

## Everything you wanted to know about cell-free RNA but were afraid to ask

Most researchers and medical professionals are familiar with RNA, from messenger RNA (mRNA) which is crucial for protein synthesis to RNA vaccines that have combated COVID-19. However, less known but equally significant is cell-free RNA (cfRNA), which circulates in the bloodstream, offering unique insights into various physiological and pathological conditions. At Floxxmics, our research focuses on cfRNA and its potential as a powerful biomarker for early disease detection. In this document, we address the most frequently asked questions about cfRNA, highlighting its transformative impact on diagnostics and research.

### What is cell-free RNA and what can it be used for?

Cell-free RNA (cfRNA) is released into the bloodstream by various tissues through processes like apoptosis, necrosis, and active secretion. These RNA molecules can originate from healthy tissues or those undergoing stress or damage, such as cancerous tissues.

cfRNA can be used as a biomarker for non-invasive liquid biopsies, offering extensive tissue-specific information for early cancer detection. It can also guide treatment selection, predict therapy responses, and monitor patients over time. Beyond cancer, cfRNA is useful in diagnosing and tracking diseases such as infectious and neurodegenerative diseases, showcasing its versatility in precision medicine.

### Why cfRNA and not cfDNA?

We prioritize the use of cell-free RNA (cfRNA) over cell-free DNA (cfDNA) for early cancer detection because of several compelling reasons.

Firstly, let's talk about cfDNA which is already in use for cancer detection, with some cfDNA-based diagnostic tests having already received FDA approval. cfDNA-based tests work by identifying specific mutations in circulating tumor DNA (ctDNA) which are DNA fragments released into the blood by tumor cells. However, this approach has notable limitations, particularly for early cancer detection. The main challenges include:

- **Mutation-specific Detection:** cfDNA-based tests look for known mutations, which can be rare and hard to detect, especially in patients who do not have these specific mutations.
- **Correlation with Tumor Size:** The amount of circulating tumor-derived cfDNA is directly related to tumor size. Smaller tumors release less cfDNA, resulting in lower sensitivity for early-stage detection.

Despite the success in later-stage cancer detection, these drawbacks make cfDNA less effective for identifying cancer at its earliest stages. This is where cfRNA offers significant advantages:

1. **Mutation Agnostic Approach:** Unlike cfDNA, cfRNA allows us to examine gene expression across all genes, not just known mutations. This comprehensive analysis provides a broader picture of tumor biology and can detect cancer irrespective of specific genetic mutations.

2. **Higher Abundance:** cfRNA is more abundant than cfDNA, enabling the detection of tumors even when the amount of cfDNA is insufficient for reliable testing. This higher sensitivity makes cfRNA a powerful tool for early diagnosis.
3. **Systemic Response Information:** cfRNA provides valuable insights not only from the tumor cells but also from the surrounding healthy cells. These healthy cells react to the presence of a tumor by changing their gene expression profiles, offering additional biomarkers for early detection.

By leveraging these unique advantages of cfRNA, Floomics enhances the accuracy and effectiveness of early cancer detection. Our commitment to cfRNA underscores our dedication to pioneering advanced diagnostic methods that can identify cancer at its earliest, most treatable stages.

## Overcoming the challenges of working with cfRNA

Despite the great potential of cfRNA as a diagnostic tool, there are several challenges that must be overcome before it can be implemented in the clinic. The scientific community currently lacks a standardized protocol for a complete cfRNA pipeline (all the way from plasma to next generation sequencing (NGS) data analysis) that consistently generates high quality data from liquid biopsy samples. Key challenges include the efficient purification of cfRNA from blood, preventing and removing DNA contamination, avoiding RNA degradation, implementing stringent quality control measures throughout the pipeline, and the development of bioinformatic pipelines optimised for working with cfRNA-derived data sets

Floomics has overcome these challenges by developing a cfRNA-seq pipeline that generates and analyses high quality cfRNA-seq data from liquid biopsy samples in a robust and reproducible manner. The Floomics cfRNA pipeline has great potential for the diagnosis of a wide range of diseases at an early stage, which will result in favourable outcomes for patients and the whole industry.

## Floomics work and services.

As cfRNA is the core area of exploration and research for Floomics, we have leveraged our learnings and expertise to support others. Beyond cfRNA we also offer additional services tailored to various genomic research needs, ranging from the nucleic acid extraction to the sequencing and data analysis. Our capabilities extend to DNA sequencing, where we provide whole genome and targeted sequencing options, enabling comprehensive genetic profiling. Furthermore, we facilitate transcriptomic research through tissue RNA-seq, providing a detailed analysis of gene expression. Our advanced bioinformatic analysis includes differential gene expression and machine learning techniques to uncover complex biological insights.

For further assistance and to explore how we can support your research endeavors, do not hesitate to contact us at [info@floomics.com](mailto:info@floomics.com).