



Using the custom library functionality in Genedata Expressionist streamlined our characterization workflow: reducing analysis times from several weeks to hours, and enabling us to progress quality candidates more rapidly.

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Industry

Pharmaceuticals

Customer Since

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About Amicus

Amicus Therapeutics is a global, patient-dedicated biotechnology company focused on discovering, developing, and delivering high-quality medicines for people living with rare metabolic diseases.

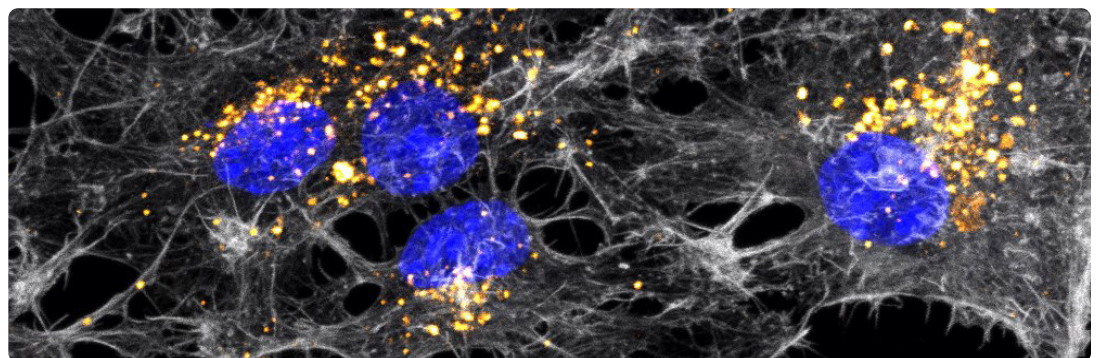
Genedata Solution

Comprehensive MS-Based Characterization of Complex Phosphorylated Glucosidases

Background

Amicus Therapeutics develops biopharmaceuticals for the treatment of rare metabolic conditions such as Pompe disease, an inherited lysosomal storage disorder caused by a deficiency of alpha-glucosidase (GAA). This disease can be treated using enzyme replacement therapy, in which recombinant GAA is targeted to the lysosome via the cation-independent mannose-6-phosphate receptor (CIMPR). The effectiveness of this subcellular targeting is dependent on *bis*-mannose-6-phosphate glycans on the biotherapeutic molecule. Consequently, thorough and comprehensive glycan characterization is critical to ensure the development of successful treatments.

To achieve in-depth characterization of these highly complex biotherapeutics, we worked together with Genedata to develop and implement tailored MS data processing workflows based on custom glycan libraries that increased not only our understanding of our drugs' glycosylation profiles, but also our analytical throughput.



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Cathepsin B positive lysosomes in cultured neurosphere cells. Image courtesy of Nadia Efimova and Brian Ranes (Amicus Therapeutics).

Main Challenges

Time-consuming data analysis workflow

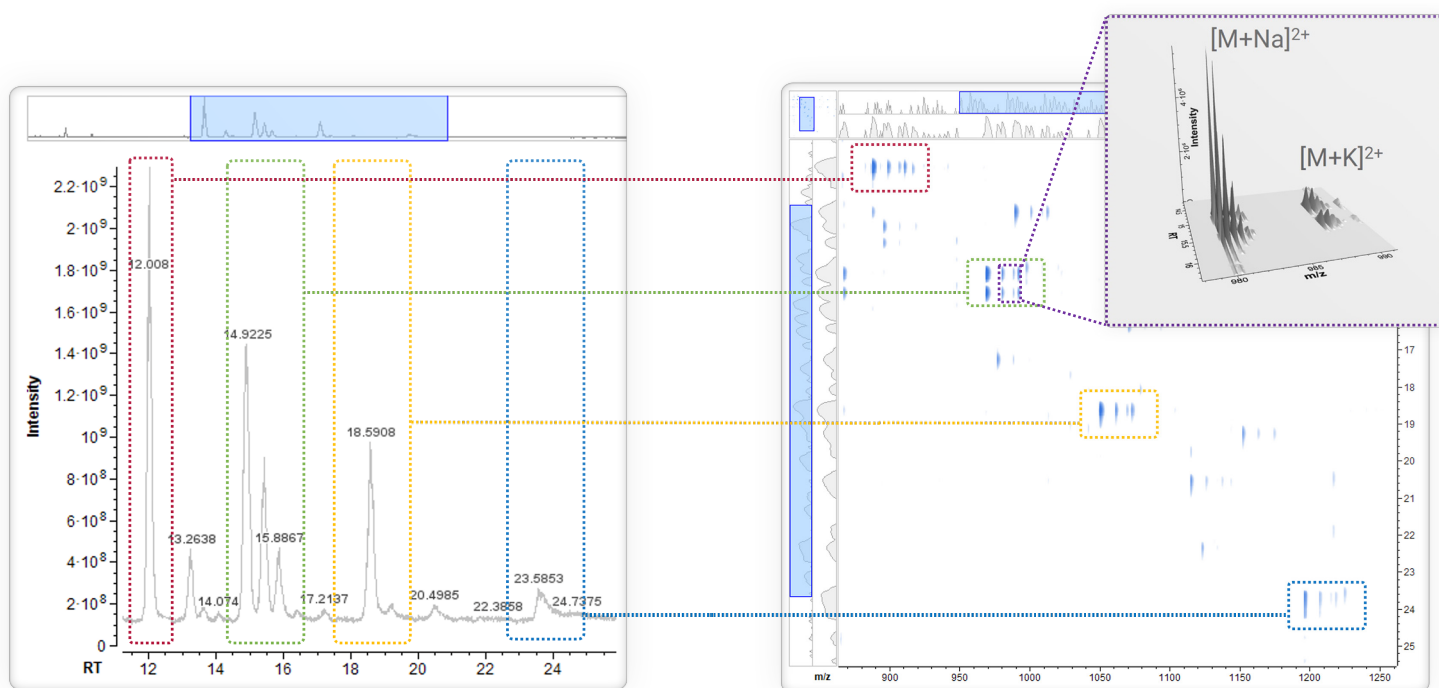
The large volumes of complex data generated during the characterization of our biotherapeutics contain signals from multiple glycan species. For each sample, identifying and annotating these signals requires weeks of an expert user's time. This highly labor-intensive process represents a serious bottleneck in our characterization efforts and delays downstream operations.

