



Millions of Droplets Matter



Unified Platform for Next-Gen Sequencing  
Target Enrichment and Digital PCR

# ThunderBolts™ NGS Target Enrichment



## Millions of Droplets Matter

The ThunderBolts™ System is a fast and efficient Next-Generation Sequencing (NGS) target enrichment system that partitions each sample into 16 million droplets. This process enhances coverage depth and uniformity, while reducing the complexities associated with multiplex PCR, such as the likelihood of competitive and non-specific amplification. ThunderBolts NGS libraries are generated using the RainDrop Source instrument following a simple workflow, and are compatible with all Illumina NGS platforms.

## Droplet PCR vs. Standard PCR

Partitioning the enrichment reaction into millions of droplets delivers a significantly higher percentage of target amplicons with greater sequence uniformity and depth of coverage compared to standard PCR enrichment (Figure 1). Variants localized to poor coverage regions associated with standard PCR enrichment methods may result in false negatives. Comparatively, these same regions can be correctly identified using the ThunderBolts System.

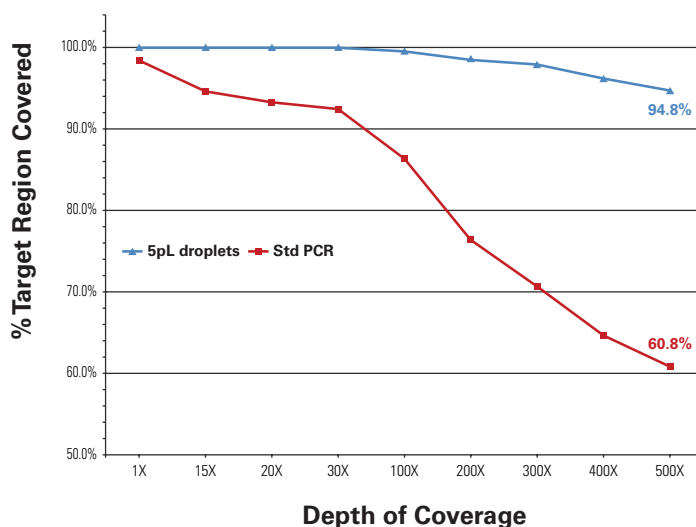
The unique molecular biology provides powerful solutions for detecting and screening clinically relevant mutations from 10 ng of starting DNA.

## Consortium Driven and Custom Panels

- **ThunderBolts™ Cancer Panel:** Interrogate mutations/hotspots in 50 oncogenes, tumor suppressors and drug resistance markers
- **ThunderBolts™ Myeloid Panel:** Profile mutations in 49 myeloid genes for research related to AML, MDS, MPN, and other myeloid disorders
- **ThunderBolts™ Open Source Consumables Pack:** Create custom gene content panels

## Key Advantages

- **Single target droplet PCR:** Reduce the likelihood of competitive and non-specific amplification bias
- **Coverage and uniformity:** Typical results include:
  - >98% coverage of amplicons at 500x (2500 avg reads/target)
  - >97% uniformity at 500x (0.2x of mean)
- **Highly sensitive:** Detect minor allele frequencies at <5%
- **High sample indexing:** 8-16x samples per MiSeq® run (v2/v3 sequencing kit, respectively)
- **Sample flexibility and input:** Sample input from as little as 10 ng of amplifiable gDNA isolated from FFPE, blood and bone marrow fluids / biopsy samples
- **Efficient time to result:** <4 hours hands-on time enabling sample-to-results in as little as 2 days



**Figure 1:** Partitioning the enrichment reaction in millions of droplets resulted in a high percentage of the target amplicons being successfully captured with greater sequence uniformity and depth of coverage compared to standard PCR enrichment.

