WHITE PAPER

From plasma to insights: Enabling reliable liquid biopsy research

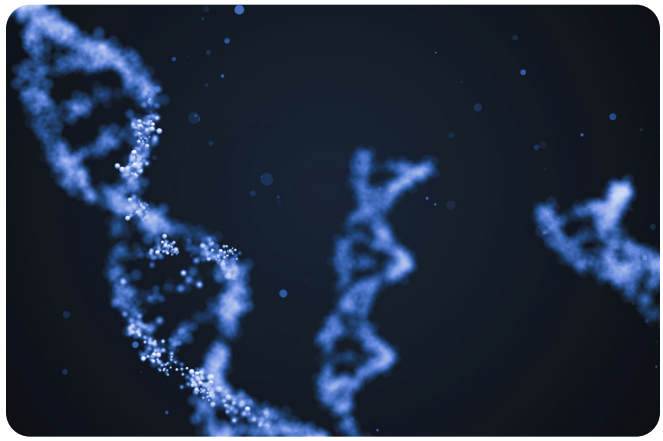
Liquid biopsy is transforming cancer research by enabling non-invasive analysis of circulating cell-free DNA (cfDNA). However, the reliability of these approaches depends heavily on the quality and consistency of cfDNA extraction.

This white paper explores how automated magnetic bead-based workflows, including the chemagic™ 360 instrument and chemagic cfDNA kits, support high-throughput, reliable cfDNA isolation. Drawing on real-world implementation at leading cancer centers and recent peer-reviewed studies across multiple cancer types, it highlights the critical role of standardized extraction in enabling sensitive, scalable liquid biopsy research.

Advancing liquid biopsy research with chemagic technology

Liquid biopsy research is reshaping how scientists investigate cancer biology, offering a non-invasive window into tumor-derived genetic material through circulating cell-free DNA (cfDNA). By enabling repeated sampling over time, cfDNA-based approaches support longitudinal studies, deeper insights into tumor evolution, and the exploration of disease heterogeneity across patient populations[1].

However, the success of circulating cfDNA analysis depends on more than downstream sequencing or analytical techniques. The quality, consistency, and recovery of cfDNA at the extraction stage play a critical role in determining the reliability of results[2]. Low DNA abundance, high fragmentation, and sensitivity to pre-analytical variation make cfDNA extraction one of the most technically demanding steps in the liquid biopsy workflow.



In this context, automated magnetic bead-based extraction technologies are increasingly central to achieving robust liquid biopsy workflows. Revvity's chemagic 360 instrument is designed to support high-throughput, consistent isolation of cfDNA from plasma and other sample types, combining scalable automation with consistent performance. By reducing manual variability and streamlining sample processing, it empowers researchers with reliable input material for downstream circulating cfDNA analysis.

This white paper explores how chemagic technology is being implemented in leading research organizations worldwide to support scalable, reliable cfDNA extraction, highlighting the key applications and research areas where chemagic technology is helping researchers achieve more consistent, reliable, and efficient liquid biopsy workflows.

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Technical challenges in cfDNA extraction and liquid biopsy workflows

Despite the growing impact of liquid biopsy research, circulating cfDNA analysis remains technically demanding. cfDNA is typically low in abundance, highly fragmented, and highly variable between samples[3], making efficient and consistent extraction essential for reliable results.

Key challenges in cfDNA extraction include:

- **Low DNA input and fragmentation:** cfDNA is often present in small quantities, particularly in early-stage disease research, increasing the risk of losing low-frequency variants during extraction.
- **Sample-to-sample variability:** differences in plasma volume and cfDNA concentration can impact recovery and downstream consistency.
- **Reproducibility across workflows:** manual and semi-automated methods can introduce variability through handling and operator-dependent steps.
- **Scaling liquid biopsy workflows:** high sample volumes and complex protocols can create bottlenecks, making it difficult to balance throughput with consistency.

These challenges highlight the need for standardized, scalable approaches to cfDNA extraction.

Unlocking scalable cfDNA extraction with automated workflows

To address the technical and operational challenges of cfDNA extraction, many research organizations are adopting automated, magnetic bead-based workflows. This approach is designed to improve consistency, reduce hands-on time, and support the high-throughput processing required for modern liquid biopsy research.

Magnetic bead-based extraction is particularly well suited to circulating cfDNA analysis, where short, fragmented DNA must be efficiently captured from low-input samples. chemagic technology harnesses Revvity's proprietary M-PVA magnetic beads to bind nucleic acids with high efficiency, supporting robust recovery of cfDNA while enabling effective removal of contaminants. This is especially important in liquid biopsy workflows, where both yield and purity directly influence downstream analytical performance.

The chemagic 360 instrument, paired with chemagic cfDNA kits, integrates this chemistry within an automated workflow that includes on-board lysis and does not require heating steps, helping to streamline processing while maintaining sample integrity. Automation reduces variability associated with manual handling and supports consistent performance across runs, even when working with variable input volumes.

