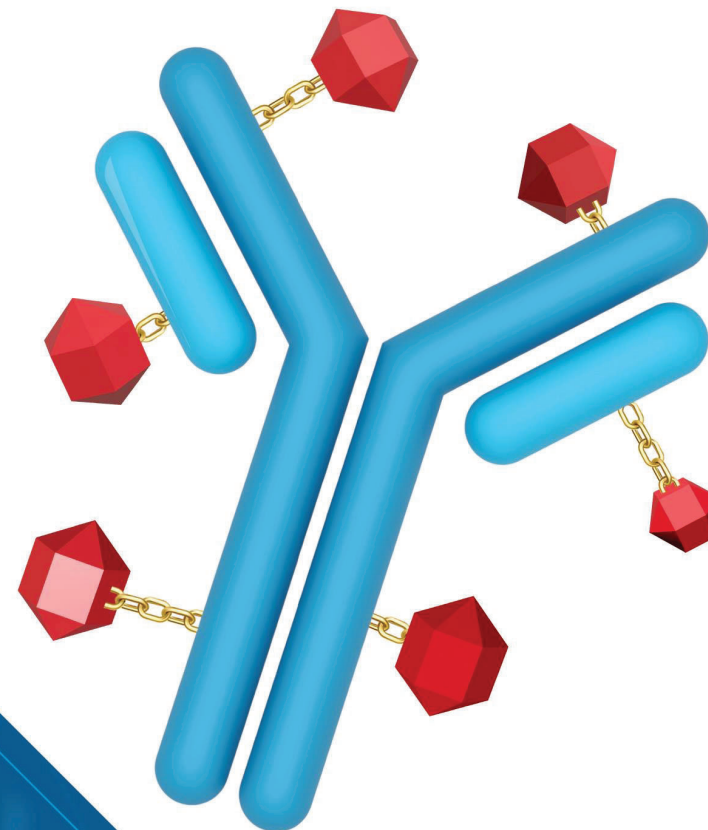
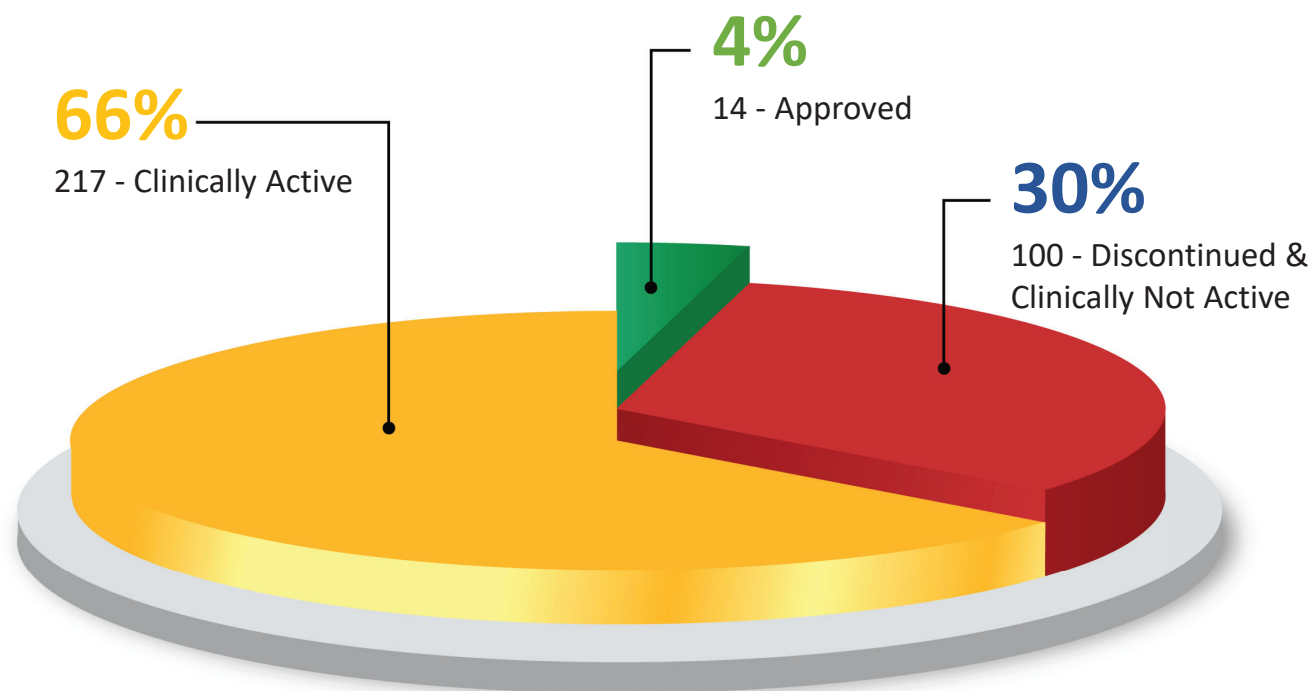


Accelerated Pathway from
Antibody
to **ADC**



Naresh Jain

Landscape of Clinical Antibody-Drug Conjugates

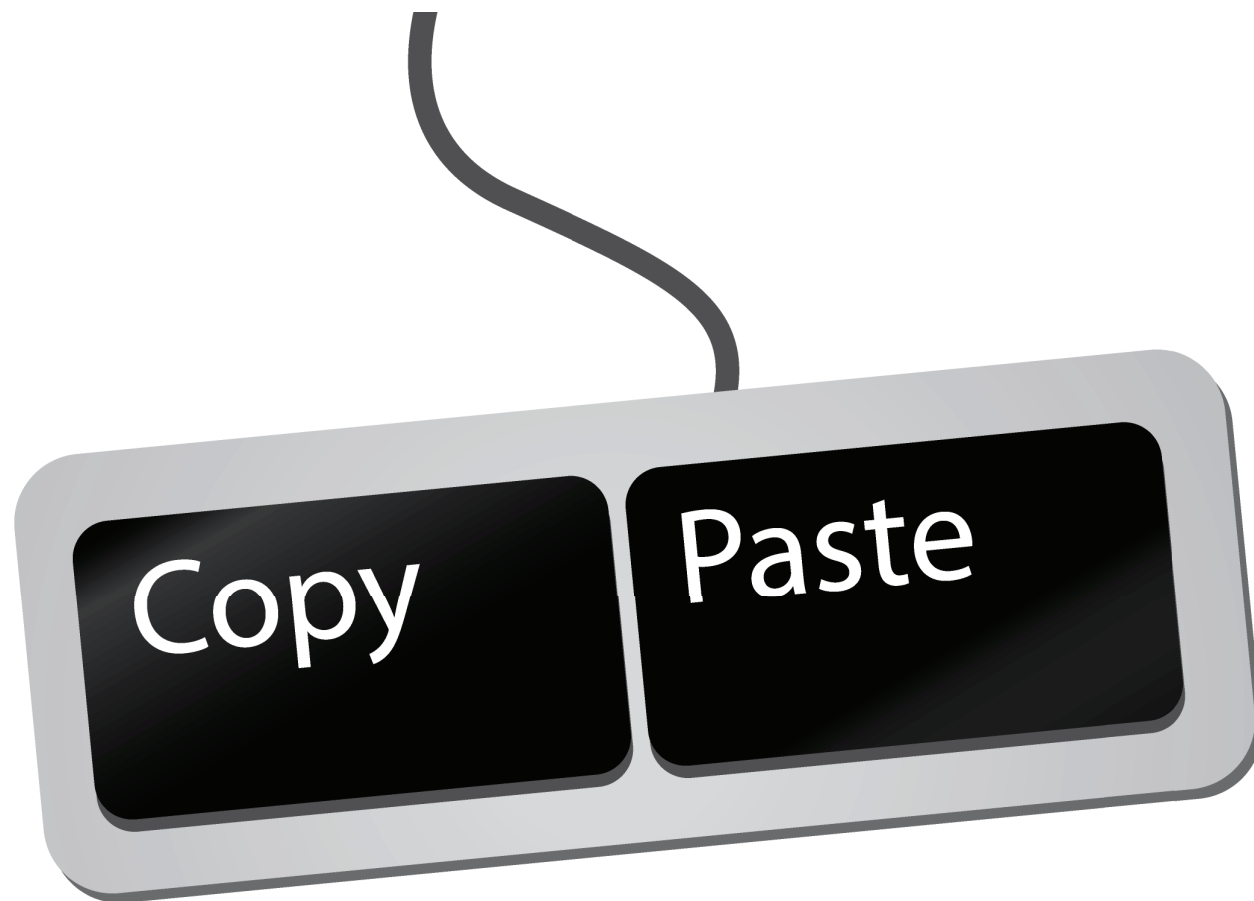


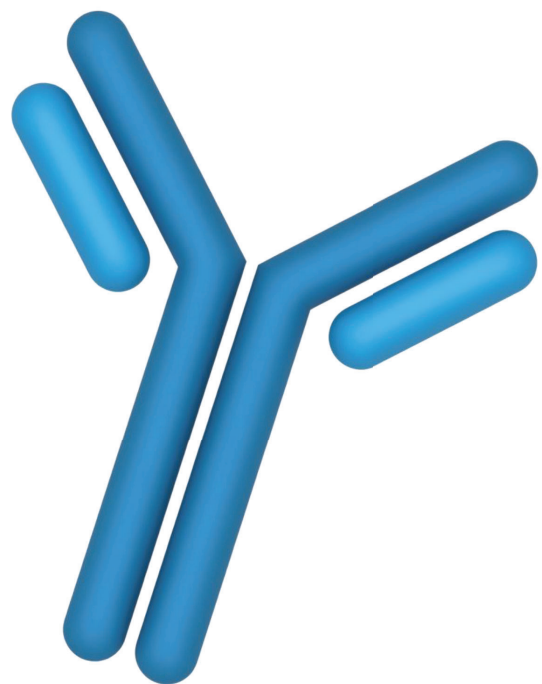
Source: **Beacon** Intelligence Database, October 2023

Discontinued & Not Active ADCs (Clinical)

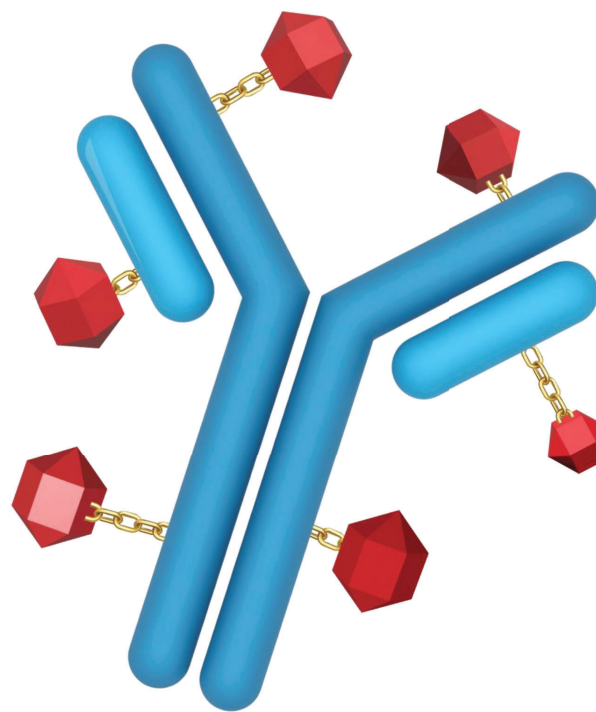
Payload Class	Tubulin Inhibitors	DNA Damaging agents	Topoisomerase inhibitor
Commonly used payloads	Auristatin (MMAE, MMAF), Maytansine(DM4, DM1), Tubulysin (AZ13599185)	Duocarmycin (DUBA), Indolino-benzodiazepine (IGN), Pyrrolobenzodiazepine (PBD)	SN-38, DXd/ DX8951, Camptothecin, Doxorubicin
Discontinued ADCs (Discontinued after PI, PII or PIII)	62	24	5
Developers	Mersana Therapeutics, Bayer, Amgen, ImmunoGen, Boehringer Ingelheim	Seagen, Roche-Genentech, Pfizer, Celltech Therapeutics, Bristol Myers Squibb	Daiichi Sankyo, Seagen, Immunomedics

Source: **Beacon** Intelligence Database, October 2023





Is this an
ADC Target?

