

Reading Cancer's Clues in the Bloodstream

Study findings support repeat molecular testing to guide more personalized care for advanced prostate cancer.

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- Researchers including Sylvester Comprehensive Cancer Center's Dr. Chinmay Jani used serial liquid biopsies to track how metastatic prostate cancer evolves under treatment pressure.
- Androgen receptor alterations consistently emerged and were linked to poorer outcomes.
- The findings support repeat molecular testing to guide more personalized care in advanced prostate cancer.

Metastatic [prostate cancer](#) does not stand still. Under the pressure of treatment, it adapts, quietly and persistently, rewiring itself to survive. For clinicians, the challenge has always been timing — knowing when the disease has changed, and how, before it outruns the next line of therapy.

[A new study](#) led by first author Chinmay Jani, MD, of [Sylvester Comprehensive Cancer Center](#), part of the University of Miami Miller School of Medicine, suggests those answers may already be circulating in patients' blood.

Using serial liquid biopsies, the research team tracked how fragments of tumor DNA known as circulating tumor DNA, or ctDNA, shift over time in patients with metastatic castration-resistant prostate cancer (mCRPC). Their findings reveal a dynamic molecular story, one that unfolds treatment by treatment, mutation by mutation.

The research was conducted as a multi-center collaboration, bringing together investigators from Sylvester, the University of California San Diego (UCSD), Moores Cancer Center, the University of California San Francisco, Scripps Research Institute and Guardant Health, reflecting the scale and translational reach of the work. The project was developed and initiated at UCSD and conducted under mentorship from Rana McKay, MD, at the Moores Cancer Center at UCSD.

"This work highlights the power of real-time molecular monitoring to inform precision medicine in advanced prostate cancer," Dr. McKay said. "As we develop the next generation of therapies,

including novel, AR-targeted agents and rational combinations, understanding how tumors evolve under treatment pressure will be critical to delivering the right drug to the right patient at the right time.

A Molecular Weather Report

Traditionally, genomic testing in prostate cancer has relied on tumor tissue often collected years earlier, sometimes from sites that no longer reflect the dominant disease. Liquid biopsy offers a different lens. Like checking the weather instead of last season's forecast, ctDNA captures what the cancer is doing now.

In this real-world analysis, researchers examined paired ctDNA samples taken before and after treatment, a window that often marks disease progression. The study included more than 1,700 patients, drawing from one of the largest linked clinical-genomic databases available.

Across all treatment groups, tumors showed a clear pattern. Mutation burden increased after therapy, underscoring the selective pressure exerted by modern prostate cancer treatments.

"Cancer adapts under stress," Dr. Jani said. "What we're seeing in ctDNA is evolution happening in real time."

The Androgen Receptor: A Common Thread

Among the many genetic shifts observed, the androgen receptor (AR), a central driver of prostate cancer growth, stood out.

After treatment with androgen receptor pathway inhibitors (ARPIs), PARP inhibitors and even taxane chemotherapy, patients were significantly more likely to develop AR amplifications or AR mutations. This was particularly the case in regions that allow the receptor to remain active, despite therapy. These alterations act like a master switch, keeping cancer growth signals turned on even when treatments are designed to shut them down.

Importantly, the presence of AR alterations was common and consequential. Across all treatment classes, patients with AR-altered tumors experienced shorter overall survival, faster treatment discontinuation and an earlier need for subsequent therapy.

"AR alterations emerged as a consistent marker of more aggressive disease," Dr. Jani said. "They mattered regardless of which therapy patients received."

The study also revealed how resistance develops to newer, targeted therapies. Among patients treated with PARP inhibitors, some tumors acquired BRCA reversion mutations, restoring DNA repair pathways and blunting the effectiveness of treatment. Others accumulated changes in genes such as TP53, EGFR and PIK3CA, hallmarks of genomic instability and treatment resistance.

Taken together, the findings suggest that a single, genomic test at diagnosis is no longer sufficient for managing advanced prostate cancer. As tumors evolve, their vulnerabilities and escape routes change.

“Serial ctDNA testing gives us a moving picture, not a snapshot,” Dr. Jani said. “That has real implications for precision oncology.”

Implications for Precision Prostate Cancer Care

By capturing tumor evolution as it unfolds, liquid biopsy may help clinicians make more informed, timely decisions, adjusting treatment strategies before resistance becomes clinically evident.

The findings also support continued development of next-generation therapies, including androgen receptor degraders and novel combination approaches designed to overcome treatment resistance.

“This approach allows us to learn from the disease as it changes,” Dr. Jani said, “and, ultimately, to tailor care more precisely for each patient.”

While observational, the study provides a strong, biological rationale for integrating serial ctDNA testing into routine care for men with mCRPC. As precision oncology continues to advance, the ability to monitor tumor evolution through a simple blood draw may prove essential for choosing the right treatment at the right moment.

In metastatic prostate cancer, the story is always changing. Thanks to liquid biopsy, clinicians may finally be able to read what comes next.

“One of the most rewarding aspects of this work is that it was led by trainees across institutions. Chinmay at Miami and Eli Tran, a fourth-year medical student at UCSD, collaborated seamlessly to move this forward,” Dr. McKay said. “I’ve always believed that mentorship should have no boundaries, not by geography, not by institution. When you create that kind of environment, trainees thrive and exceptional science follows.”

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