# RainDrop™ Digital PCR



## Millions of Droplets Matter

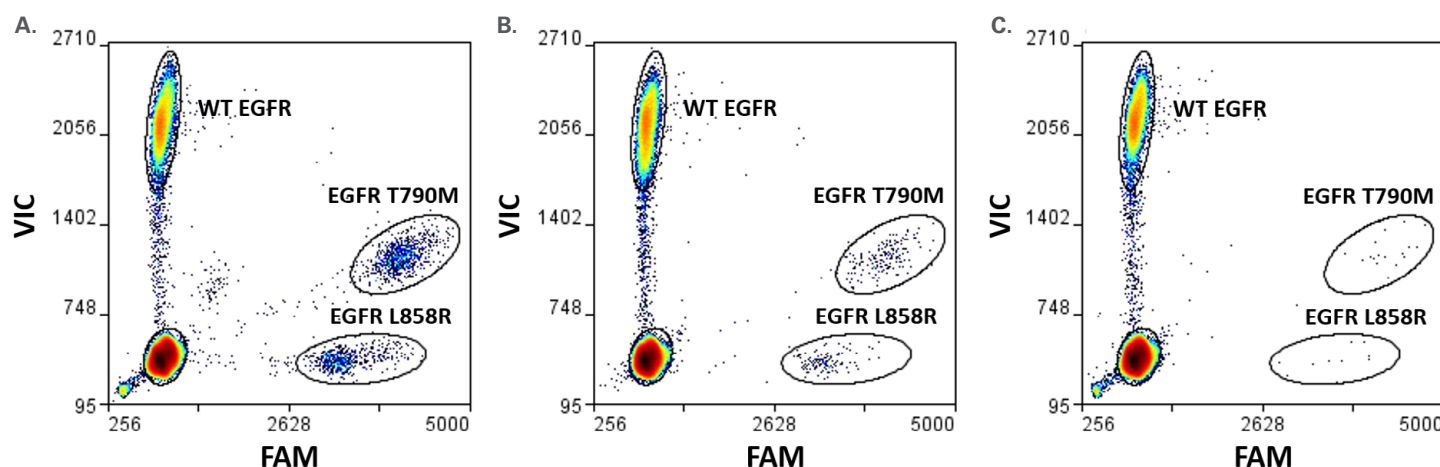
The RainDrop® Digital PCR System is the most sensitive and precise platform for nucleic acids detection and monitoring of cell-free and cell-based biomarkers for cancer, viruses, pathogens, or infectious diseases. The RainDrop System enables absolute quantification of targets by partitioning a standard qPCR reaction into millions of picoliter-sized droplets such that each droplet contains either 0 or 1 molecules of interest. Every droplet is measured for fluorescence to generate a negative or positive signal, providing a true digital result.

## Droplet PCR vs. Standard PCR

An important characteristic of PCR assay performance is specificity, which can be a challenge for mutation detection with qPCR. In qPCR, allele-specific probes can compete with one another for template DNA. This can lead to non-specific binding and false positive detection if one allele is in excess compared to the minor allele. This lack of qPCR specificity prevents accurate quantitative measurement of mutant-positive samples. By partitioning the reaction into droplets, the RainDrop Digital PCR System reduces probe competition for template and maximizes reliable quantification of the two alleles (Figure 2).

## Key Advantages

- **Sensitivity and precision:** Up to 6 log dynamic range provide a limit of detection down to 1 in 1 million
- **Absolute quantification:** Accurate and precise detection without a standard curve
- **Single molecule PCR:** Reduce the likelihood of competitive and non-specific amplification bias
- **True multiplex dPCR:** Millions of partitions and multi-color detection techniques enable robust multiplexing
- **Versatile platform:** Run both RainDrop dPCR and ThunderBolts NGS target enrichment applications
- **Flexible reaction volume:** Up to 21  $\mu$ L of starting sample material in a 50  $\mu$ L reaction



**Figure 2:** Two common mutations in lung cancer, EGFR p.L858R and p.T790M, detected simultaneously from 80 ng of cell-free DNA at 5% (A), 1% (B) and 0.1% (C). The multiplexing capability of the RainDrop System removes the need to divide valuable sample to detect multiple mutations to maximize the detection of rare variants.



