ACTREC's CRISPR-based test detects a rare blood cancer

The new test developed using CRISPR technology can quickly and accurately diagnose acute promyelocytic leukemia (APL), a rare and aggressive form of leukemia, under three hours and costs less than existing tests

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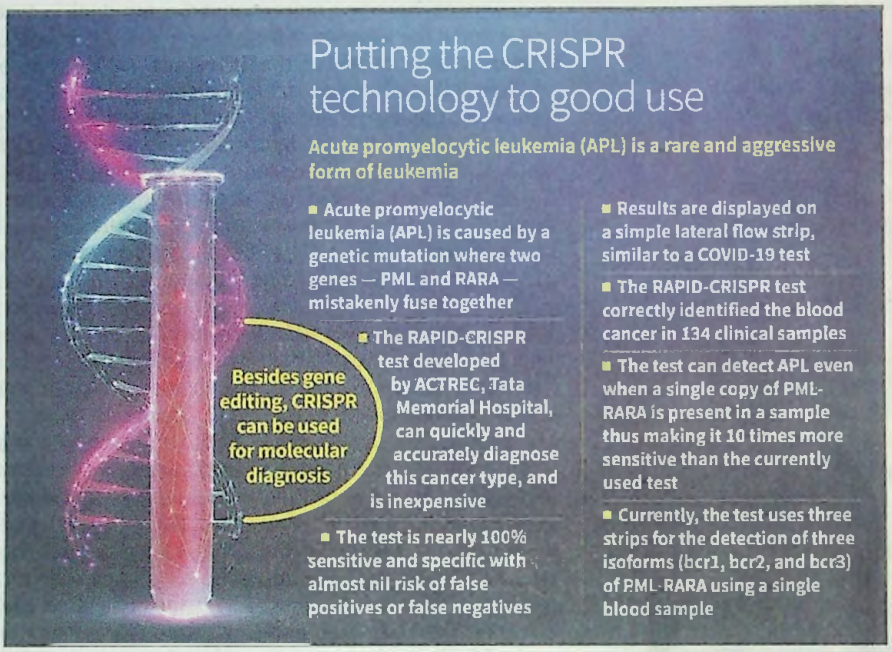

Acute promyelocytic leukemia (APL) is a rare and aggressive form of leukemia, a cancer that affects blood cells. It is caused by a genetic mutation where two genes, PML and RARA, mistakenly fuse together. The fusion of the two genes leads to the production of fewer white blood cells and platelets, which reduces the body's ability to fight infections and control bleeding.

What sets this cancer apart from other types of cancer is that it can cause severe internal bleeding in organs such as the lungs and brain, which can result in death within a few days if not treated immediately. But the brighter side is that acute promyelocytic leukemia is highly curable if diagnosed and treated early. Current treatments can cure most patients.

Acute promyelocytic leukemia (APL) is a subtype of acute myeloid leukemia (AML) and accounts for about 10-15% of newly diagnosed AML cases. At Tata Memorial Hospital, we see nearly 50-60 new APL cases annually. The median age at diagnosis is around 34 years, with a male: female ratio of 1.5:1.

The problem, however, is that the tests that are currently available to diagnose this rare type of blood cancer take a long time, which delays life-saving treatment. Moreover, these tests require expensive machines and trained specialists, making them difficult to use in smaller hospitals, rural areas, and developing countries.

Using the CRISPR technology, our team at ACTREC, the cancer research division of Tata Memorial Hospital, Mumbai, has developed a new test called RAPID-CRISPR, which can quickly and accurately diagnose this cancer type. Given the limitations of the currently available tests, the test developed at ACTREC can deliver results in under three hours, costs less than existing tests, and does not require complex laboratory equipment. While the name RAPID-CRISPR reflects the speed of diagnosis, RAPID stands for Redefined Apl IDentification. The study, which was supported by the Department of Atomic Energy, has been published in the journal *Blood Advances*.

The CRISPR-based technology has two applications – besides the well-known role of gene editing, CRISPR can also be used for molecular diagnosis. In this case, the RAPID-CRISPR test is added to a patient's peripheral blood sample in a test tube. The test looks for the cancer-causing PML-RARA gene mutation, which is the cause of this rare blood cancer, in the sample and automatically cuts it. The process of detection of the mutation and cutting it triggers a signal that is detected using a simple, easy-to-read strip similar to a home pregnancy test.

Peripheral blood is sufficient for the diagnosis in 80% of cases. In 20% of cases where the white blood cell count is very low (less than 1,000 cells per microlitre; normal range is 4,000-10,000 cells per microlitre), bone marrow aspiration is an ideal sample for diagnosis.

Since the test is designed to detect the mutation, it has nearly 100% sensitivity and specificity with almost nil risk of false positives or false negatives. Unlike the currently available test that requires specialised equipment to extract and amplify the genetic material, the RAPID-CRISPR test uses a simple process that works directly on patient samples. Hence, the test does not require extensive laboratory setups, expensive machines, or highly trained personnel, thereby making the test affordable and accessible to people. The results are displayed on a simple lateral flow strip (similar to a COVID-19 test), making it easy for doctors to read and act quickly.

Our team evaluated the RAPID-CRISPR test on 134 clinical samples, and in every case, the test correctly identified the blood cancer without any mistakes. Impressively, it detected even when a single copy of PML-RARA was present in a sample, thus making the RAPID-CRISPR test 10 times more sensitive than the currently used gold-standard test (RQ-PCR).

Many hospitals and clinics in developing countries lack the resources to perform complex genetic tests, leading to delays in diagnosis and even deaths where the patients could be saved if the cancer were detected at an early stage. The RAPID-CRISPR test can bridge this gap and ensure that patients receive the right treatment as soon as possible.

Currently, the test uses three strips for the detection of three isoforms (bcr1, bcr2, and bcr3) of PML-RARA using a single blood sample. Our team is working to optimise the assay for a single-tube reaction that can detect isoforms using a single strip.

Since the test does not rely on complex technology, we hope that with further development, this test can become a standard tool in hospitals. The team also intends to refine the technology to make it even easier to use, potentially allowing at-home testing in the future.

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