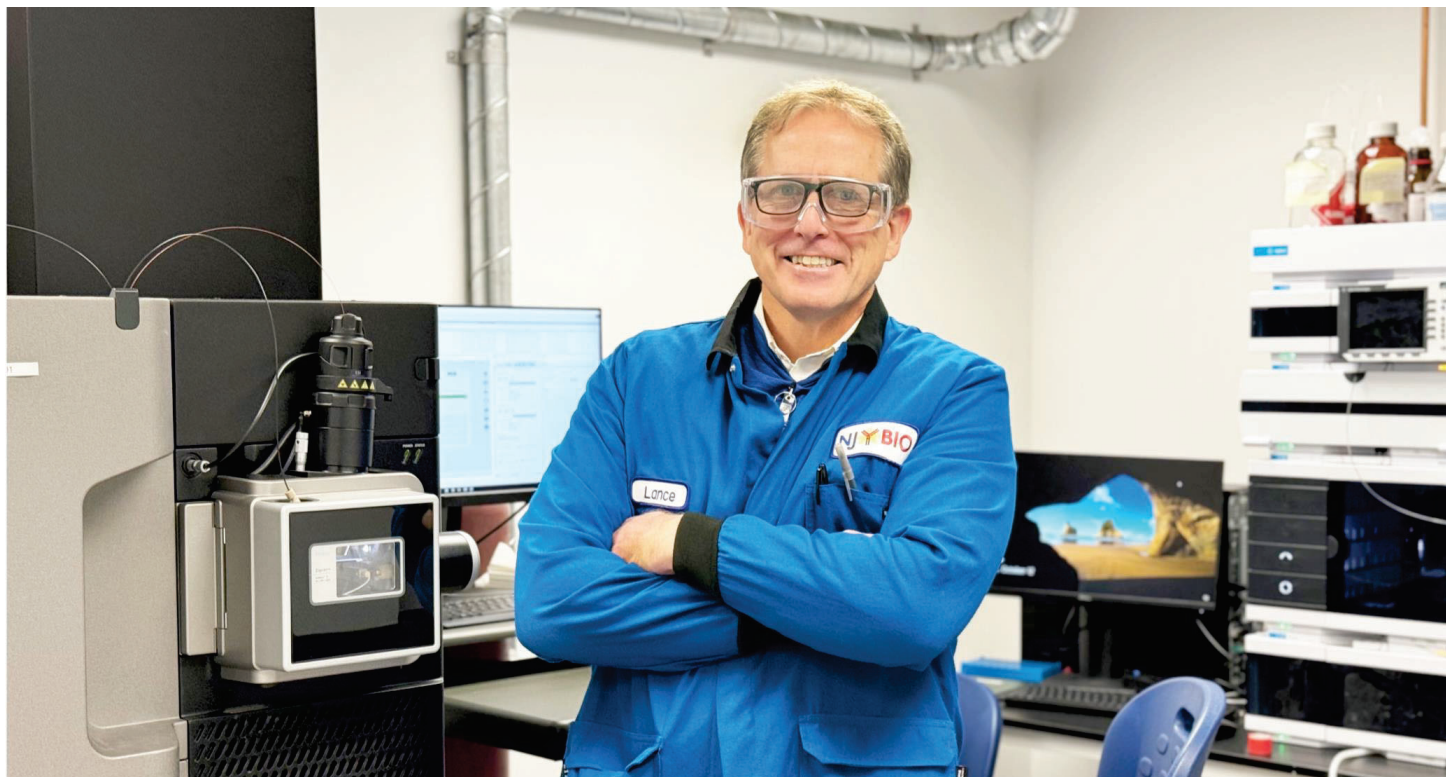


Do you have right
Payload linker?





SiteDAR

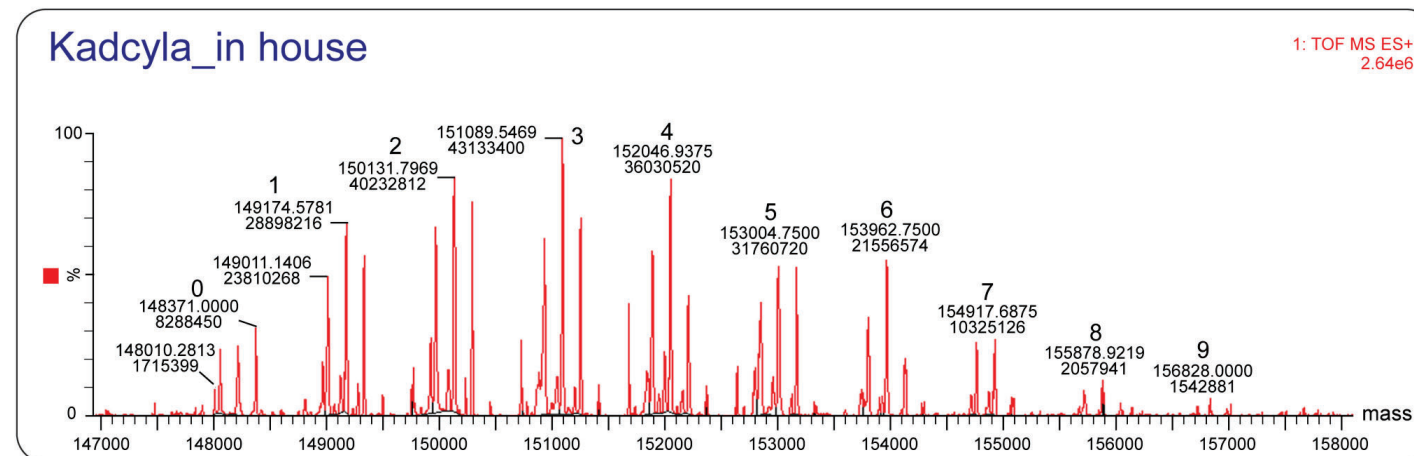
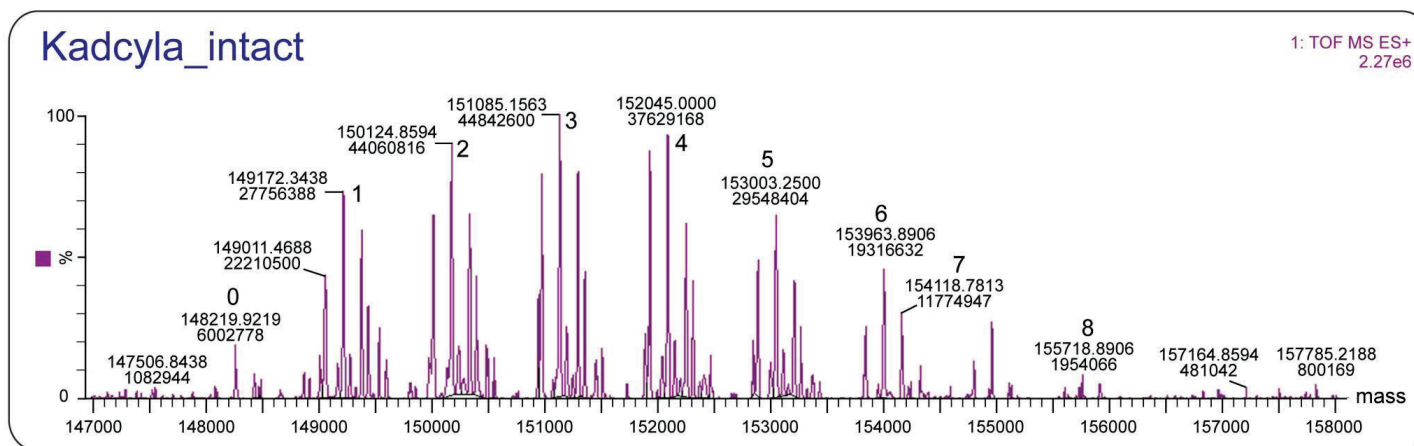


