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Automating Solid Tumor Characterization from a Liquid Biopsy (LB)

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Introduction

The demand for precise, minimally invasive cancer diagnostics is driving rapid adoption of **liquid biopsy (LB)-based assays for solid tumors**. These assays offer **critical insights for early detection, treatment selection, and disease monitoring** through comprehensive genomic profiling conducted from a single blood draw. However, realizing this potential requires integrating advanced sequencing platforms with robust, scalable bioinformatics frameworks to ensure accuracy, reproducibility, and clinical readiness.

Objective

The aim of this project was to automate the bioinformatics workflow and validate the analytical sensitivity and specificity of a **combined DNA/RNA-based LB assay for detecting a broad spectrum of somatic alterations relevant to solid tumors**, including **SNVs, INDELs, CNVs, RNA gene fusions**, and quantification of **tumor mutation burden (TMB) and microsatellite instability (MSI)**, with added focus on scalability.

Challenges

- Develop bioinformatics workflows and coordinate assay development for successful product launch
- Create VAF summarization framework for positive controls (DNA mutations, RNA fusions, MSI, TMB) at known titrations
- Validate assay sensitivity/specificity and align results with prior sequencing platforms, and integrate bioinformatics across primary–secondary–tertiary analysis
- Build API-driven automation to replace manual scripts and streamline cross-system data flow
- Implement data/sample management system for live batch and sample tracking through the pipeline

Methods

We developed a bioinformatics workflow consisting of the following steps:

1) Sequencing performed on a benchtop short-read sequencing system, with FASTQ files as output

2) Alignment, variant detection, TMB, and MSI performed using a commercially available secondary analysis pipeline

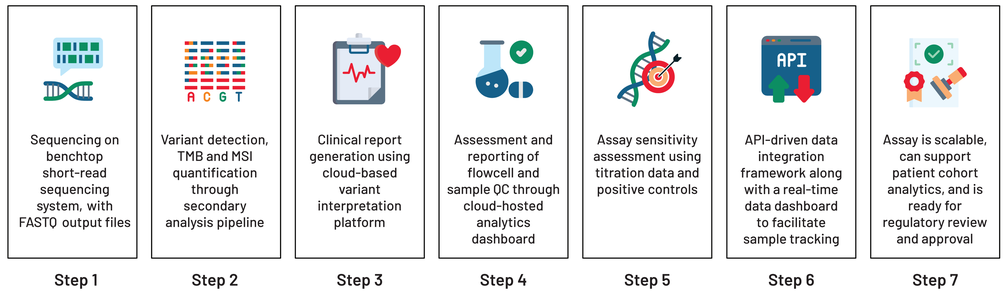
3) Clinical reports generated as PDFs via a secure, cloud-based variant interpretation platform

4) Flowcell and sample QC were assessed via scripts and reported using a cloud-hosted analytics dashboard.

5) Assay sensitivity was assessed using titration data and positive controls to confirm detection of low-frequency allele variants (≥5%). Computational pipelines for artifact detection and removal were also developed to improve bioinformatics QC and reliability.

6) An automated, API-driven data integration framework, along with a real-time data dashboard to facilitate sample tracking, was implemented to streamline data transfer across systems and replace manual processes, improving consistency and reducing processing time.

7) All assay components were documented to support CLIA and CAP-compliant validation. The resulting assay is equipped to support future scalability and inclusion of patient cohort analytics, and is ready for regulatory review and approval.



Achievements

- Complete implementation in just **3 months**
- The effective use of lambda functions by the Strand team **reduced overall costs by by 50%**
- Processed close to **17,000 samples**, with over **14,000 samples** processed for tertiary analysis
- Strand's **API-driven data integration framework** substantially reduced manual workload and time.

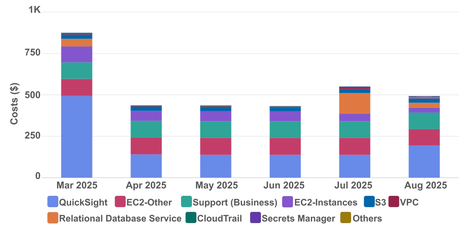


Figure 01: The incorporation of various AWS into the bioinformatics workflow resulted in substantial reductions in the cost of the LB assay.

Results and Conclusions

The assay reached clinical application readiness, supported by a scalable data infrastructure capable of incorporating patient cohort analytics. Moreover, the study demonstrated the feasibility of developing a scientifically rigorous and clinically efficient liquid biopsy assay for solid tumors on a new sequencing platform. It further underscored the importance of coupling technical assay development with robust computational frameworks to enable high-throughput precision oncology diagnostics. These findings also highlight the potential for extending this approach to additional cancer types and for supporting real-time genomic monitoring in clinical care.