Key workflow capabilities include:

- **Consistent cfDNA recovery across input ranges:** a wide range of sample volumes (approximately 0.5-18 mL), enabling flexibility for different study designs and sample availability.
- **Efficient, streamlined processing:** automated workflows with integrated lysis reduce hands-on time and minimize potential sources of variability.
- **Consistency at scale:** standardized protocols help ensure consistent extraction performance across large cohorts and longitudinal studies.
- **Traceability and workflow integration:** barcode-based sample tracking and bidirectional LIMS connectivity support full traceability within complex lab environments
- **Broad downstream compatibility:** extracted cfDNA is suitable for a range of analytical methods, including NGS, qPCR, and ddPCR.
- **Flexible sample compatibility:** applicable to fresh or frozen plasma and serum collected in commonly used tube types.

By combining optimized magnetic bead chemistry with automated workflow control, the chemagic 360 instrument enables researchers to move from variable, labor-intensive extraction toward standardized, high-throughput cfDNA workflows that support reliable results.

This reliability is particularly important in high-throughput plasma workflows, where consistent recovery across large sample volumes helps minimize sample dropouts and maintain dataset integrity.

Explore how Revvity chemagic supports cfDNA research.

Insights from a cancer research institution

The performance of cfDNA extraction workflows is ultimately defined by how they operate under real-world laboratory conditions. High-throughput research environments require not only consistent extraction performance but also ease of use, flexibility across sample types, and the ability to integrate seamlessly into existing workflows.

At a leading cancer research organization, the chemagic 360 instrument has been implemented as part of routine workflows for nucleic acid extraction across multiple sample types. The system can be used for circulating cfDNA extraction as well as for other applications, including formalin-fixed paraffin-embedded (FFPE) tissue, blood, and bone marrow samples.

Cancer research organizations benefit from several practical advantages of the chemagic 360 instrument in liquid biopsy workflows:

- **Scalability across instruments:** multiple systems operating in parallel support high sample throughput in large research environments.
- **Ease of adoption and usability:** a straightforward setup enables consistent execution across teams with varying levels of experience.
- **Rapid turnaround times:** extraction in under 45 minutes supports time-sensitive workflows and improves overall lab efficiency.
- **Versatility across sample types:** a single platform supporting plasma, FFPE, blood, and bone marrow enables broader application within research workflows.

Importantly, these operational benefits extend beyond convenience. In high-volume liquid biopsy research, consistency in sample processing and turnaround time directly contributes to the reliability and reproducibility of downstream circulating cfDNA analysis.

Applications of cfDNA extraction in liquid biopsy research

The growing body of peer-reviewed research leveraging cfDNA highlights the expanding role of liquid biopsy across a range of oncology research applications. From early detection studies to longitudinal monitoring and multi-cancer analysis, these applications place increasing demands on cfDNA extraction workflows, particularly in terms of sensitivity, reproducibility, and scalability.

The following studies utilizing chemagic technology, including the chemagic 360 and chemagic cfDNA kits, demonstrate how robust cfDNA extraction supports reliable data generation, preserves biological signal integrity, and enables efficient, scalable liquid biopsy workflows across diverse research applications.

Early detection and cancer classification

Early detection remains one of the most demanding applications of liquid biopsy research, where tumor-derived cfDNA is often present at extremely low levels.

A recent study in *Communications Medicine*[4] demonstrated how integrating 5-methylcytosine (5mC) and 5-hydroxymethylcytosine (5hmC) signals from cfDNA can significantly improve early-stage colorectal cancer detection, achieving high diagnostic accuracy through combined epigenetic profiling. The success of this approach depends on preserving subtle epigenetic signatures within fragmented cfDNA, placing strong emphasis on extraction workflows that can deliver high-quality, intact DNA with minimal bias or loss.

Another study, published in *Scientific Reports*[5] explored the use of combined methylation and fragmentomics features to classify lung cancer from plasma-derived cfDNA, using machine learning models to improve detection performance. In this type of multi-feature analysis, consistent cfDNA recovery across samples is critical to ensure that fragmentation patterns and methylation signals are not distorted.

Together, these studies reflect a broader shift toward multi-dimensional cfDNA analysis for early cancer detection. As analytical methods become more sensitive, the requirements placed on upstream workflows increase accordingly. Reliable cfDNA extraction, supported by chemagic technology, helps ensure that low-frequency and multi-layered signals are preserved, enabling more confident interpretation of early disease signatures.

Treatment response monitoring and longitudinal studies

Liquid biopsy research is increasingly used to track tumor dynamics over time, enabling researchers to monitor treatment response and disease progression through serial cfDNA sampling. In these longitudinal settings, the ability to generate consistent, comparable data across multiple timepoints is critical.