W. Lance Martin, PhD



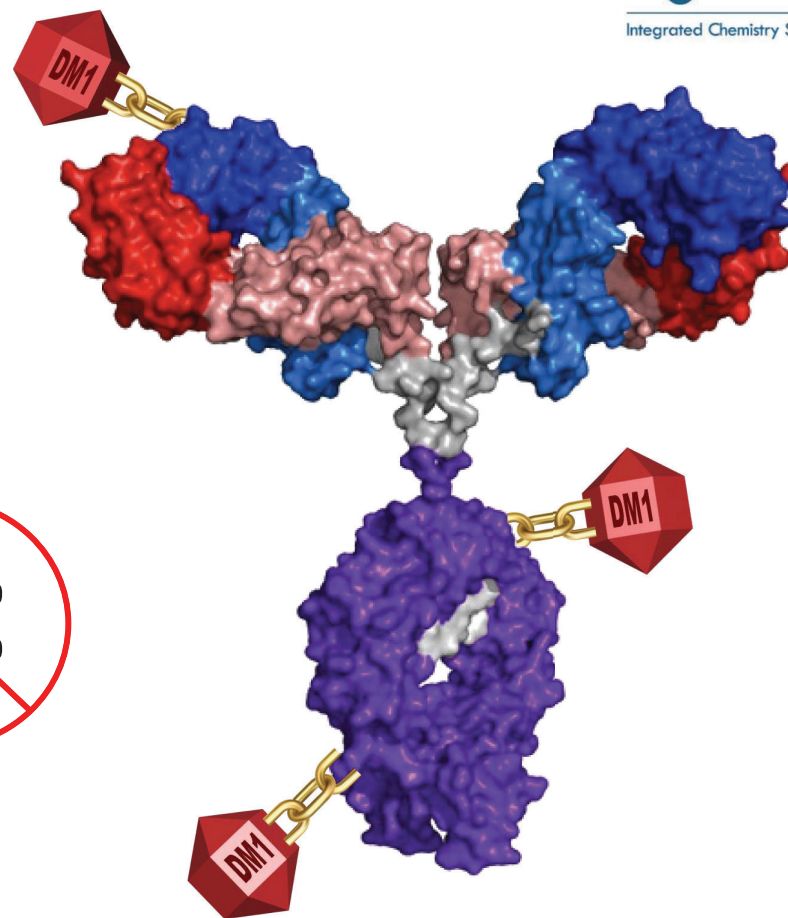
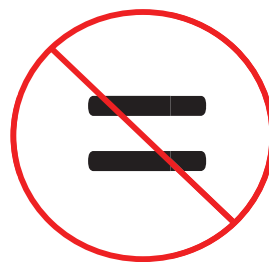
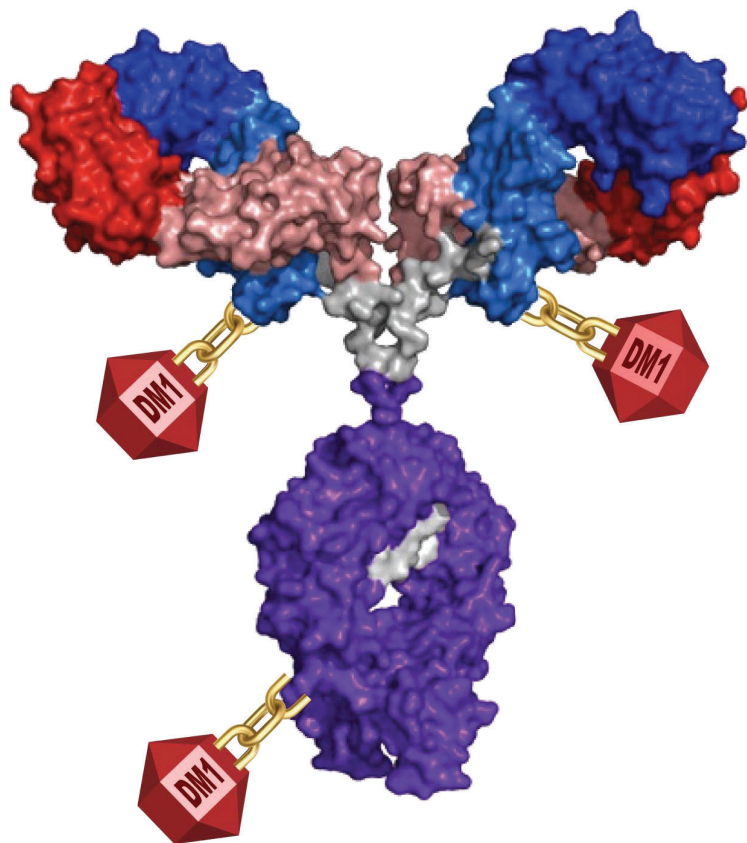
DAR conventional

DAR 3.4

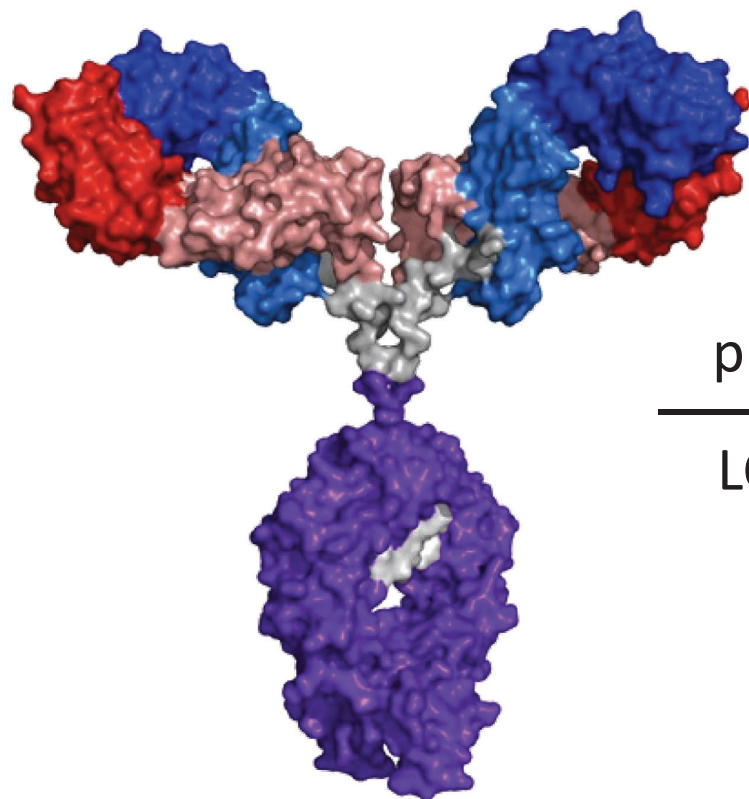


DAR 3.5

Biodistribution: the ADC cQA



Multi-Attribute Mapping (MAM)

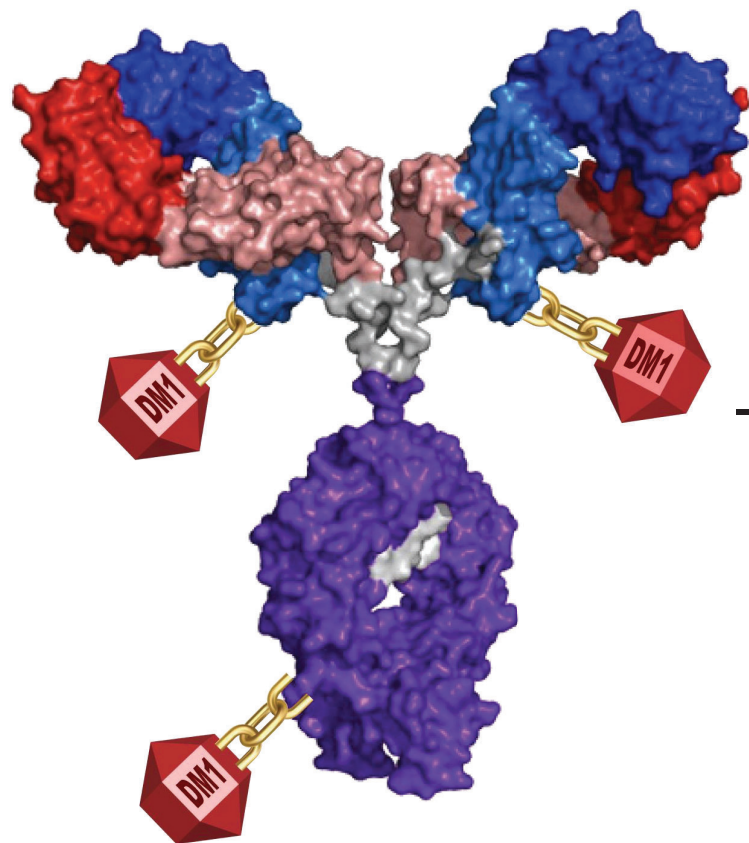


proteolysis
→
LC-MSMS

Oxidation?
Deamidation? → batch
Glycation? release

< specification?

SiteDAR



proteolysis
→
LC-MSMS

Drugs at
same sites?

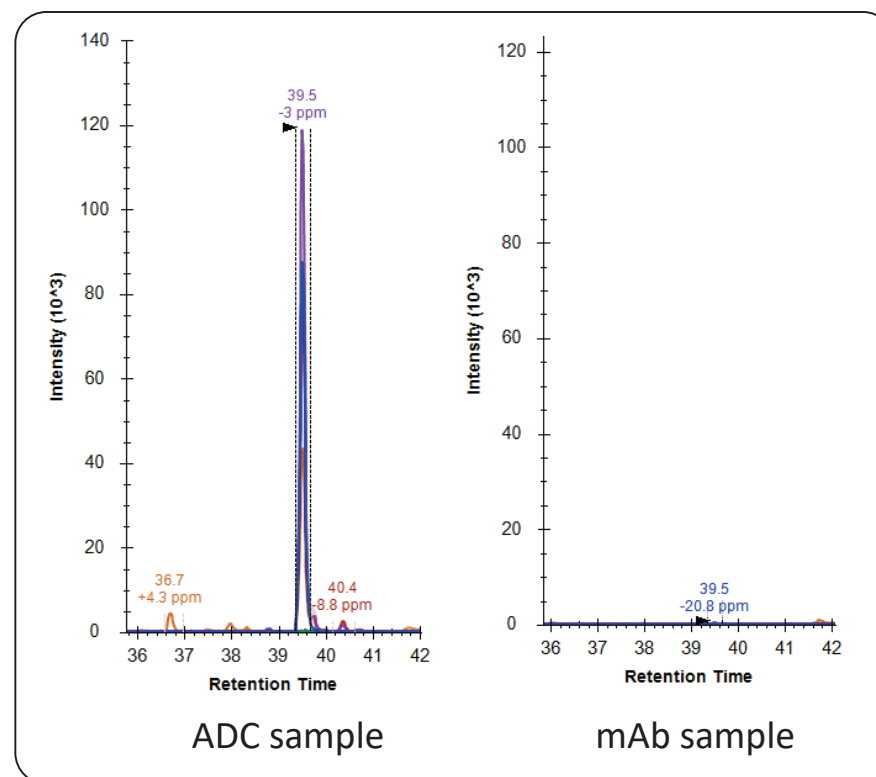
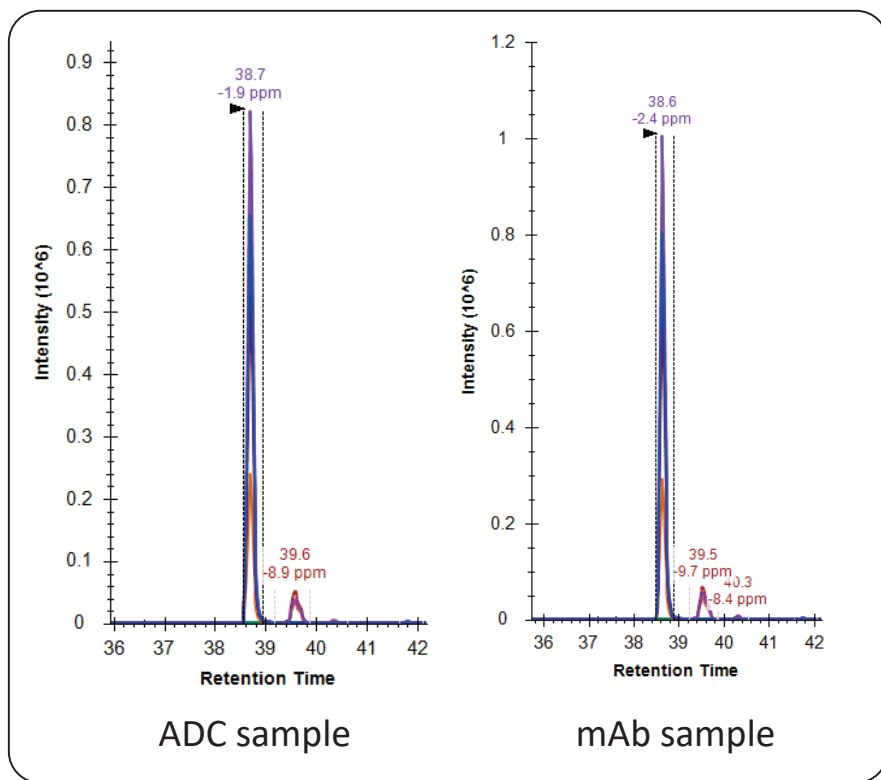
VVSVLTVLHQDWLNGKEYK
[DM1]

In the same
amounts?

