POTELLIGENT® Technology

Overview from a Science Perspective

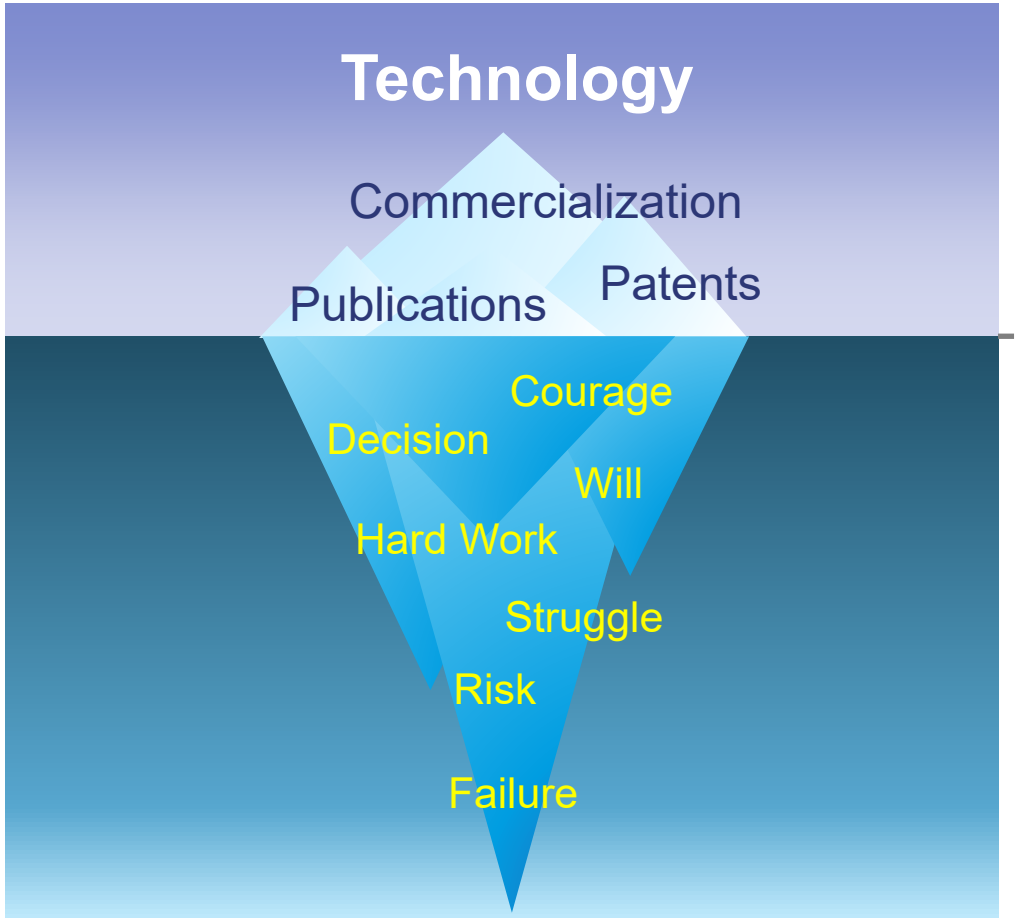
September 10, 2026

Kyowa Kirin Co., Ltd. Research Headquarters, Research Planning Department

Tokyo Research Park

Rinpei Niwa

The Iceberg Model of Research



What shows is the success story

Supports the entire R&D process
The invisible part

© Kyowa Kirin Co., Ltd.

1990s: Antibody Drugs Emerge as a Key Discovery Platform

~Mid-1990s

Antibody drugs are still at their dawn: no blockbusters yet, no proven path to success

Japan excels in small-molecule drugs but lags the world in antibodies

Amidst this, **Kirin Pharma** and **Kyowa Hakko Kogyo** leveraged their biotech strengths and each launched its own antibody research

Late 1990s

Major FDA approvals are coming one after another: Rituxan (1997), Herceptin (1998) are approved

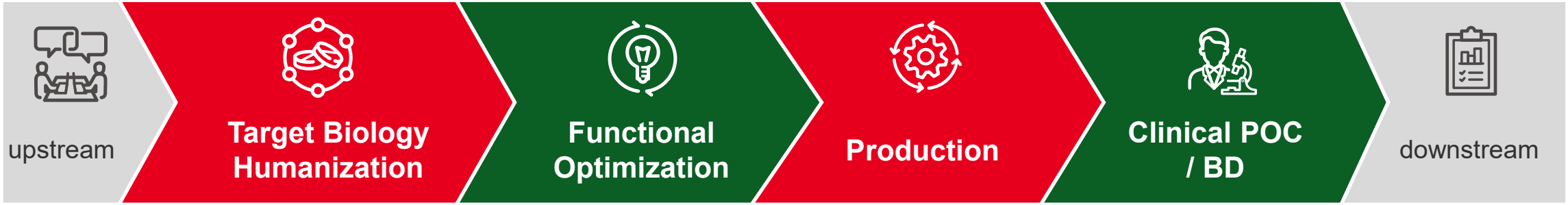
In Japan, regulations and clinical trial infrastructure have finally begun to be developed

© Kyowa Kirin Co., Ltd.

Kyowa Kirin's Birth: An Antibody Researcher's View (2008)

Kirin Pharma: Upstream discovery strengths in target biology, human antibody platforms, and biologics production know-how from EPO

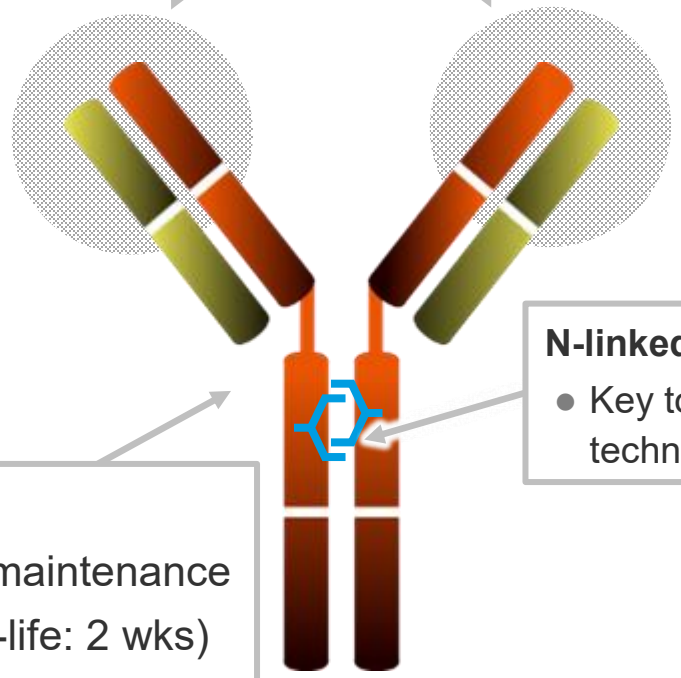
Kyowa Hakko Kogyo: Antibody engineering for enhanced function, plus clinical POC and licensing built on POTELLIGENT technology



© Kyowa Kirin Co., Ltd.