Complex characterization of highly diverse glycan structures

Determining the nature and extent of post-translational modifications (PTMs) such as glycosylation represents a key analytical challenge during the development of innovative biotherapeutics. In the case of GAA, glycan phosphorylation adds another layer of complexity to an already highly heterogeneous molecular profile that cannot be easily characterized with off-the-shelf mass spectrometry (MS) data analysis software.

Siloed data limiting information flow

Significant resources are invested to analyze novel biotherapeutics throughout their development phases. However, analytical data and metadata remain dispersed across instruments: limiting data interoperability, hindering collaboration, and greatly reducing opportunities to obtain and leverage insights from MS-based analytics.



Conventional results display using Total Ion Chromatogram (TIC) signal

Innovative Ion Map and 3D visualization provide easy-to-recognize patterns for glycoanalysis

Figure 1. Powerful visualizations enable swift identification of related structures and provide detailed molecular information for all glycosylation signals.

Solution

Powerful processing and intuitive visualizations

Genedata Expressionist is built on a central server architecture that provides powerful and scalable data processing. Intuitive visualizations enable the user to quickly identify target glycan signals and flag them for further in-depth analysis. For example, the ion map provides an easy-to-understand representation of the entire MS data set, demonstrating the *m/z* and retention time (RT) relationships between core glycan structures and their fragments and adducts (Figure 1).

User-friendly analysis workflows customized to our needs

Flexible MS data processing workflows—built and implemented together with Genedata experts—streamline released glycan and glycopeptide mapping analytical processes. Built-in glycan libraries provide a comprehensive database for MS-based analysis of complex glycans. A dedicated glycan editor facilitates the ready expansion of existing libraries, or the creation of new customized databases tailored to our specific needs (Figure 2).

A single, open enterprise software platform for all MS data

Genedata Expressionist provides a centralized infrastructure for capturing and accessing all information related to our MS data. Analytical data, metadata, methods, results, reports, etc., are consolidated in a single platform to provide a corporate analytical knowledge base. For example, glycan libraries can be easily generated and continuously augmented and leveraged throughout a molecule's life cycle. This information becomes an asset that can also be applied to the development of future biotherapeutics.



Figure 2. Through an intuitive editor, Genedata Expressionist enables users to create custom-built glycan libraries that utilize corporate nomenclature.

Benefits

Increased productivity

The time required to characterize each sample was reduced from many weeks to just a few hours. The resulting increase in analytical throughput dramatically accelerates evaluation of drug candidates and is key to providing more timely feedback to our colleagues in other departments.

Improved candidate quality reduces risk

Implementing our MS data processes into custom-built data workflows enables us to tailor and optimize each step of our data processing, analysis, and reporting. For example, building a custom library using our specific glycan nomenclature greatly simplifies data analysis and internal knowledge sharing. This flexibility enables us to achieve unique molecular insights into our biotherapeutics that greatly helps us to identify and progress high-quality candidates.

From siloed data to corporate knowledge

By ensuring easy access to critical information, Genedata Expressionist facilitates knowledge sharing and collaboration, providing stakeholders with relevant information and supporting our decision-making processes. Centralized project- and knowledge-management also streamlines MS analytics across our organization, and establishes standardized processes for MS data processing, analysis, and reporting.

Summary

Highly laborious and inefficient procedures in MS data analysis are major bottlenecks during the characterization of glycosylated biotherapeutics.

Working in close collaboration with Genedata, we quickly implemented a dedicated software solution that facilitates and dramatically accelerates MS data analysis of complex glycans.

The implemented solution reduced the time required to characterize each sample from weeks to hours and enabled us to fully leverage the insights from our MS analyses, providing faster time to clinic with the highest quality biotherapeutics.