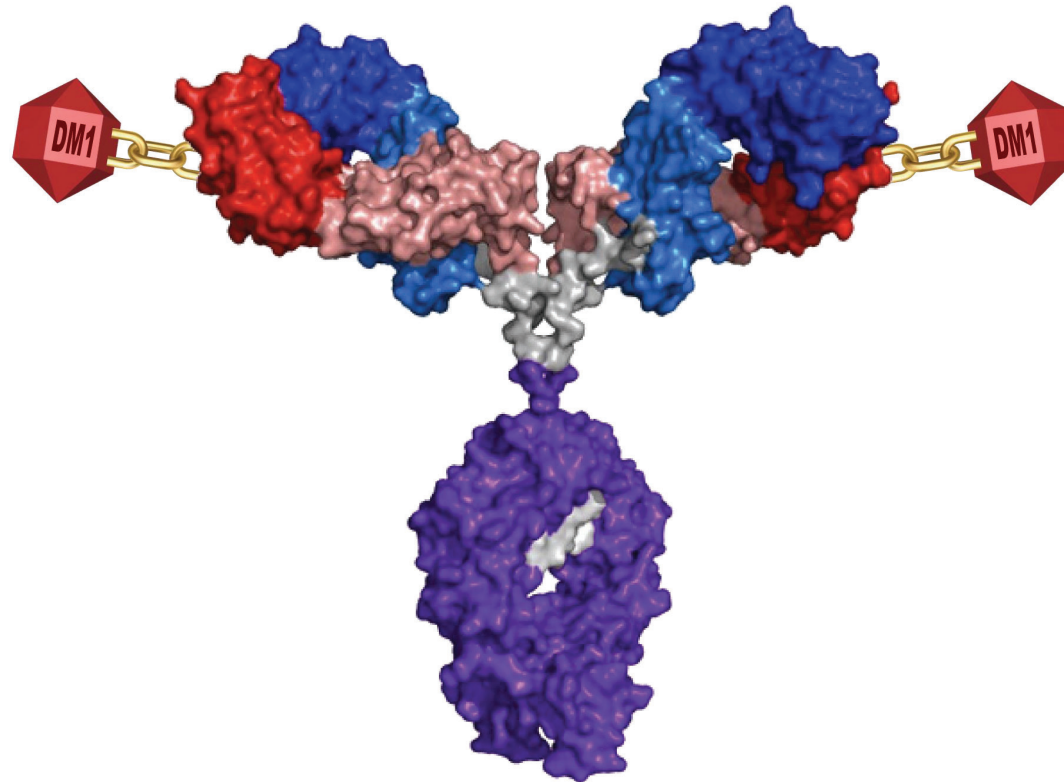
Which site? How much?

VVSVLTVLHQDWLNGKEYK

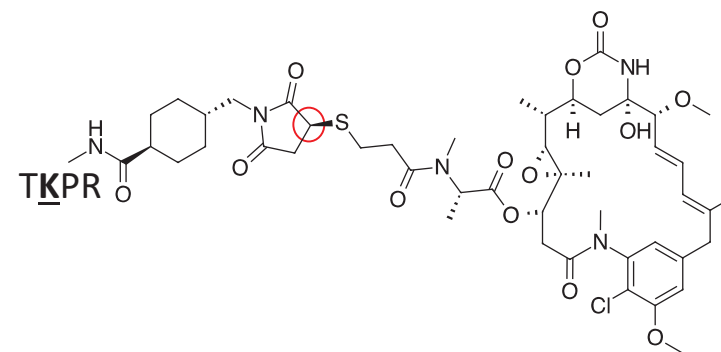
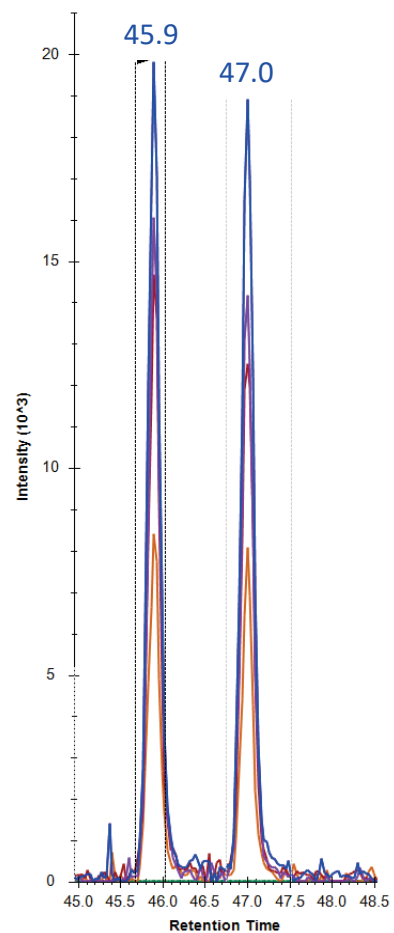
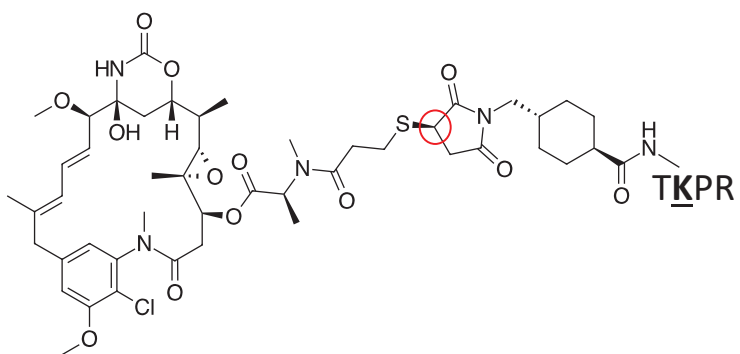
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[DM1]



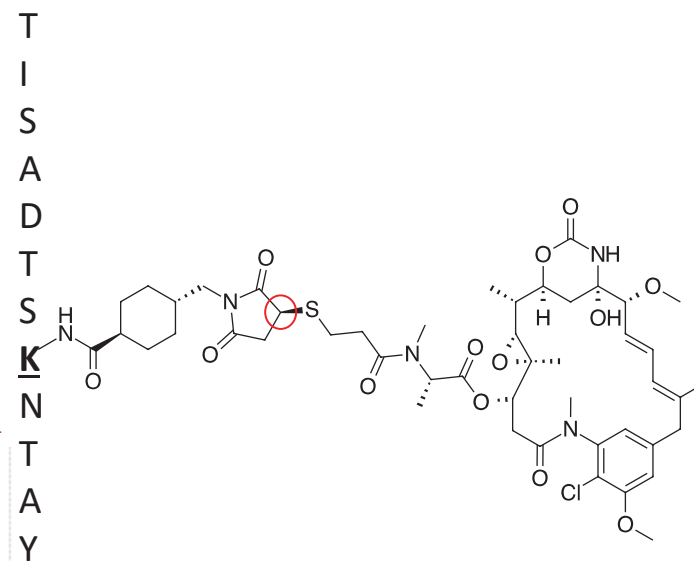
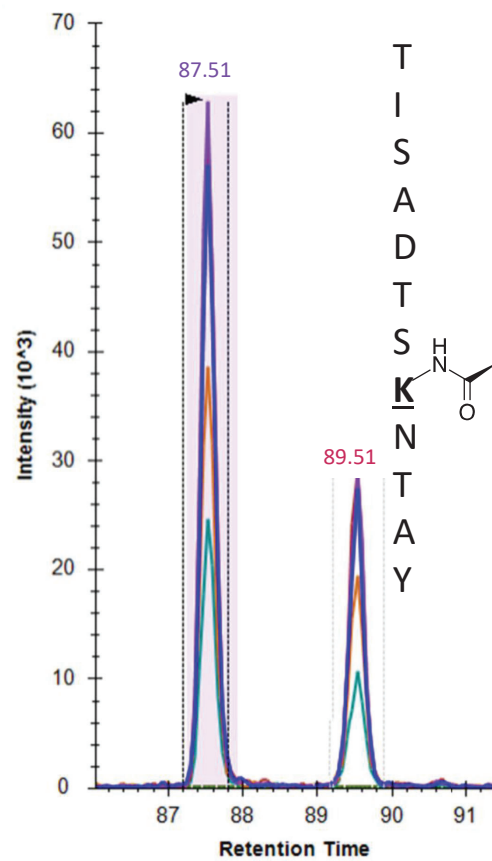
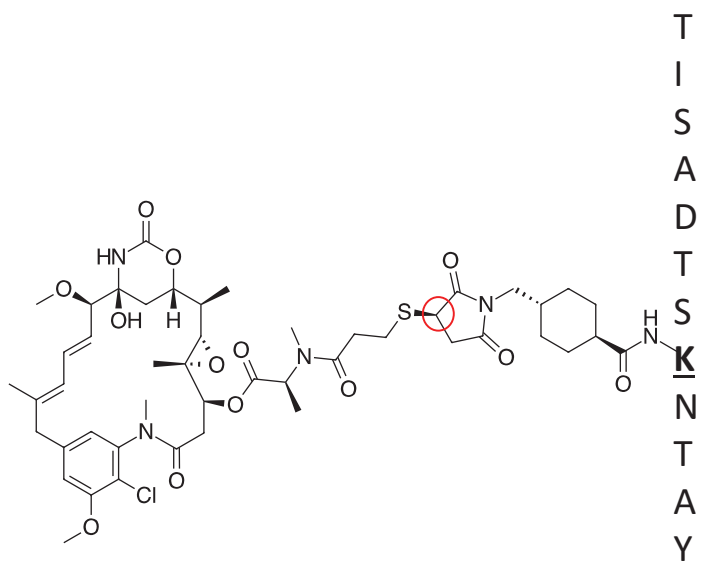
mAb modified at antigen site



Diastereomers!

