

# Pioneering Advanced Nucleic Acid Analysis for Gene and Cell Therapy Development at TATAA Biocenter

## Leading in bioanalysis and biomarker discovery

The rise of advanced cell, gene, and RNA therapies has heightened the need for sophisticated nucleic acid analysis techniques that adhere to rigorous drug development standards. These therapies depend on precise methods such as quantitative PCR (qPCR), digital PCR (dPCR), and next-generation sequencing (NGS), setting them apart from traditional small molecule bioanalysis.

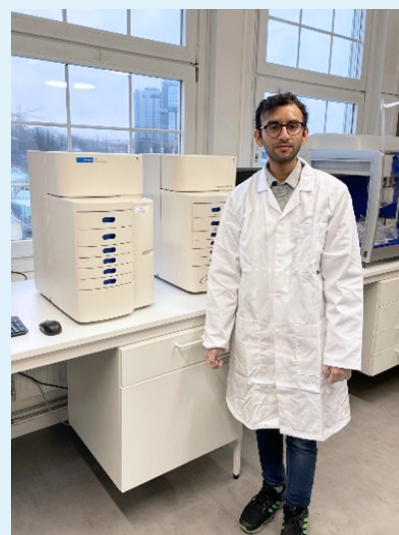
TATAA Biocenter, a specialized contract research organization (CRO) in Gothenburg, Sweden, excels in bioanalysis, biomarker discovery, and validation through the development of highly sensitive assays and high-throughput analyses specifically designed for advanced therapies. The facility's GLP-accredited laboratory is well-equipped to conduct complex biodistribution studies, analyze transgene expression, and perform comprehensive transcriptome-wide investigations, essential for delivering actionable insights throughout the drug development process.



## Ensuring safety and efficacy

For therapies involving the administration of genetically modified cells or viral vectors, safety and efficacy testing is crucial. Methods include biodistribution studies of the therapeutic agents and transgene expression measurement across target and nontarget tissues. The assays developed for these purposes must be highly sensitive, specific, precise, and accurate.

Furthermore, working with diverse and often challenging sample types, such as limited-volume samples, fibrous tissues, fecal samples rich in PCR inhibitors, or degraded formalin-fixed, paraffin-embedded (FFPE) samples, adds an additional layer of complexity. This makes stringent quality control (QC) paramount as high-quality data forms the foundation for regulatory decisions on safety and efficacy. "The data is the basis for decisions on whether a drug proceeds to market or human trials. Therefore, it must be accurate. We must perform QC at every step during assay development to ensure that it performs equally well every time," said Johanna Nilsson, a facility representative.



TATAA Biocenter Lab Scientist Karthik Ganganna with the Agilent 5200 and 5300 Fragment Analyzer systems.

## Applying advanced techniques and robust QC

At TATAA, vector copy number and transgene expression are measured using advanced qPCR and dPCR platforms. RNA-seq is also used for transcriptome-wide profiling, siRNA knockdown efficiency evaluation, and differential gene expression analysis across various treatments and response parameters.

Robust QC measures are in place to ensure reliable results. The lab uses the Agilent 5200 and 5300 Fragment Analyzer systems, featuring 12 and 96 channels, respectively, to meet the standards of high sensitivity, specificity, precision, and accuracy. The instruments also enable full sample traceability through integration with the lab's LIMS system. "We have two different Fragment Analyzers, a 12-channel and a 96-channel," explained Elina Ekedahl, NGS specialist and project manager at TATAA. "Purchasing the 96-channel system a few years back has significantly improved our workflows in terms of throughput."

## Evaluating RNA integrity

Degraded RNA can cause a converted cDNA library to inaccurately represent the transcriptome by overrepresenting shorter transcripts or fragments. Therefore, TATAA recognizes that having an easy and fast method to evaluate RNA integrity is essential for all downstream processes conducted in the lab. Degraded RNA can lead to false negatives or inaccurate results, making proper sample handling critical, especially for low-abundance transcripts and high-sensitivity applications like biodistribution and viral shedding studies.

"Using the Fragment Analyzer systems to check the quality of extracted material sets the baseline for downstream processes," mentioned Elina. "If a sample has low quality, you must decide whether to include it in your analysis." Assessing RNA quality with the Fragment Analyzer and receiving an RNA Quality Number (RQN) provides valuable insights into sample integrity, helping to ensure accurate and reliable downstream analyses. "To know the quality is our goal with the Fragment Analyzer," mentioned Johanna. "For FFPE or degraded samples, we need to know how impacted the quality is and how much we can trust the data going forward."

## Focusing on NGS library preparation QC

In addition to RNA QC for assay development and biomarker analysis, the Fragment Analyzer systems also play a key role in QC during NGS library preparation. These instruments are used to determine average fragment sizes, detect adapter-dimer artifacts, and identify over- or underamplification of the library.

During library generation for small RNA sequencing, small fragments, including miRNAs and other noncoding RNAs, are amplified during PCR. The Fragment Analyzer helps the TATAA team confirm that the size-selected library sample contains only the correctly sized fragments and verify the presence of specific isolated fragments when required.

"The systems are very straightforward to use. They've been working well for our applications," said Elina.

## Driving innovation in advanced therapies

The Fragment Analyzer is a critical tool for TATAA Biocenter in the chain of quality controls necessary for developing and validating assays for advanced therapies. With the instrument, labs can provide precise and reliable results, driving innovation in the pharmaceutical industry.

Looking ahead, TATAA Biocenter is poised to expand its work in cell and gene therapy projects, anticipating an increase in GLP-regulated work. "We look forward to taking on even more GLP work," emphasized Johanna. Despite the current lack of clear FDA and EMA guidelines on validating qPCR assays compared to traditional methods like mass spectrometry and flow cytometry, TATAA is leading the way. She added, "Regulatory guidance for cell and gene therapies is evolving, and we are at the forefront." TATAA's recent publication on validating qPCR and dPCR assays for bioanalysis and cell and gene therapies<sup>1</sup> positions them as a knowledge leader, ready to drive innovation and compliance as new regulations emerge.

Overall, the Agilent 5200 and 5300 Fragment Analyzer systems are an indispensable tool for maintaining the integrity and quality of sequencing libraries, ultimately leading to more efficient and effective research outcomes.

Discover more about TATAA Biocenter and their mission:

[Your CRO for molecular analysis - TATAA Biocenter](#)

## Reference

1. Hays, A.; Wissel, M.; Colletti, K.; Soon, R.; Azadeh, M.; Smith, J.; Doddareddy, R.; Chalfant, M.; Adamowicz, W.; Ramaswamy, S. S.; et al. Recommendations for Method Development and Validation of qPCR and dPCR Assays in Support of Cell and Gene Therapy Drug Development. *AAPS J.* **2024**, 26 (1), 24. DOI: 10.1208/s12248-023-00880-9.

[www.agilent.com/genomics/fragment-analyzer](https://www.agilent.com/genomics/fragment-analyzer)

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