Structure of Antibody Molecules

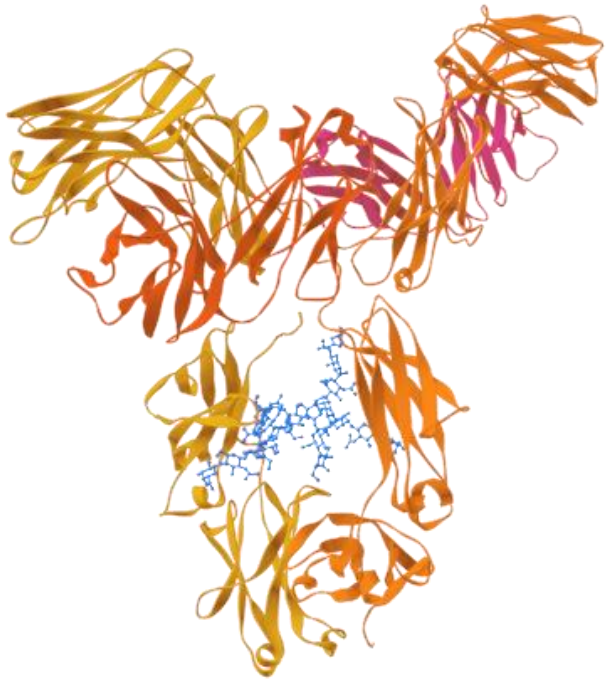
Variable Domain (×2)
- Antigen binding site... Extremely high target specificity



Orange: Heavy chain
Yellow: Light chain

N-linked glycan (×2)
- Key to Potelligent technology

Constant domain
- Molecular structure maintenance
- Blood retention (half-life: 2 wks)
- Various Effects Activations

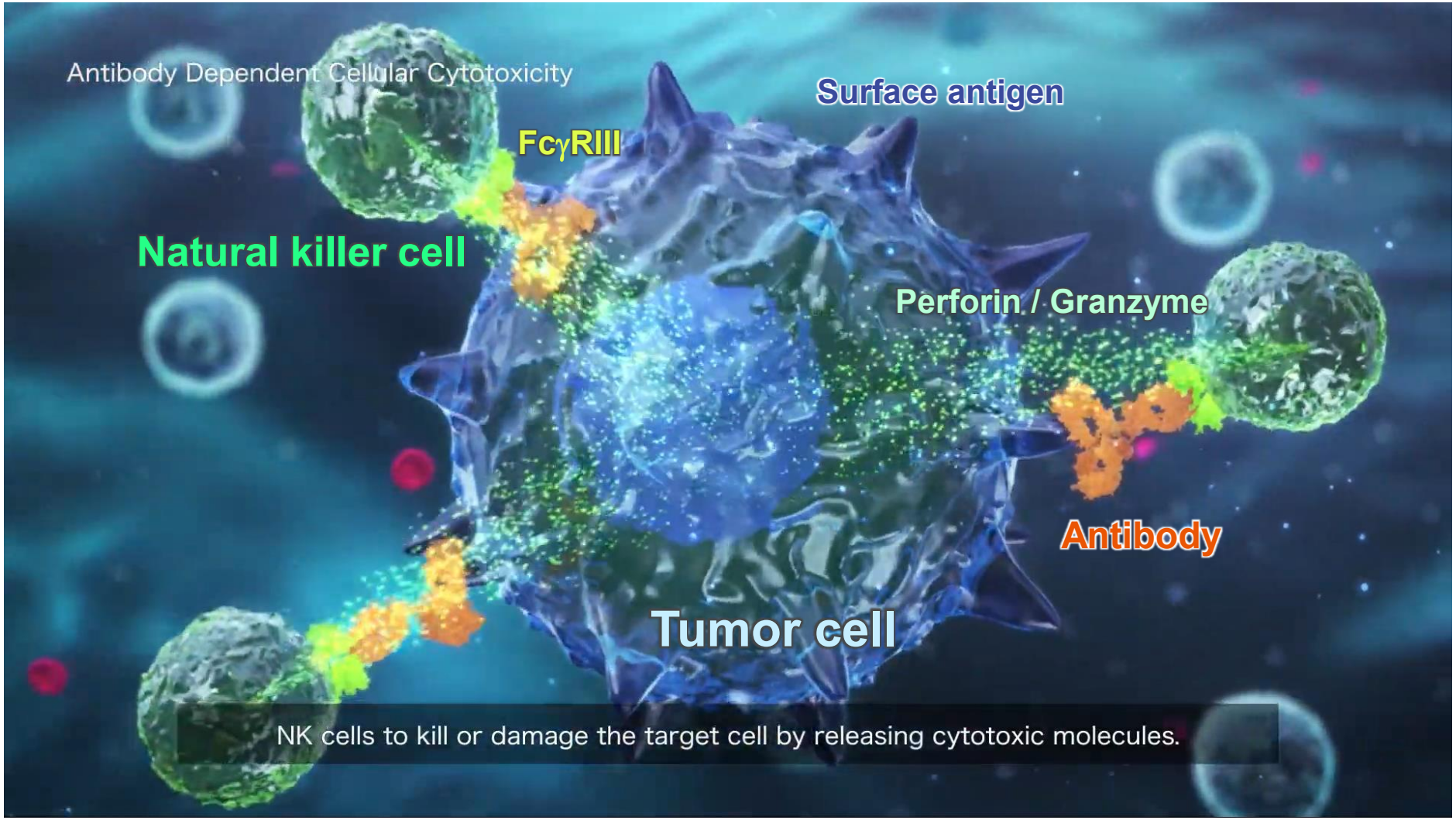


IgG antibody
Molecular weight: approximately 150,000

© Kyowa Kirin Co., Ltd.

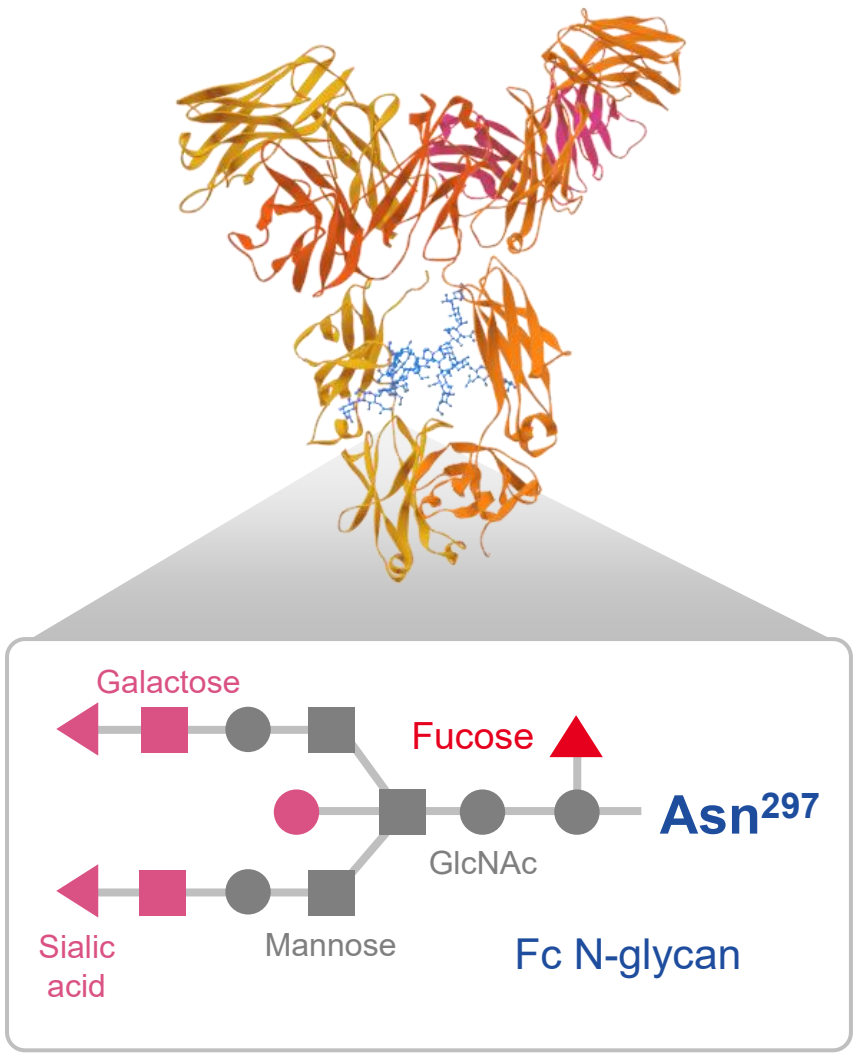
ADCC (Antibody-Dependent Cellular Cytotoxicity)