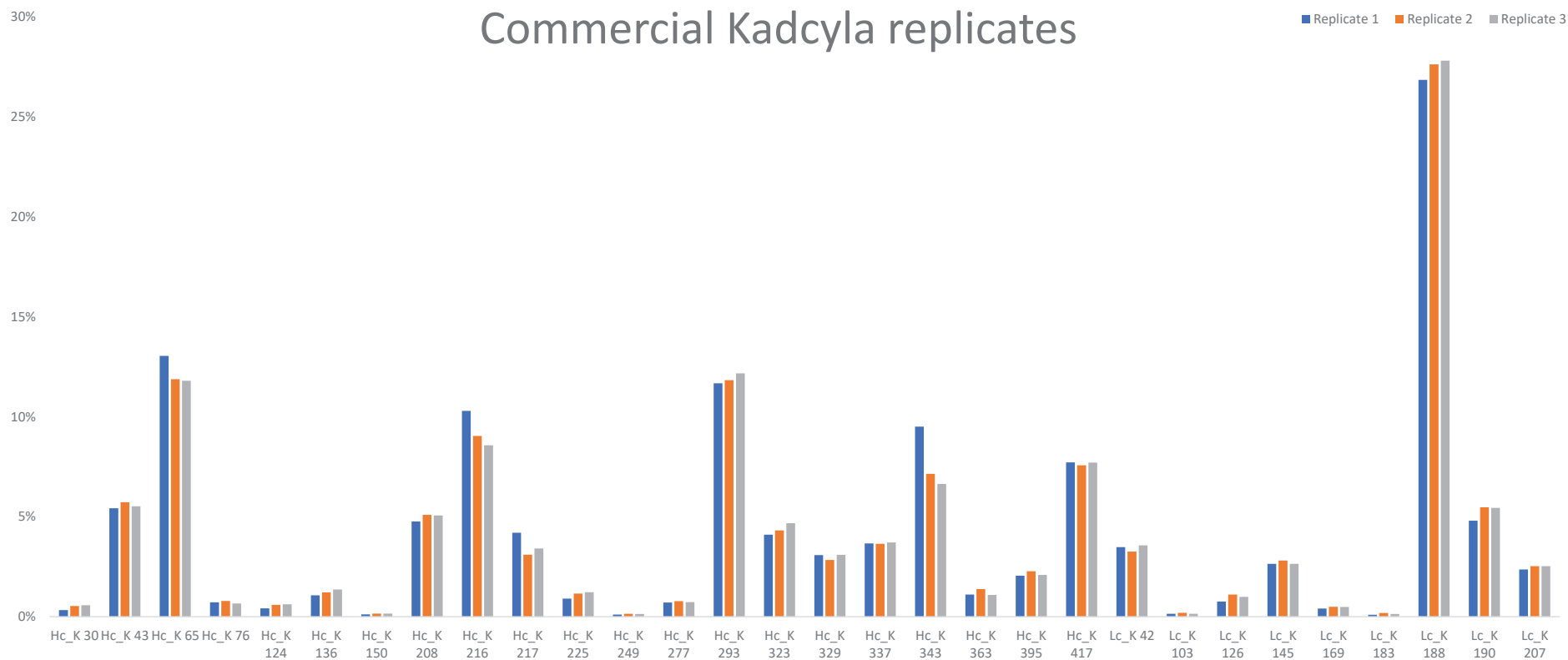


At different ratios



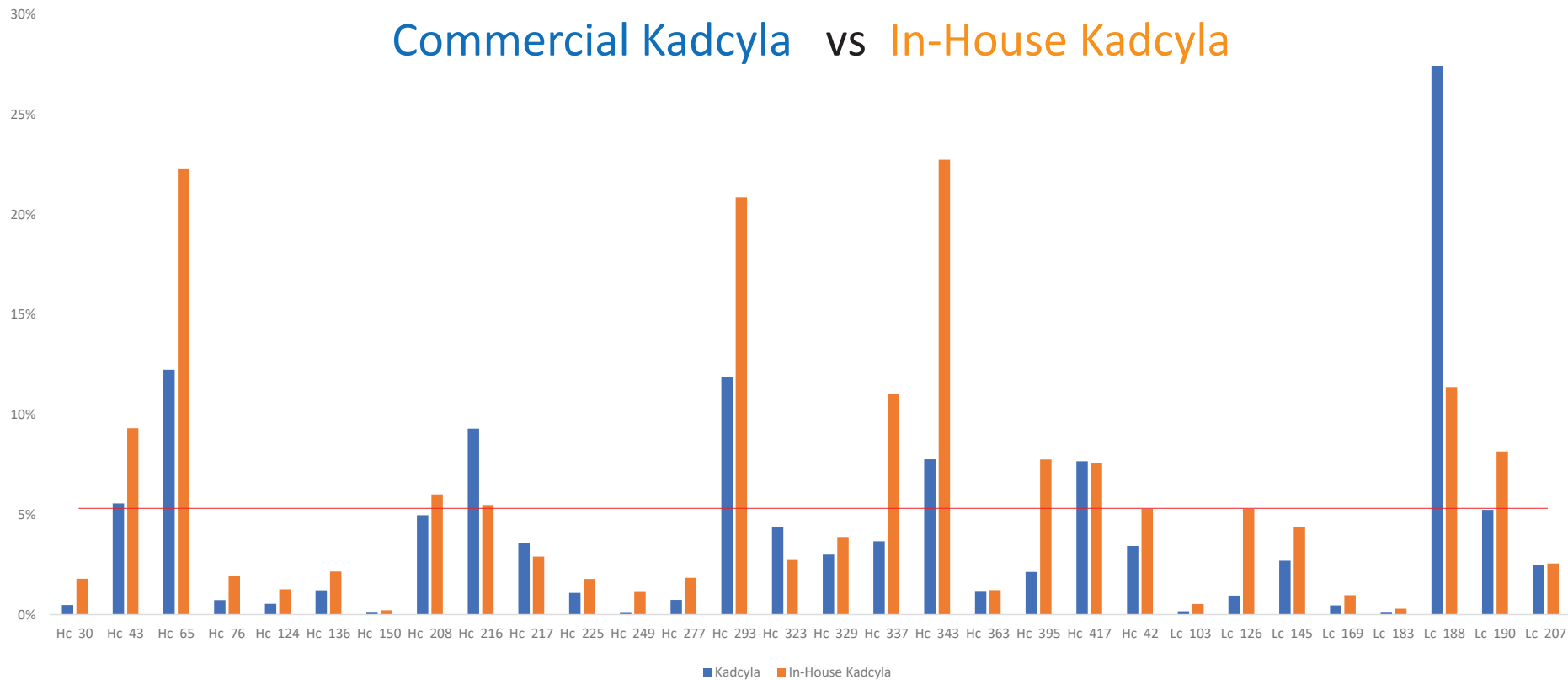
Measurement reproducible of SiteDAR

Commercial Kadcyła replicates



Same DAR – different sites

Commercial Kadcyła vs In-House Kadcyła

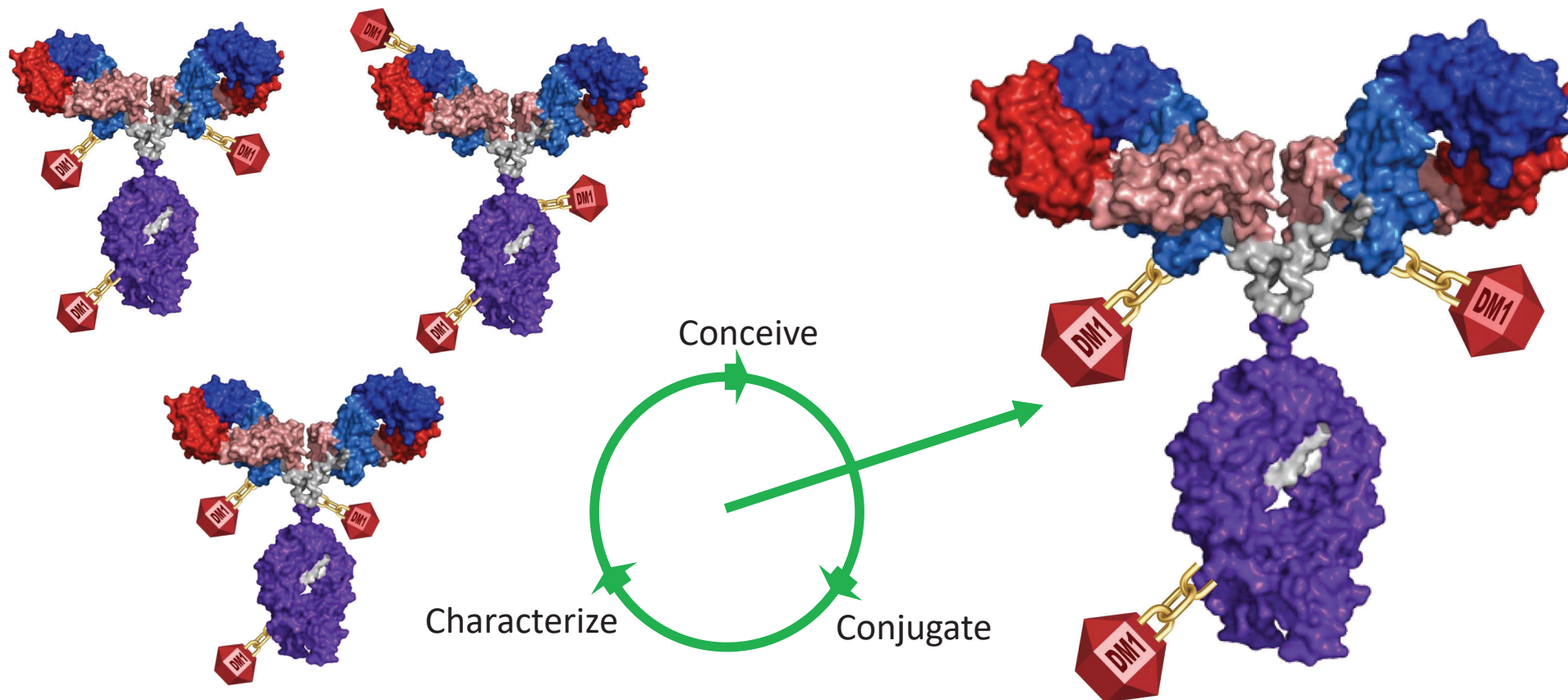




9 out of **11**



ADC biodistribution by design





BioNMR



David Fry

Richa Vartak

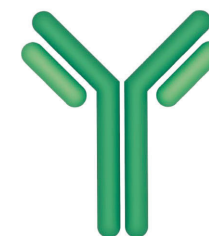
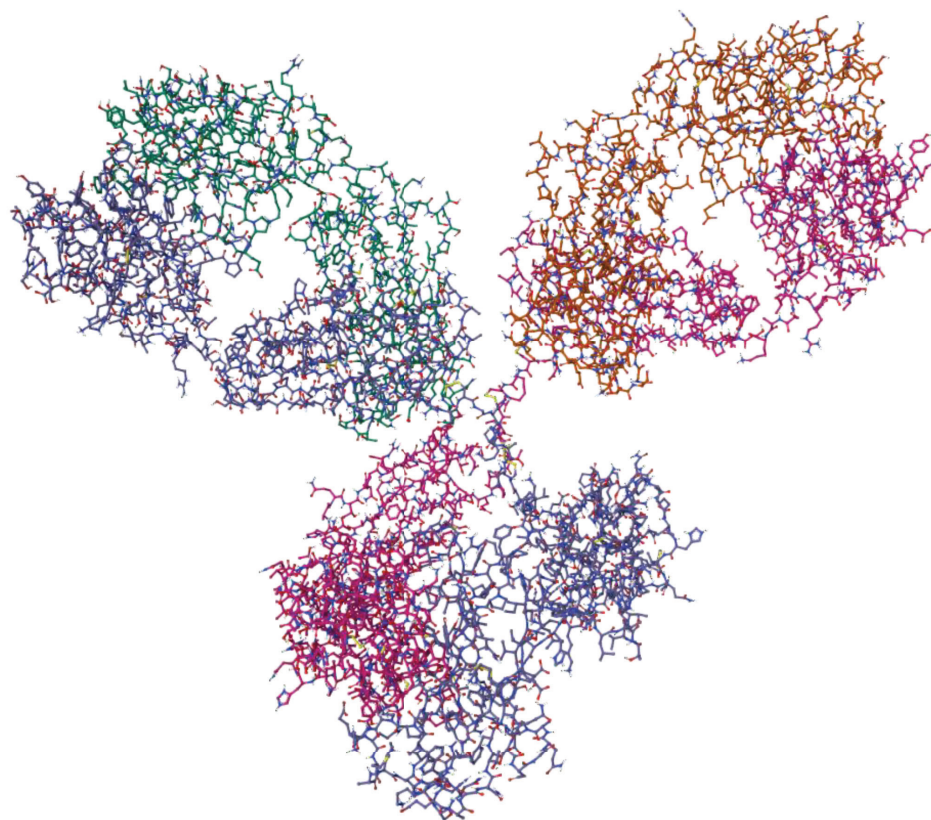
Steven Murkli



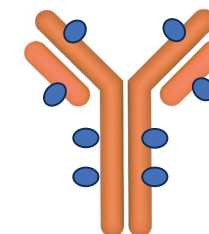