Recent studies have demonstrated how changes in circulating tumor DNA (ctDNA) profiles can provide a window into therapeutic response and emerging resistance. For example, longitudinal analyses in pancreatic cancer have shown that ctDNA levels correlate with tumor burden and clinical outcomes, supporting its use as a dynamic biomarker[6]. Studies like this rely on standardized cfDNA extraction across treatment timelines, with automated chemagic 360 workflows providing the consistency needed to support reliable analysis.

Similarly, a study on metastatic gastroesophageal cancer demonstrated that early changes in ctDNA levels, extracted using the chemagic 360, could predict treatment response significantly earlier than conventional imaging approaches[7]. Applications such as these rely on stable and consistent cfDNA workflows, where consistent DNA recovery across timepoints is essential to ensure that observed changes reflect true biological dynamics rather than workflow variability.

In addition to the standardization and reproducibility that chemagic technology provides, the ability to process multiple samples efficiently supports the practical demands of longitudinal research, where frequent sampling and rapid turnaround are often required. Together, these capabilities help enable more accurate interpretation of treatment response and disease evolution.

Multi-cancer and large-scale genomic profiling

Beyond individual cancer types, liquid biopsy research is increasingly being applied at scale to support large, multi-cohort studies that aim to uncover shared and disease-specific molecular signatures across diverse patient populations. These approaches often integrate genomic, epigenetic, and fragmentomic data, placing significant demands on upstream workflows.

A landmark study published in *Nature Communications*[8], demonstrated the application of large-scale sequencing to improve the clinical assessment of hematological malignancies. The study leveraged high-throughput workflows across multiple sample types, including blood, bone marrow, and FFPE tissue, to generate comprehensive molecular profiles at scale.

chemagic 360 based extraction workflows were used to support consistent nucleic acid isolation across diverse and often challenging sample inputs. This level of workflow standardization is critical in studies of this scale, since variability in DNA extraction can introduce bias and impact cross-sample comparability.

In a separate *Nature Communications* study[9], the researchers explored optimized DNA extraction strategies for cytology and other low-input sample types, demonstrating how alternative sources of DNA can be used to support genomic profiling when conventional samples are limited[9]. Studies such as this highlight the importance of robust extraction workflows when working with degraded or low-abundance material; frequently encountered in real-world oncology research.

Together, these studies illustrate how chemagic technology is being applied within complex, high-throughput research environments, where reliable DNA recovery across diverse sample types is essential. As liquid biopsy research continues to scale, the ability to standardize upstream workflows becomes increasingly important, not only for operational efficiency, but for ensuring that downstream insights are driven by biological signal rather than workflow variability.

Key considerations for cfDNA extraction in liquid biopsy workflows

As liquid biopsy research continues to evolve, the demands placed on cfDNA extraction workflows are increasing. From early detection studies to longitudinal monitoring and large-scale genomic profiling, the ability to generate high-quality, reliable cfDNA is central to reliable downstream analysis.

From the wide-ranging research applications discussed, several key considerations emerge for researchers when selecting and validating cfDNA extraction workflows:

- **DNA yield and quality:** efficient recovery of fragmented cfDNA, while preserving integrity and minimizing contaminants, is essential for supporting sensitive downstream analyses such as methylation profiling, fragmentomics, and mutation detection.
- **Reproducibility across samples and timepoints:** consistent extraction performance is critical in both large cohort studies and longitudinal designs, where variability can obscure true biological signals.
- **Scalability and throughput:** as studies expand in size and complexity, workflows must support the processing of large sample volumes without introducing bottlenecks or compromising consistency.

- **Compatibility with diverse sample types:** research workflows increasingly incorporate a range of inputs, including plasma, serum, FFPE tissue, and low-input or degraded samples, requiring flexible and robust extraction approaches.
- **Integration with downstream workflows:** seamless compatibility with analytical methods such as NGS, qPCR, and ddPCR ensures that extracted cfDNA can be readily used without additional processing steps.
- **Workflow standardization and traceability:** automation, sample tracking, and integration with laboratory information management systems (LIMS) support reproducibility, data integrity, and compliance in complex research environments.

These important factors highlight the importance of selecting extraction workflows that not only deliver high-quality cfDNA, but also support the broader operational and analytical demands of modern liquid biopsy research.

Building a reliable foundation for liquid biopsy research

Liquid biopsy research is advancing rapidly, enabling new approaches to early detection, treatment monitoring, and large-scale cancer profiling. Across these applications, one requirement remains constant: the need for high-quality, consistent cfDNA input.

As workflows become more complex and data-driven, variability at the extraction stage can limit sensitivity, comparability, and overall confidence in results. Standardized, automated approaches are therefore essential to ensure that downstream insights reflect true biological signals.

That is why chemagic technology is trusted by leading research organizations at the forefront of liquid biopsy research. By combining robust magnetic bead chemistry with scalable automation, chemagic workflows enables consistent, high-quality cfDNA extraction, providing the reliable foundation needed to support the next generation of cancer research.

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