https://www.kyowakirin.co.jp/antibody/movie/index.html

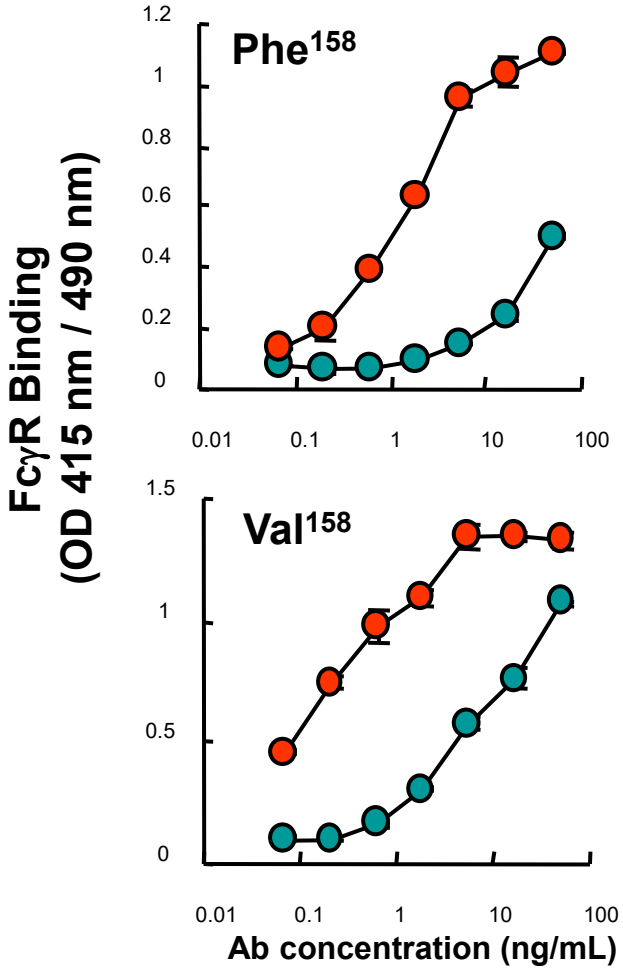


© Kyowa Kirin Co., Ltd.

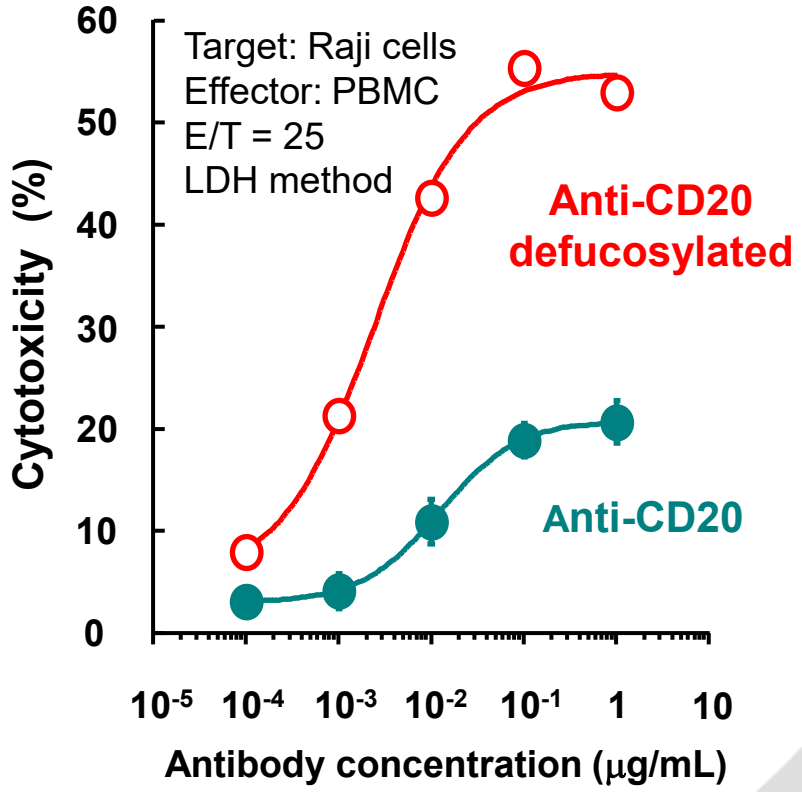
POTELLIGENT® Technology: Defucosylation Strongly Enhances ADCC



FcγRIIIa binding



ADCC



Based on Fig.2 from Niwa et al., Cancer Res., 64, 2127-2133, the presenter recreated it

© Kyowa Kirin Co., Ltd.

POTELLIGENT® technology born from research failures

1990s~

Anti-X Antibody Project

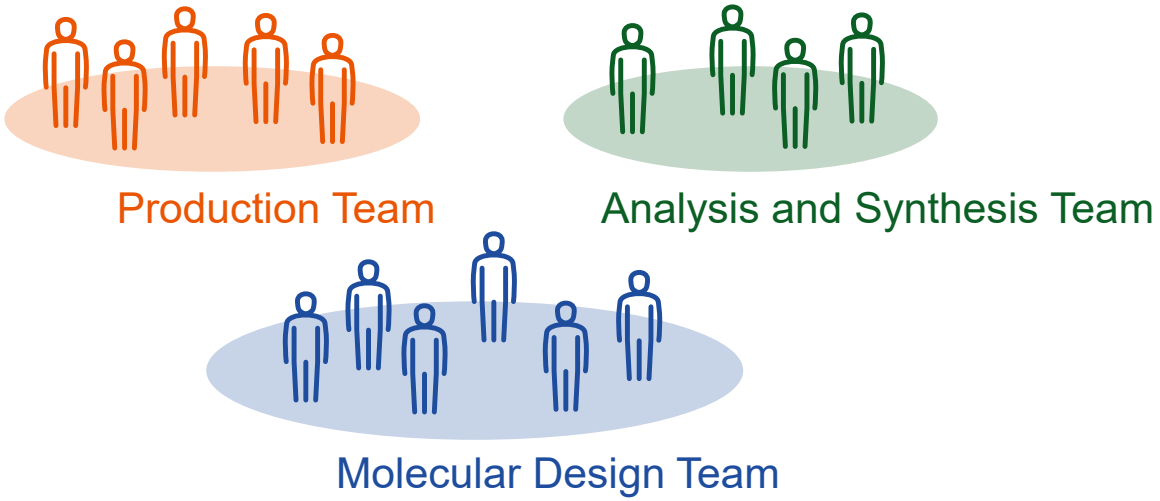
Sharp ADCC drop in CMO-made non-clinical samples