Center for NMR Excellence



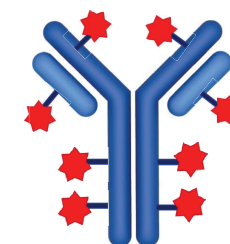
NMR Can Help Answer How Does Conjugation Change 3D Ab Structure



Herceptin (Native)

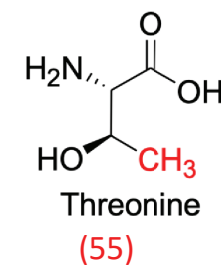
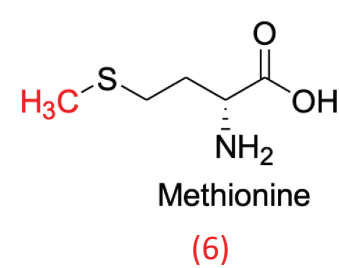
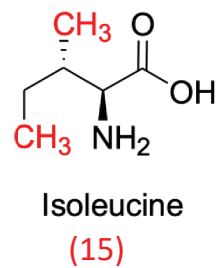
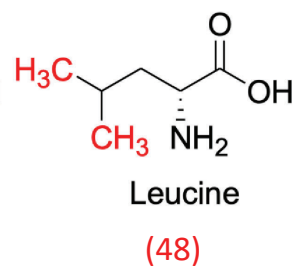
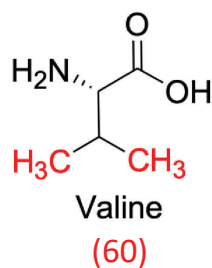
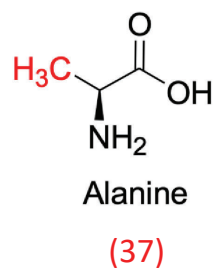


Herceptin-NEM (Capped)



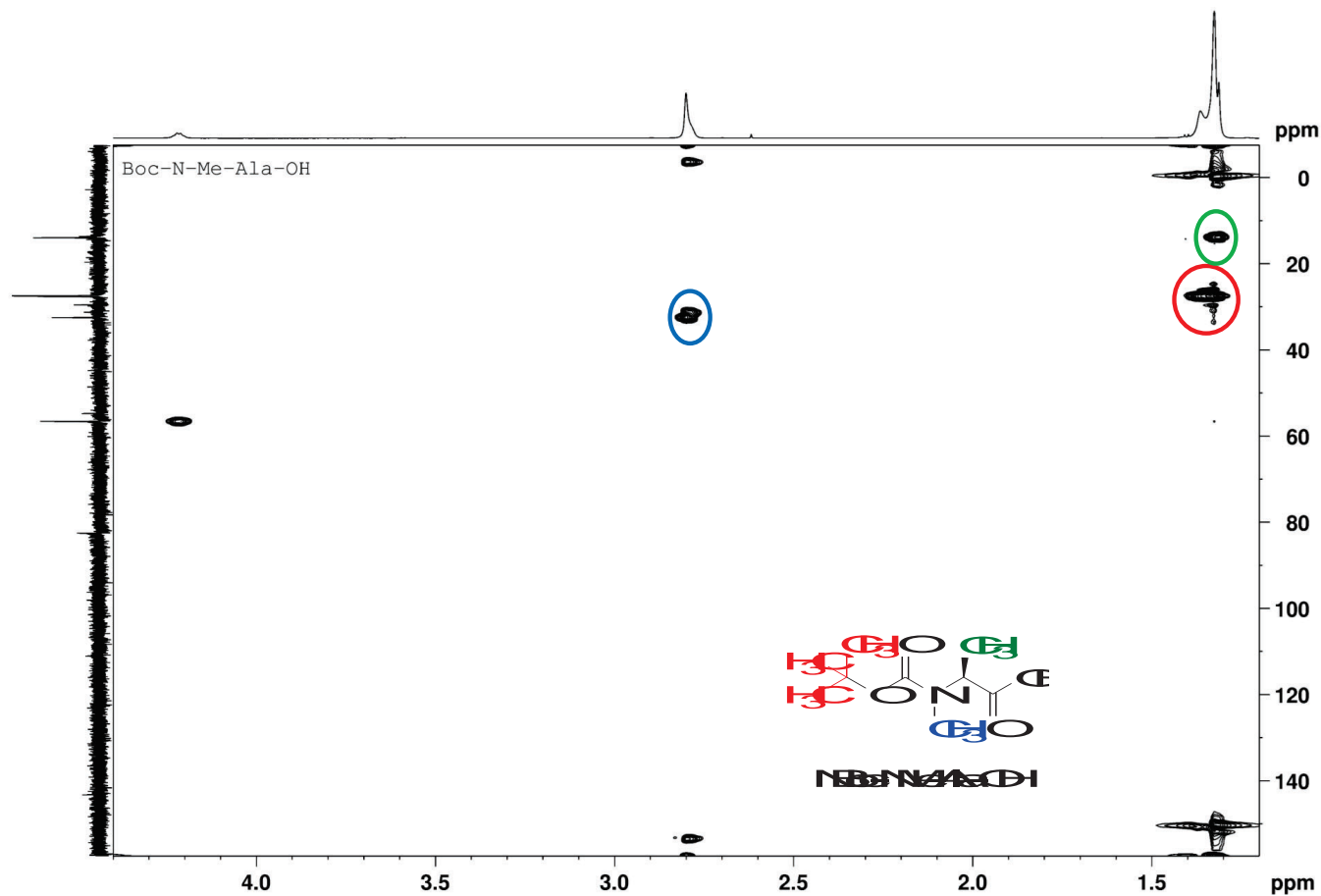
Herceptin-DXD (Linker Payload)

