

Alpha-Gal-containing biologics

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Glycans containing the non-human epitope Gal α 1-3Gal (alpha-gal) can significantly decrease the clinical performance of therapeutic monoclonal antibodies (mAbs). The presence of Gal α 1-3Gal can affect the safety profile and lead to a potential adverse reaction and neutralisation of the drug by anti- α -galactose antibodies reducing therapeutic efficacy. Given the potential impact on patients, Gal α 1-3Gal are a high priority Glycosylation Critical Quality Attribute (GCQA) and drug developers must effectively optimise, measure and control the glycosylation of their products to limit Gal α 1-3Gal levels throughout the product life cycle.

Detecting and quantifying the amounts of Gal α 1-3Gal can be very difficult as these epitopes are often hidden by the complexity of the glycan profiles.

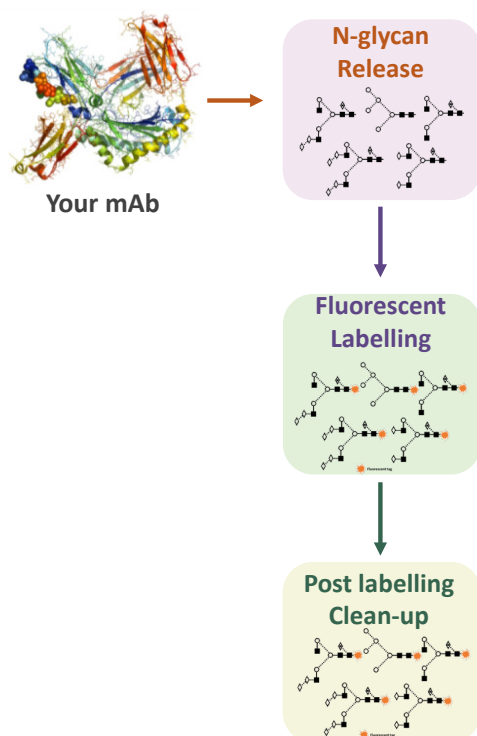
How Ludger can help?

1. Ludger's Technology

Ludger offers a range of products for analysis of biologics containing alpha-gal epitope. This includes: (a) kits for N-glycan release; (b) kits for glycan labelling; (c) glycan clean-up systems; (d) buffers for HILIC-UPLC systems; (e) System Suitability Controls; (f) Process Controls and Reference Standards.

Ludger's strategy that mAb developers can use for detection and quantification of Gal α 1-3Gal bearing glycans:

Ludger's Technology - for more info click on product code (or guide)



- N-glycan release kit: **LZ-rPNGaseF-kit (product guide)**
- Process Control to assess the release, labelling, clean-up and analyses: **GCP-IGG-100U** (100 μ g human IgG glycoprotein).
- Procainamide tag: **LT-KPROC-24 (product guide)**
- 2-AB Tag: **LT-KAB-A2 (product guide)**
- 2-AA Tag: **LT-KAA-A2 (product guide)**
- Process Control to assess the labelling, clean-up and analyses: **CLIBN-IGG-01** (N-glycans released from human IgG glycoprotein).
- Clean-up plate for procainamide labelled glycans: **LC-PROC-96 (product guide)**
- Clean-up cartridges for 2-AB or 2-AA labelled glycans: **LC-T1-A6 (product guide)**
- Buffer for HILIC-UPLC: **LS-N-BUFFX40 (product guide)**
- System Suitability Standard and Reference Standard for GU allocation: **CPROC-GHP-30 / CAB-GHP-30 / CAA-GHP-30** - Procainamide or 2-AB or 2-AA Labelled Glucose Homopolymer (GHP). *GU values can be used as a primary identification for glycans based on reported values in the literature and databases.*
- Reference Standards: Mixtures of N-glycans Common to mAb Samples: www.ludger.com/products/glycan-standards

- HILIC-FLR-UPLC
Or
- HILIC-FLR-UPLC-ESI-MS/MS (LC-MS/MS)

Exoglycosidase Digestions followed by:

- HILIC-FLR-UPLC
Or
- HILIC-FLR-UPLC-ESI-MS/MS (LC-MS/MS)

- Exoglycosidases:
 - Sialidase (removes α 2-3,6,8 sialic acids)
 - Fucosidase (removes α 1-2,3,4,6 fucose)
 - Beta Galactosidase (removes β 1-4 galactose)
 - Alpha Galactosidase (specific for α -galactose)
 - Beta-N-acetylglucosaminidase (specific for GlcNAcs β -linked to mannose)
 - Mannosidase (removes α 1-2,3,6 mannose)
www.ludger.com/products/exoglycosidases
- Post-exoglycosidase Cleanup Plate: **LC-PBM-96 (product guide)**
- Process Control to assess the exoglycosidase digestions and analyses: Mixtures of N-glycans Common to mAb Samples:
www.ludger.com/products/glycan-standards
- Process Control to assess the alpha galactosidase digestions and analyses: **CAB-ALPHA-GAL-01** Native or fluorescently labelled glycan containing the Gal α 1-3Gal

If you require any further information on how we can help you select products, please contact us at: info@ludger.com

2. Ludger's Glycan Analysis Services

Our strategy is to offer a range of complementary analytical methods (e.g. HILIC-UPLC, exoglycosidase sequencing, HILIC-FLR-ESI-MS/MS) to answer questions about the structures of glycans on glycoproteins. The complexity of the analysis reflects the detail of the information required. We work closely with clients **to design and execute appropriate glycoprofiling programmes** and can work up to GMP standard. Our data and **customised reports** are used: (i) in process optimisation; (ii) to support regulatory submissions; (iii) for lot release of drug batches during biomanufacturing.

We can also transfer and validate these optimised glycoprofiling methods to your laboratories.

Glycan Analysis Services



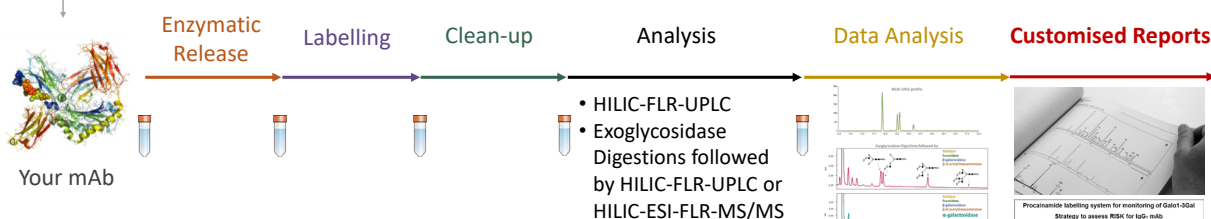
Dr Radoslaw Kozak
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- Discussion with Client regarding requirements
- CDA/MSA if required



Study Proposals
&
Quotation

- Client Purchase Order
- Client Samples

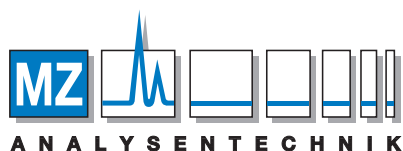


Ludger's reports are used by companies around the world:

- in process optimisation
- to support regulatory submissions
- for lot release of drug batches during biomanufacturing

We can transfer these methods to your laboratory

We can provide Compliance documentation for GMP



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