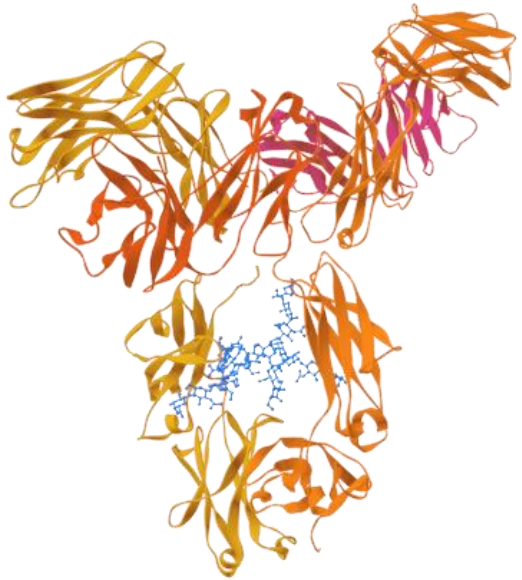
How do in-house and CMO samples differ...?

Research into the cause begins

© Kyowa Kirin Co., Ltd.

The team thoroughly investigated the cause





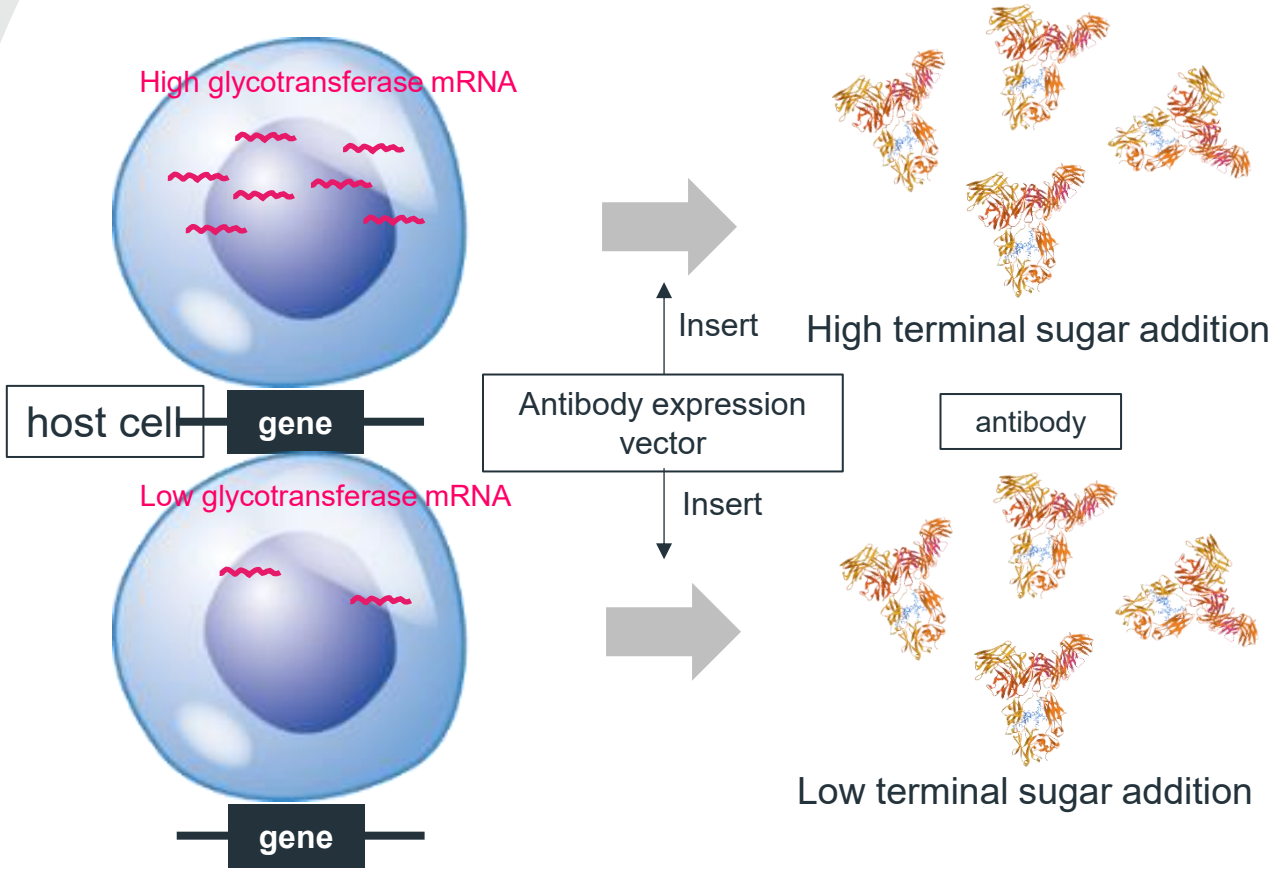
Investigating the Cause

What's the difference between in-house samples and CMO samples...?

- Same expression vector in both samples...
  Amino acid sequence is identical
- Only the **host cells differ**

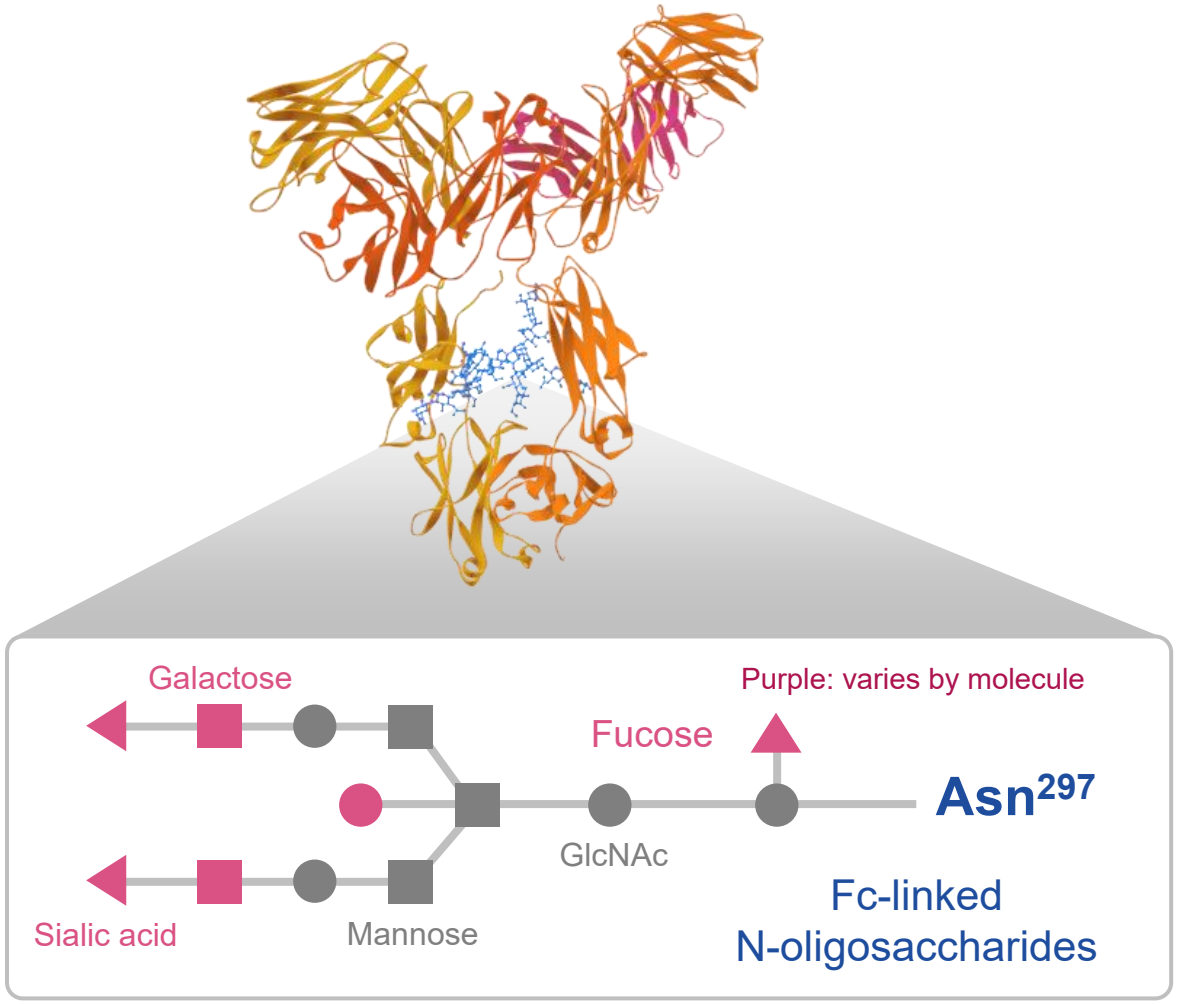
© Kyowa Kirin Co., Ltd.