Methyl Groups Present in Amino Acids

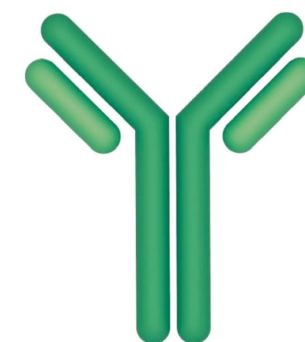


(221) Methyl-group containing amino acids in Trastuzumab

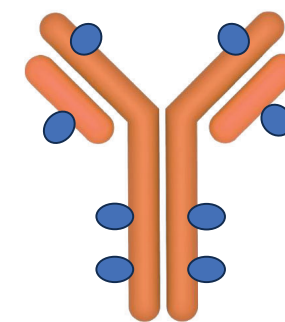
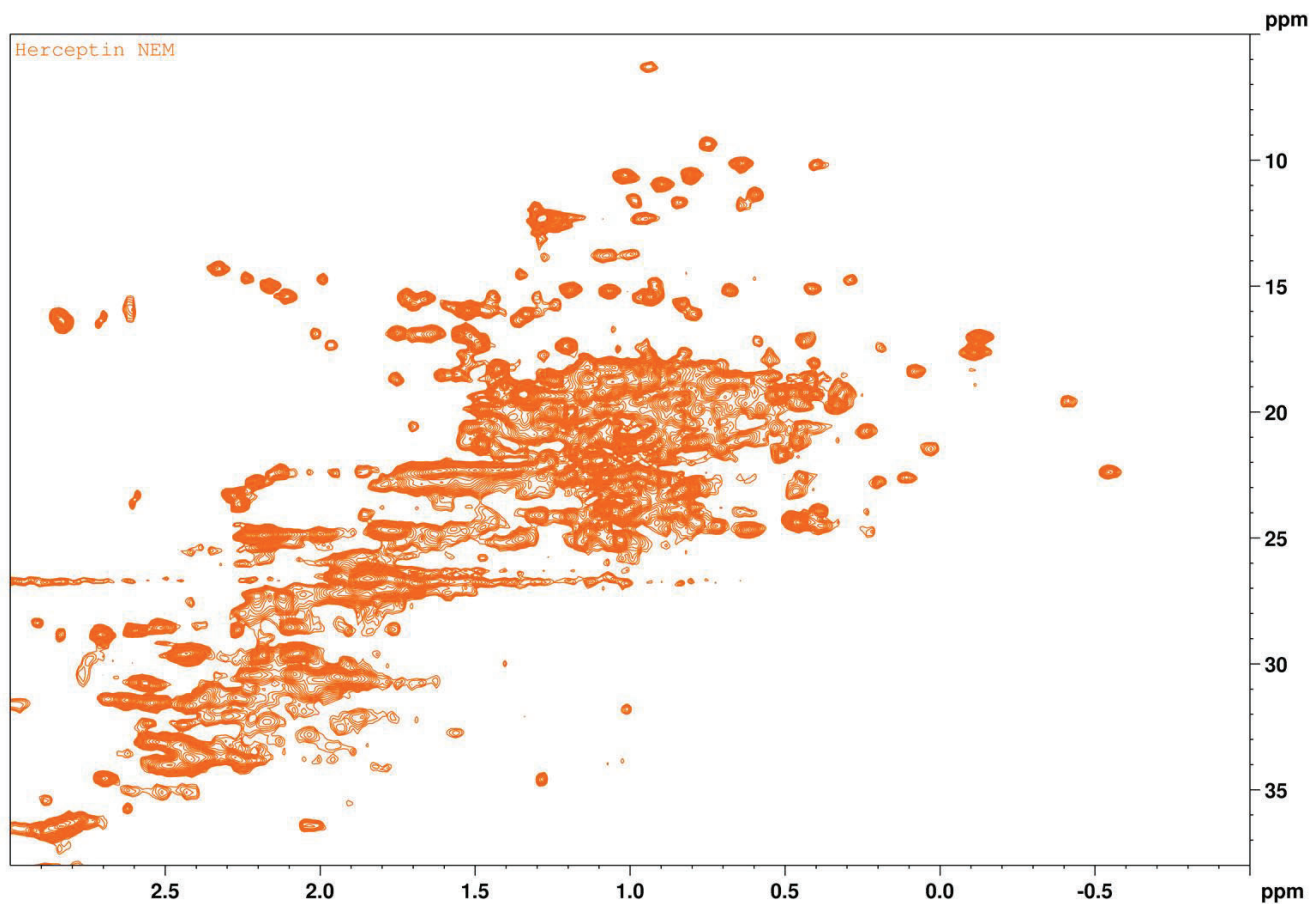
HSQC as A Method To Visualize Methyl Groups



HSQC of Herceptin



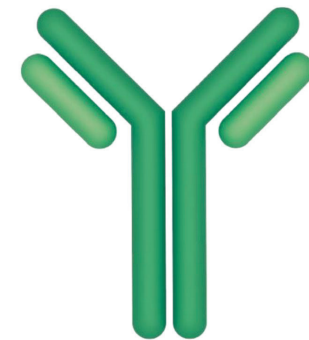
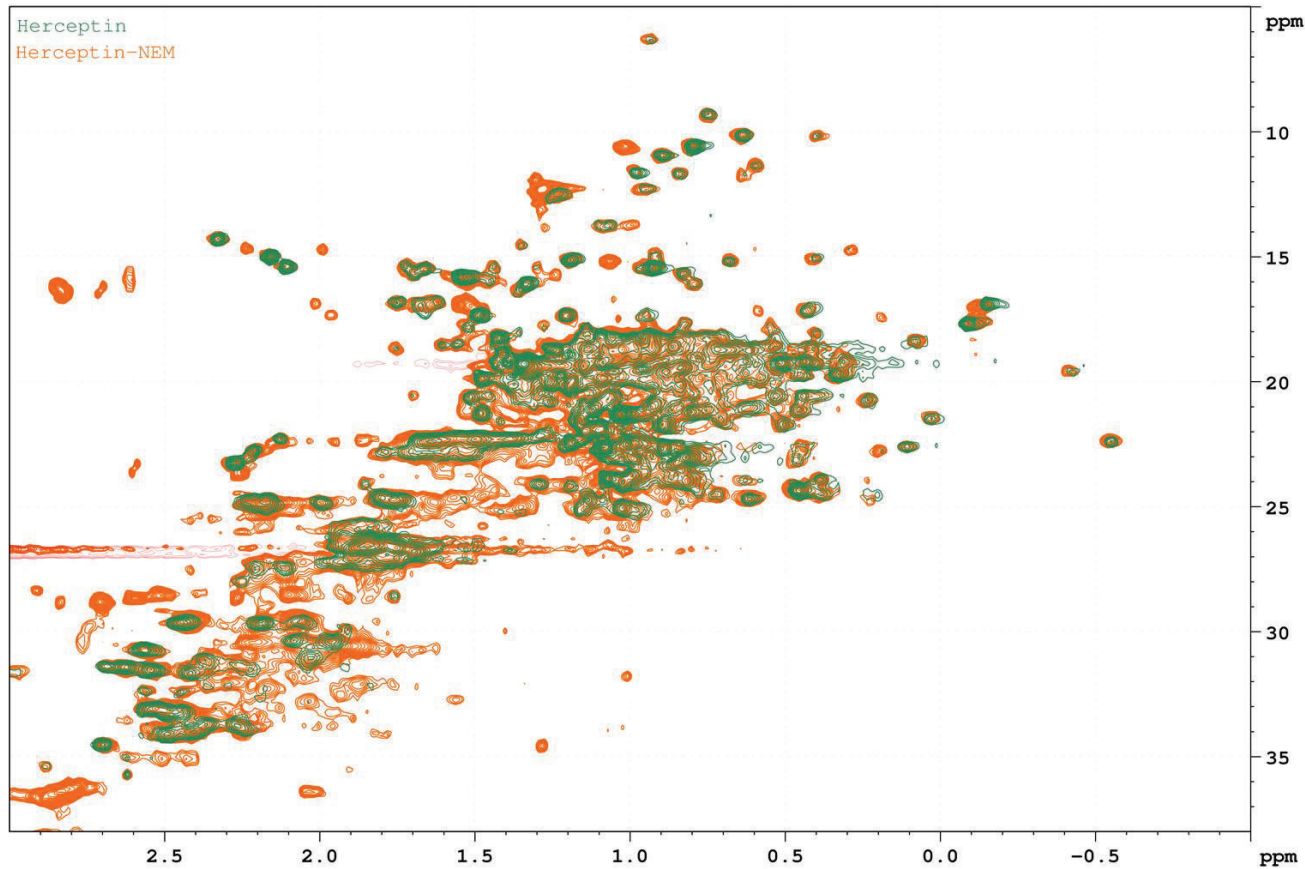
HSQC of Herceptin-NEM



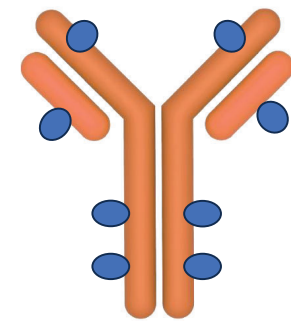
Herceptin-NEM (Capped)



Overlay of Herceptin with Herceptin-NEM



Herceptin (Native)

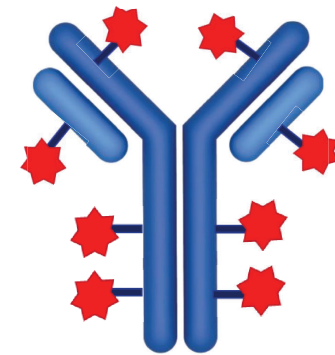
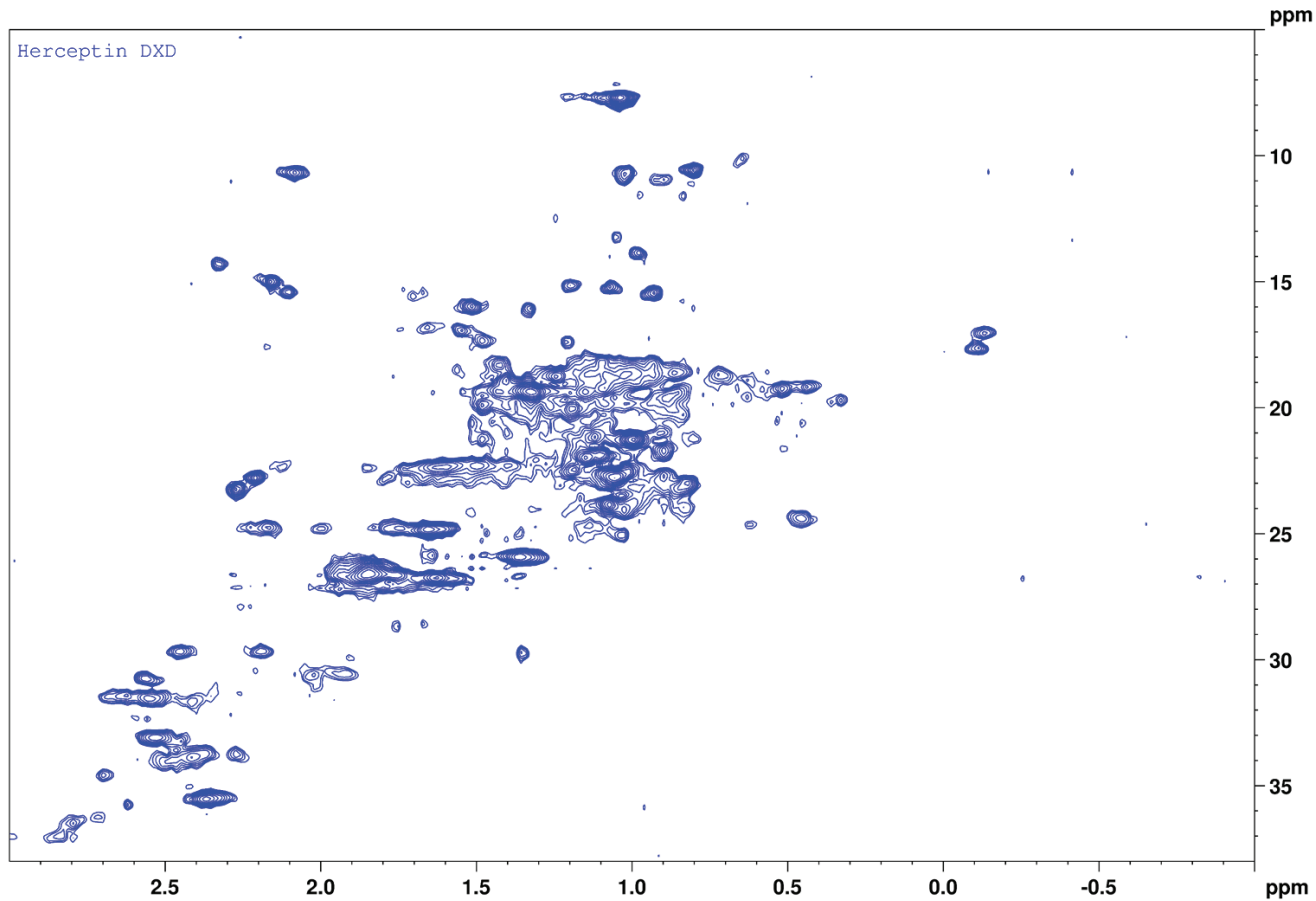


