CASE STUDY

Liquid Biopsy Provides an Accurate Snapshot of Cancer Following Surgery

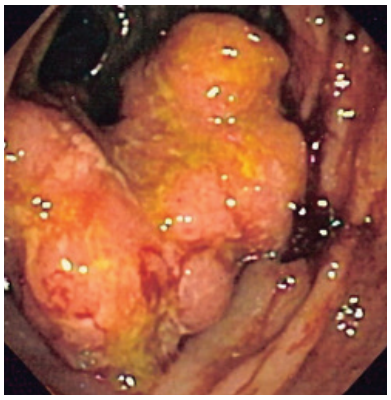
Quick Summary

- Mridula*, a 63- year-old cancer patient was referred to Strand Life Sciences for genetic analysis by prominent oncologist in Hyderabad.
- Genetic profile of the solid tumor was established using the StrandAdvantage 152-Gene Test.
- Concordance between genetic profile of the solid tumor and cell-free DNA obtained *vide* a liquid biopsy was established.
- Patient prognosis can be monitored as early as three months post-surgery using this minimally-invasive, fast and highly sensitive technique allowing timely therapeutic interventions.

Patient Profile

Mridula*, a 63-year-old owner of a curio shop had persistent digestive issues throughout 2015. She had episodes of diarrhea alternating with constipation. Sometimes, blood was also spotted in her stool, along with cramping pain in the stomach. She also experienced fatigue. Initially, she put down these minor irritating issues to her advancing years. However, when the pain and discharge of blood became all too frequent, she consulted a leading oncologist in Hyderabad.

Her doctor suspected colorectal carcinoma and prescribed investigations, including a colonoscopy and biopsy to ascertain this possible diagnosis. Colonoscopic imaging and histopathological analysis of the tumor biopsy confirmed his suspicions of colorectal carcinoma.



Representative Image: Colonoscopic Image of Colorectal Carcinoma
(Source: https://upload.wikimedia.org/wikipedia/commons/c/c8/Colorectal_cancer_endo_2.jpg)

Treatment Plan

Mridula's oncologist scheduled a surgery to remove the tumor mass from her colon. Along with the resection surgery, he also advised her to get a genetic analysis of the tumor tissue done.

He had two objectives in mind:

1. A mutation profile of the solid tumor would help to choose drugs for additional chemotherapy, possibly targeted drugs which have a higher success rate than generic chemotherapy.
2. Genetic profile of the tumor combined with a new test - liquid biopsy - to help monitor a patient's progress after surgery, as often as desired.

Accordingly, a biopsy sample of the solid tumor as well as a 10ml blood sample from Mridula were sent to Strand Life Sciences, Bangalore.

** Name changed to protect patient privacy*

Genetic Analysis

The StrandAdvantage 152-gene test was used to analyse the solid tumor biopsy of Mridula's colorectal cancer. This is a pan-cancer test designed to assess the most frequently mutated genes in most cancers. Additionally, the identification of gene mutations, using this test, is also helpful in choosing targeted therapies for cancer.

Mutations in two genes - *KRAS* and *TP53* - were identified from the solid tumor biopsy of Mridula's colorectal tumor.

Summary of Previous Tests

Sample Collection Date	Test	Gene	Mutation	Result	Details
Solid Tumor Result (DNA Source: FFPE)					**Supporting Reads**
20-Jul-2016	StrandAdvantage 152 Gene Cancer Test	*KRAS* *TP53*	G13D R273C	Detected Detected	20.98% 25.69%

A blood sample from the patient was also analysed for the presence of the same mutations in cell-free DNA. Normal as well as cancerous cells shed their DNA into the bloodstream when they die. This DNA - essentially a trail of breadcrumbs - can be harvested and checked for the presence of tumor-specific mutations (Bettegowda et al. 2014; Tie et al. 2016). Since all this can be done with a blood sample, without the need for a solid tumor biopsy, these tests are known as liquid biopsy tests for cancer.

In Mridula's case, a blood sample was analyzed to check whether the same mutations as in the solid tumor biopsy could be identified in her blood or not.

Sample Collection Date	Test	Gene	Mutation	Result	Copies/ ml plasma
Previous Liquid Biopsy Results (DNA Source: cfDNA from blood)					**Copies/ml plasma**
20-Jul-2016	Strand Liquid Biopsy	*KRAS* *TP53*	G13D R273C	Detected Detected	1200 2900

Tumor-associated mutations, namely $KRAS^{G13D}$ and $TP53^{R273C}$, were also identified in cell-free DNA extracted from her blood sample. This agreement between the solid and liquid biopsies created a window of opportunity for monitoring the effects of adjuvant therapy.

Following surgery, chemotherapy was prescribed to Mridula to tackle residual cancer.

In the follow-up period, another liquid biopsy sample was obtained in October 2016 to understand whether the therapy was effective or not.

Sample Collection Date	Test	Gene	Mutation	Result	Copies/ ml plasma
20-Oct-2016	Strand Liquid Biopsy	*KRAS*	G13D	Detected	2800

The results showed that the genetic mutations characteristic of Mridula's colorectal cancer were still present in cell-free DNA in high quantities. This can be attributed to the fact that the cancer might have spread to other locations in the body and is growing actively. Her therapy is under revision and her oncologists are considering other options for her.
Liquid biopsy tests for additional follow-up have been advised to Mridula.

Conclusions

- Genetic profiling of a somatic cancer led to the identification of two characteristic genetic mutations - *KRAS*^{G13D} and *TP53*^{R273C}.
- Concordance between liquid and solid biopsies was established during the tumor resection surgery.
- A follow-up liquid biopsy sample obtained 3 months post-surgery has allowed oncologists to understand that residual disease is persistent in the patient, perhaps at other metastatic sites.
- Liquid biopsy provided a quick snapshot of the tumor soon after initiation of a therapeutic regimen. This advantage is not conferred by traditional assessment techniques like PET/CT scans.

Strand Liquid Biopsy Tests For Tumor Monitoring

Strand Life Sciences offers a combination of their Strand Advantage 48-Gene and 152-Gene Cancer Tests and liquid biopsy-based tests as personalized cancer monitoring tests. Solid tumor biopsies as well as liquid biopsies (blood samples) from cancer patients are analyzed to identify a set of mutations present in cancer at the time of diagnosis / initiation of treatment.

These unique, personalized genetic profiles of cancer can then be used in a patient-specific manner to track the progression of cancer in every patient, at the desired time intervals.

Identification of genetic mutations from liquid biopsy samples is carried out at a sensitivity of 1:1000 (ten-fold higher than the industry average).

References

Bettegowda, C. et al., 2014. Detection of circulating tumor DNA in early- and late-stage human malignancies. Science translational medicine, 6(224), p.224ra24. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24553385 [Accessed January 7, 2017].

Tie, J. et al., 2016. Circulating tumor DNA analysis detects minimal residual disease and predicts recurrence in patients with stage II colon cancer. Science Translational Medicine, 8(346), p.346ra92-346ra92. Available at: http://www.ncbi.nlm.nih.gov/pubmed/27384348 [Accessed February 16, 2017].

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