Are host-cell-driven glycan differences the cause?



Investigating the Cause

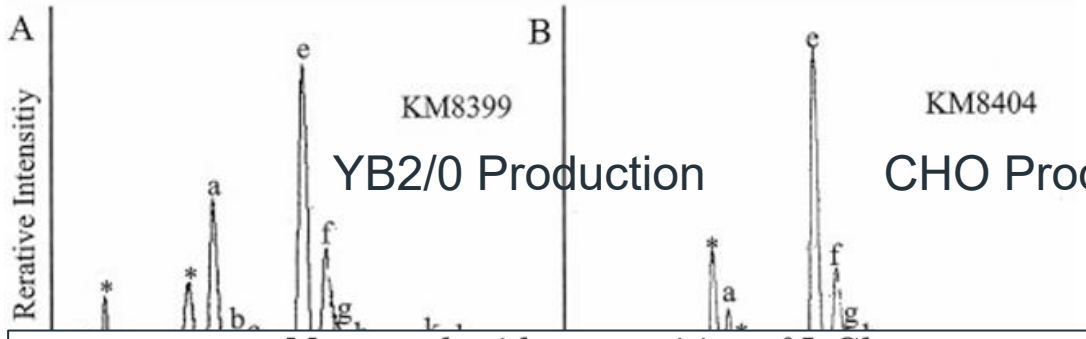
How do in-house and CMO samples differ?



© Kyowa Kirin Co., Ltd.

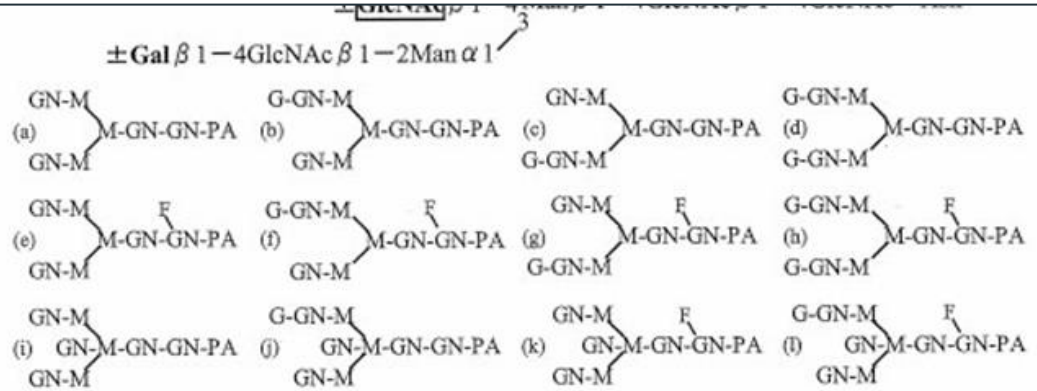
Do glycan structure differences cause the ADCC gap?

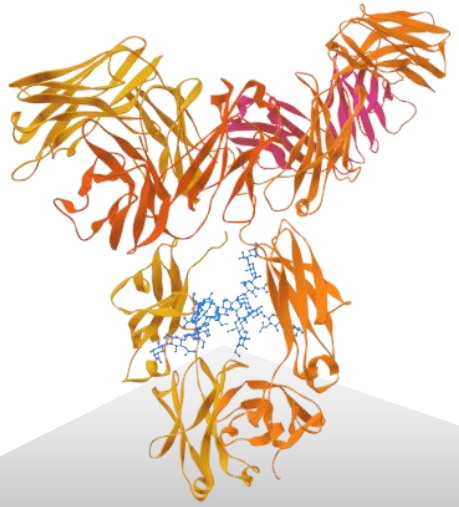
Comparing Fuc, Gal, and GlcNAc variants showed Fuc content is key to ADCC activity

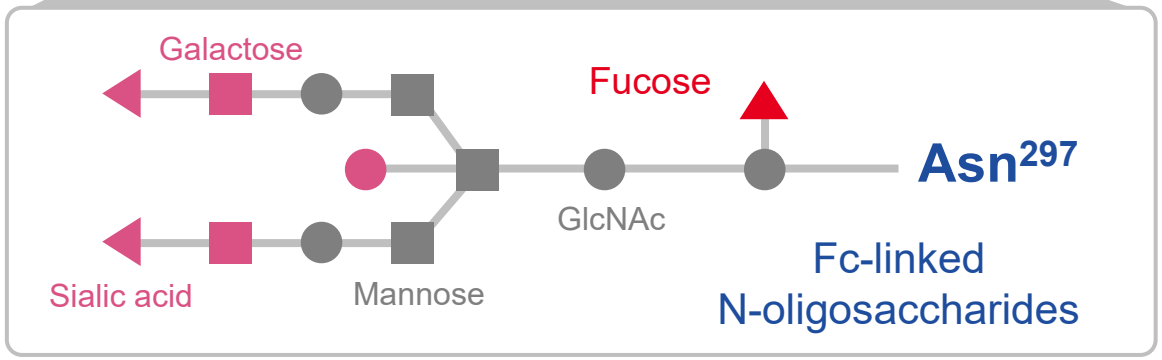


Monosaccharide composition of IgGls

IgGl	Cell line	Fuc	Gal	GlcNAc	Man[a]
KM8399	YB2/0	0.72	1.01	4.51	3
KM8404	CHO	0.91	0.27	3.80	3