Herceptin-NEM (Capped)

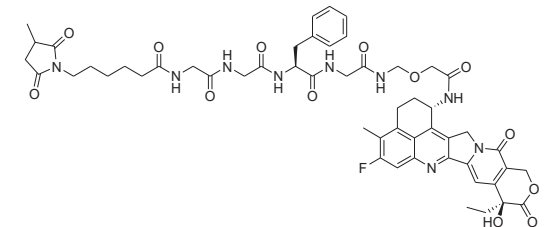




HSQC of Herceptin-DXD



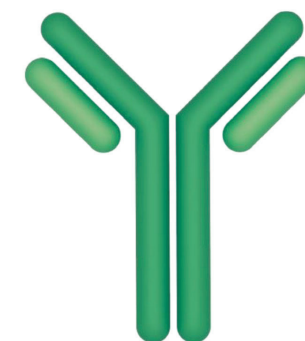
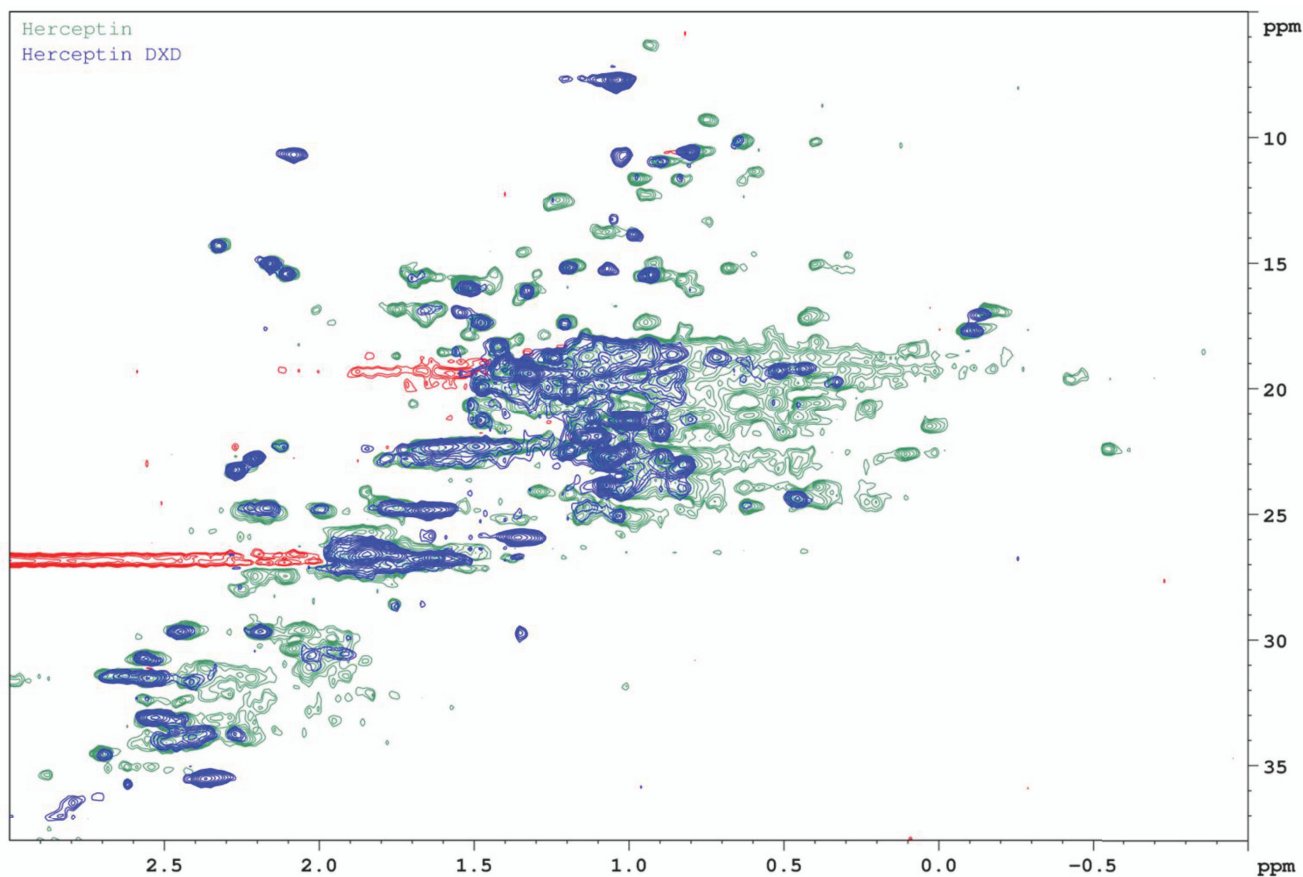
*Herceptin-DXD
(Linker Payload)*



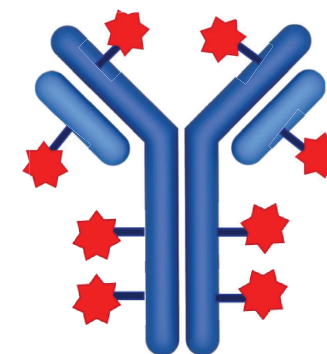
 *Deruxtecan (DXD)*



Overlay of Herceptin with Herceptin-DXD

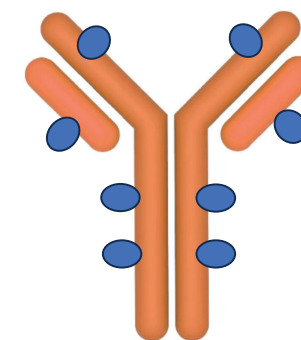
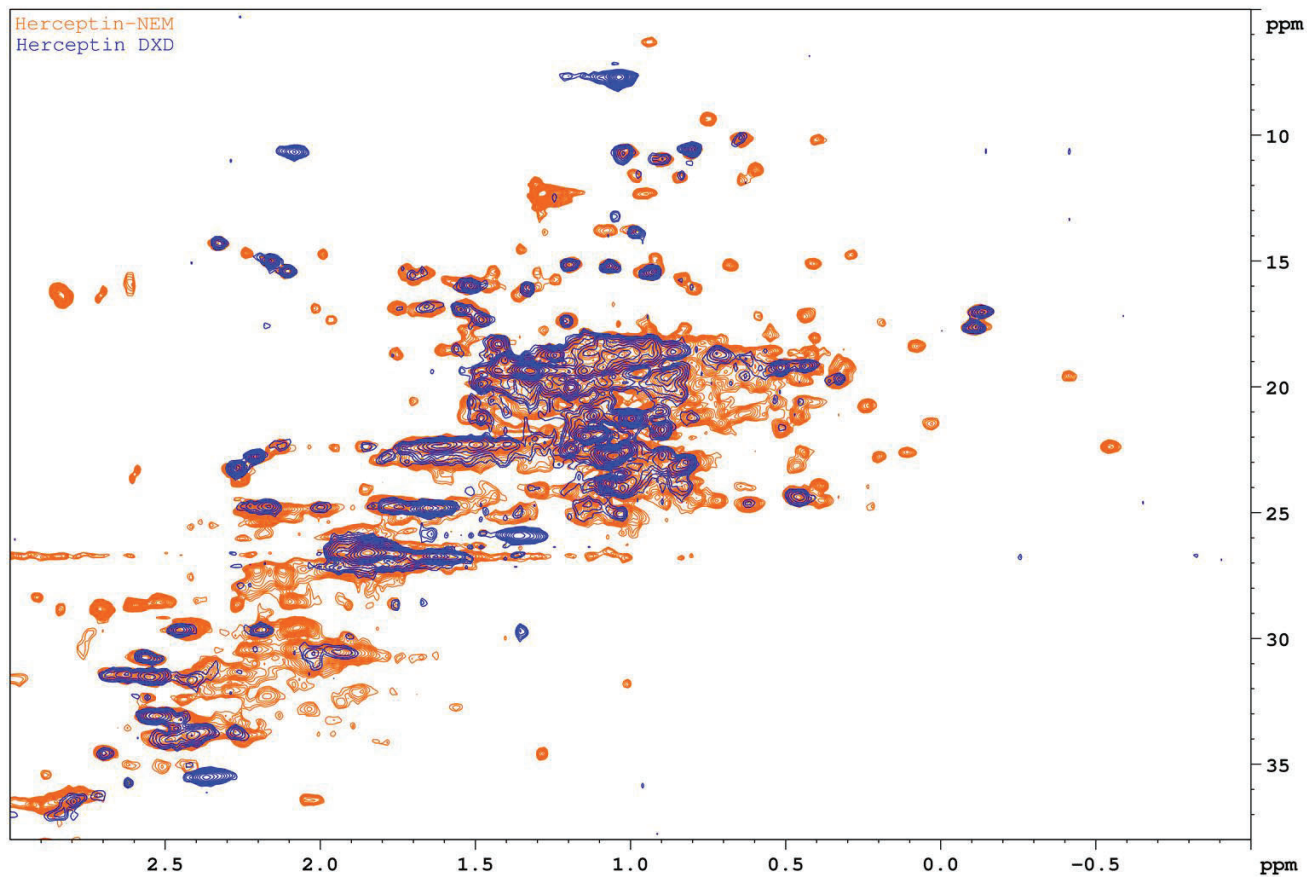


Herceptin (Native)

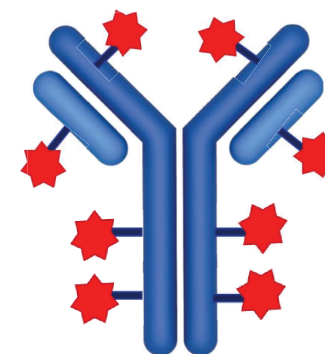


*Herceptin-DXD
(Linker Payload)*

Overlay of **Herceptin-NEM** with **Herceptin-DXD**



Herceptin-NEM (Capped)



*Herceptin-DXD
(Linker Payload)*



Princeton, NJ



Mumbai, India





**Bioanalytical
Services for
ADC**



Bioconjugation



**Payloads &
Linkers**



**Oligonucleotide
Services**



**Protein
Degraders**



**BioNMR
Services**



**mRNA
Services**

**R&D
Services**

**GMP
Services**
1st Q 2024



Thank You!



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