# The Only Unified Platform

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Droplet generation and single molecule PCR is the hallmark of RainDance's dPCR and NGS target enrichment platforms. The ability to generate up to 10 million highly uniform 5 picoliter droplets enables superior genomic variant analytics, particularly:

## Sensitivity

- Utilization of up to 10 million droplets yields more than 6 logs of linear dynamic range
- Increased sample loading capability to quantify very low frequency events
- Ability to detect minor allele frequencies down to 0.0001% (1 in 1 million)

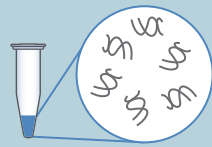
## Specificity

- Ensures that each individual droplet contains either 0 or 1 molecules of interest
- Eliminates drawbacks associated with bulk and co-occupancy multiplex PCR
- Absolute counting of both positive and empty droplets

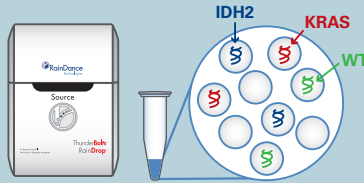
## Ordering Information

Product	Description	Part Number
RainDrop® System	RainDrop Digital PCR System: <ul style="list-style-type: none"><li>• Source instrument with dedicated control computer and instrument control software</li><li>• Sense instrument with dedicated control computer and instrument control software (Vic &amp; Fam Dye Compatible)</li><li>• On-site installation and training</li></ul>	20-04400
RainDrop® 96 Consumable Kit (96 Samples)	Source and Sense chips (12), PCR tube caps, carrier oil	20-04410
RainDrop® 96 Consumable Kit 5 Pack (96 Samples)	Source and Sense chips (60), PCR tube caps, carrier oil	20-04411
ThunderBolts™ System	Source instrument with computer and instrument control software	20-07700
ThunderBolts™ Cancer Panel Pack (24 Samples)	ThunderBolts Cancer Panel primers, chips (6), carrier oil, stabilizer solution, destabilizer solution	20-07217
ThunderBolts™ Cancer Panel Pack (48 Samples)	ThunderBolts Cancer Panel primers, chips (12), carrier oil, stabilizer solution, destabilizer solution	20-07215
ThunderBolts™ Myeloid Panel Pack (24 Samples)	ThunderBolts Myeloid Panel primers, chips (6), carrier oil, stabilizer solution, destabilizer solution	20-07218
ThunderBolts™ Myeloid Panel Pack (48 Samples)	ThunderBolts Myeloid Panel primers, chips (12), carrier oil, stabilizer solution, destabilizer solution	20-07216
ThunderBolts™ Myeloid Panel Starter Pack (48 Samples)	Source instrument with computer and instrument control software, on-site installation and training, ThunderBolts Myeloid Panel primers (48-samples), chips (12), carrier oil, stabilizer solution, destabilizer solution	20-07701
ThunderBolts™ OS Pack (96 Wells)	Source chips (12 x 8 wells), carrier oil, stabilizer solution, destabilizer solution	20-07206

# NGS Target Enrichment



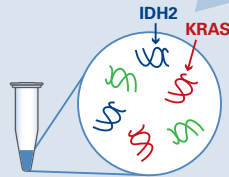
Prepare Blood,  
Soft Tissue, FFPE,  
cf/ctDNA Samples



Generate Millions of Droplets  
Enabling Single Molecule PCR



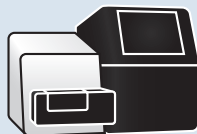
Thermal Cycle



Break Emulsion and  
Purify Sequences

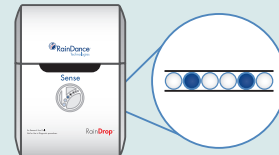


Thermal Cycle and  
Add Standard Illumina  
Adapter and Indexes

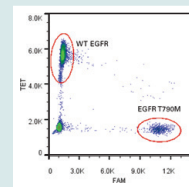


Produce NGS Ready Libraries

# Picoliter Digital PCR



Detect Fluorescent



Analyze Data with RDA II



#### About RainDance Technologies

RainDance Technologies is making complex genetics simple. The company's ultra-sensitive genomic tools enable research of novel non-invasive liquid biopsy applications that should result in more accurate, reliable, cost-effective, and early detection of cancer and other inherited and infectious diseases. Major research institutions and laboratories around the world rely on the performance of RainDance systems. Based outside Boston, Massachusetts, the company supports customers using RainDrop® Digital PCR, as well as the ThunderStorm® and ThunderBolts™ Next-Generation Sequencing Enrichment Systems through its international sales and service operations, as well as a global network of distributors and commercial service providers.

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