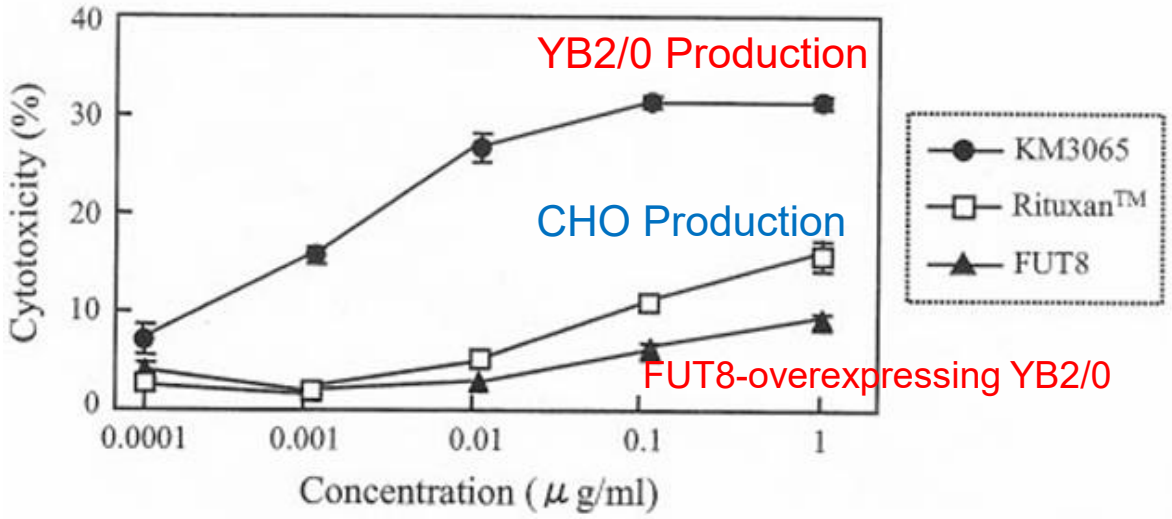
(Modified) Shinkawa et al., J Biol Chem 2003 (Figure 2& Table 1) Licensed under CC-BY 4.0

© Kyowa Kirin Co., Ltd.

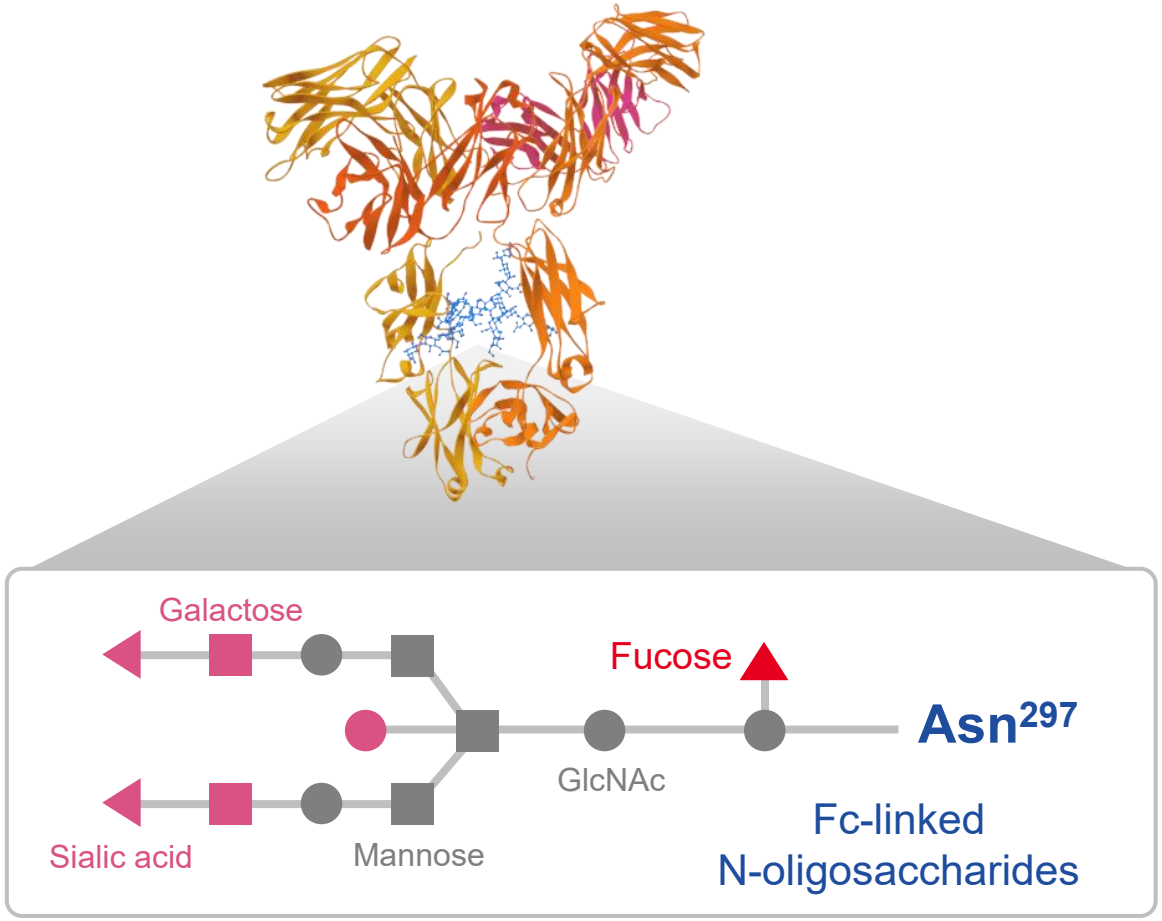
Does glycan structure differ by production cell?

When host cells with low FUT8 expression were forcibly expressed, the obtained high-fucose antibodies showed a significant decrease in ADCC

*FUT8 (α1,6-fucosyltransferase)
The only enzyme that adds fucose to N-linked glycans



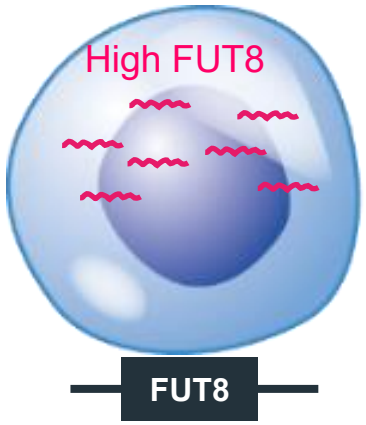
(Modified) Shinkawa et al., J Biol Chem 2003 (Figure 5) Licensed under CC-BY 4.0



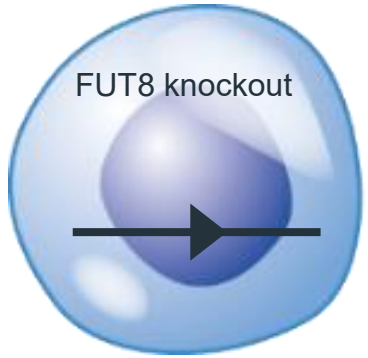
© Kyowa Kirin Co., Ltd.

Stable Potelligent antibody-producing cells via host-cell FUT8 knockout

*FUT8 (α1,6-fucosyltransferase)
The only enzyme that adds fucose to N-linked glycans



CHO cells
NS/0 cells



FUT8$^{-/-}$ CHO cells

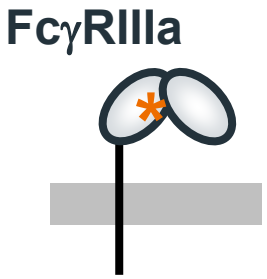
Yamane-Ohnuki et al., Biotechnol Bioeng 2004 Sep 5; 87(5):614-22

- Standard commercial production hosts
- High FUT8 yields highly fucosylated antibodies

- Uniform production of fully afucosylated antibodies

© Kyowa Kirin Co., Ltd.

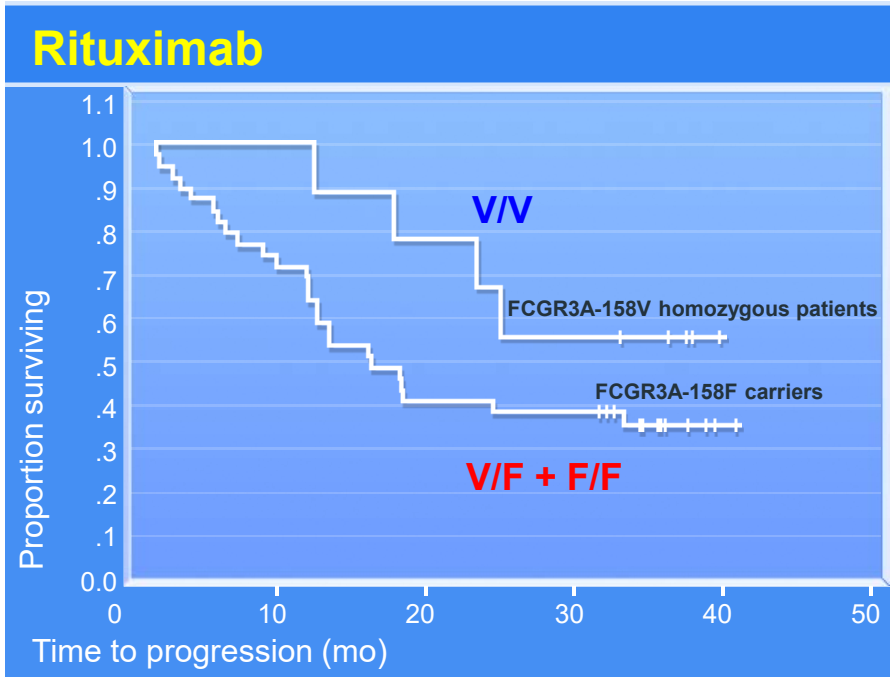
Key external factors
ADCC's clinical value repeatedly shown in trial cohorts



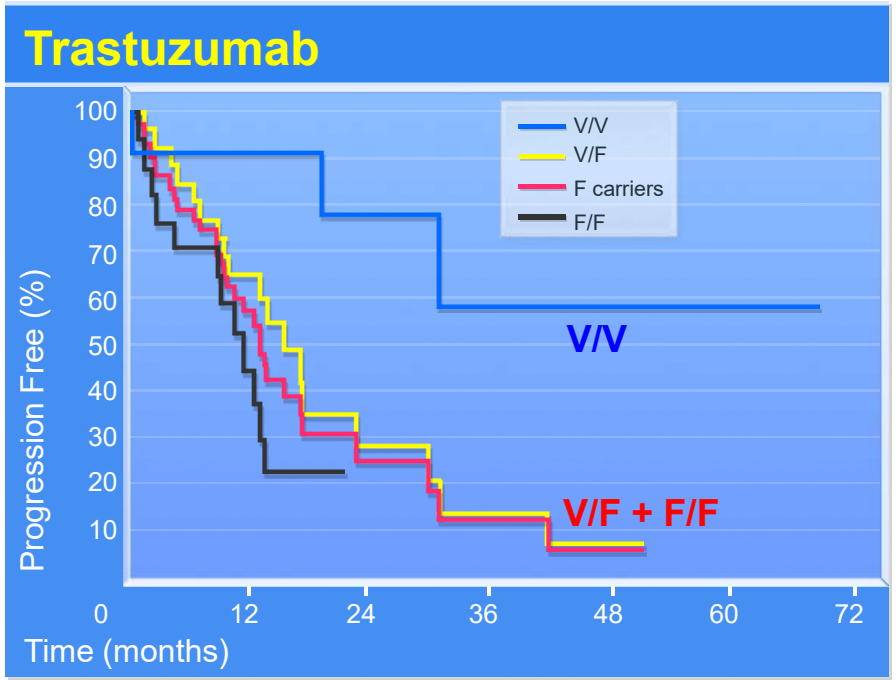
* Val / Phe polymorphism at position 158

FcgRIIIa-^{158}Val : Strong Fc binder -> **High ADCC**

FcgRIIIa-^{158}Phe : Weak Fc binder -> **Low ADCC**



Cartron et al., BLOOD, 99, 754-8 (2002)
Based on Figure 1, the presenter recreated it.

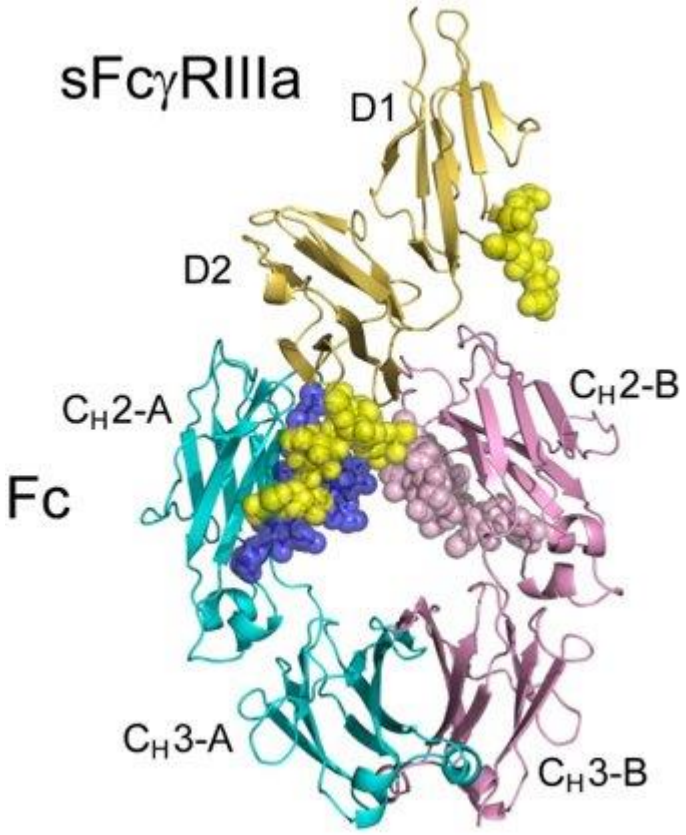


Musolino et al.,J Clin Oncol 26: 1789-96 (2008)
Based on Figure 1, the presenter recreated it.

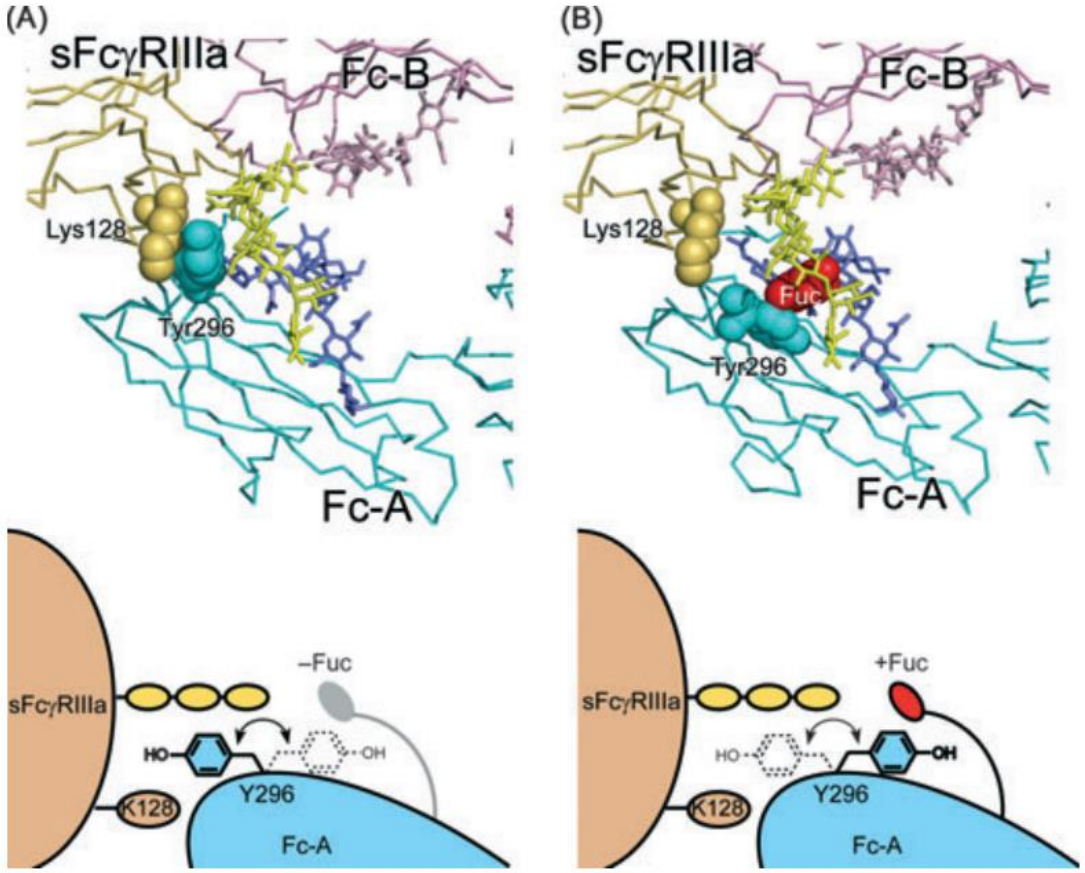
© Kyowa Kirin Co., Ltd.

Potelligent structural biology: more interactions, same contact pattern

A strong Interaction between plus charge of Lys128 of FcgRIIIa and minus charge of Tyr296 of the Fc is formed by removing fucose



Mizushima T et al. Genes to Cells 16, 1071

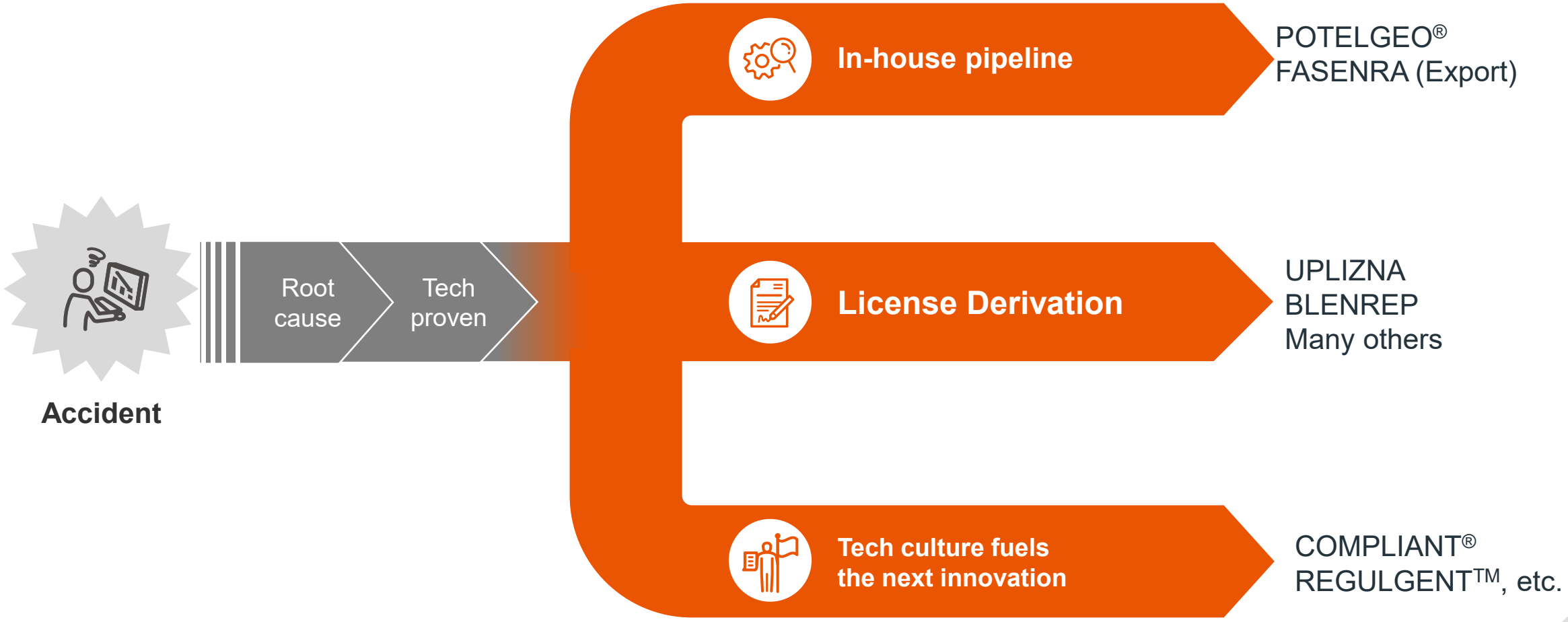


A: Nonfucosylated Fc

B: Fucosylated Fc

© Kyowa Kirin Co., Ltd.

POTELLIGENT® technology born from research failures



© Kyowa Kirin Co., Ltd.

Keys to Potelligent’s Success: A Researcher’s View

Organizational Strength that created the technology

- Insight and perseverance to never miss serendipity
- Teamwork integrating production, analysis, and molecular design
- A technology-driven culture that turns failure into a starting point for identifying causes

The Strength of the Technology Itself

- Subtle sugar chain modification, not amino acid changes
  - High developability
  - Mechanism of action identical to natural antibodies
- “Sense of security” drives client adoption

Demonstration in our own pipeline

- Installation in POTELIGEO and FASENRA
- Blood cells were selected as the optimal target for ADCC
- The courage and speed to advance "first-in targets" × "unidentified technologies"

Licensing Business and Trends

- Proved commitment via in-house POT and FAS development
- Many publications showcasing innovative science
- Total package offered via LONZA partnership
- Tailwind: clinical value of ADCC recognized in early 2000s

© Kyowa Kirin Co., Ltd.

たった一度の、いのちと歩く。