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Molecular diagnostics for early diagnosis of diseases- the way forward

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Molecular diagnostics are a set of tools and techniques to analyse biological markers in the genome or sometimes even in the proteome, which would indicate the presence of diseases including various types of cancers, infections such as TB, Pneumonia, UTIs, prenatal testing for diseases such as Thalassemia or Down Syndrome. Molecular diagnostics at the point of care presents a significant opportunity, not just in the clinical diagnostics industry, but also in allied industries such as livestock- poultry, fish and seafoods as well as in food testing.



We are living in the age of genomics- where DNA is the new currency. The cost of sequencing the entire human DNA has dropped from $10,000 dollars in 2011 to less than $1000 today, thanks to advanced ‘Next Generation Sequencing’ (NGS) technologies. As costs have reduced, access to sequencing has improved. COVID-19 was a shot in the arm as many new laboratories installed NGS machines. Lower costs, higher throughput and easier access has meant faster genomic data generation and in large quantities. Novel biomarkers have been identified for various types of cancers, infectious diseases and this has driven the growth of the molecular diagnostics industry.

Molecular diagnostics are a set of tools and techniques to analyse biological markers in the genome or sometimes even in the proteome, which would indicate the presence of diseases including various types of cancers, infections such as tuberculosis (TB), Pneumonia, urinary tract infections (UTI)s, prenatal testing for diseases such as Thalassemia or Down Syndrome. Apart from human diseases, molecular diagnostics also has applications in plant and livestock disease diagnosis. One of the major advantages of molecular diagnostics solutions is the ability to detect the biomarkers at very low concentrations, thereby enabling early diagnosis. These tests are cost effective and can be performed at the point of care. The detection for the tests is done using DNA sequencing, fluorescent probes, microarrays or Fluorescence In Situ Hybridization (FISH).

Rising investments

Although molecular diagnostics tools have been around for more than 30 years, investments into startups in this space have seen a rise since 2013, driven by the advancements in sequencing technologies and gene editing tools such as CRISPR, as well as new isothermal molecular diagnostic technologies. Investments in molecular diagnostics increased from around $1 billion in 2013 to more than $4 billion in 2019. However, COVID-19 gave a major push towards investments into this sector, driven by a major requirement for early detection of the infection. RT-PCR and other isothermal tests such as Loop Mediated Isothermal Amplification (LAMP) became a standard for diagnosis during 2020-21. Investments rose to more than $6 billion in 2020-21, a rise of 1.5 times from the previous year. Molecular diagnostics market saw a growth of more than 200 per cent YoY in 2019-20 and was expected to be worth more than $15 billion in 2023.

Some of the largest companies in India in this sector include Medgenome which has raised a total of $185 million, MolBio Diagnostics ($117.5 million), Strand Life Sciences ($13 million) which was acquired by Reliance Industries Limited’s subsidiary Reliance Strategic Business Ventures Ltd for Rs 393 crore or close to $50 million, Mylab Discovery Solutions and Tata MD who developed kits for COVID-19 detection along with molecular diagnostics solutions for TB detection. New generation companies such as D-Nome are using advances in synthetic biology and protein engineering to develop room temperature PCR solutions for point of care diagnostics.

From RT-PCR to isothermal solutions - the path towards point of care (POC) molecular diagnostics

The PCR technique was invented in 1985 by Kary B. Mullis. It enables scientists and technicians to make many copies of a scarce sample of DNA. Using “primers”, which map to a desired gene or DNA fragment of interest, the PCR technique can be used to amplify and hence detect the presence of the target DNA. Further, PCR technique is quantitative: it can be used to determine the amount of target DNA that is present in a sample.

Diagnostic tests commonly utilise PCR or RT-PCR techniques. Here, “RT” stands for reverse transcription, which means that the technique can also be used to detect RNA. Once the target DNA or RNA of a pathogen is isolated, a PCR test for it can be formulated. PCR-based tests also have high sensitivity and specificity, which translates to low false negative and low false positive rates. These characteristics have made it the gold standard for various diagnostic tests. Most famously in recent years, the PCR technique was used to construct the gold-standard RT-PCR tests for COVID-19. Further, the quantitative nature of the PCR technique means that they can be used for applications beyond yes/no diagnostic tests.

However, diagnostic tests that use PCR also have a few drawbacks. Firstly, they require expensive equipment, skilled technicians and multiple reagents for the different steps involved. They also require many cycles alternating between high and low temperatures to amplify the target DNA. These drawbacks have resulted in PCR tests having long turn-around times and being performed only in well-equipped central labs. Thus, alternatives to PCR tests are needed which can be performed at the point of care (POC) itself.

Several alternatives to PCR-based diagnostics have been developed in research laboratories around the world with the aim of overcoming some of the drawbacks that PCR tests face. The core at each of these techniques is the ability to amplify nucleic acids: DNA and RNA. Some of the techniques developed are loop-mediated isothermal amplification (LAMP), nucleic acid sequence-based amplification (NASBA), strand-displacement amplification (SDA), rolling circle amplification (RCA) and recombinase polymerase amplification (RPA). Their major advantage over PCR is that they take place at constant temperature, i.e., they are isothermal processes. This means that they are good candidates for accessible tests that can be done cost-effectively and at the POC.

However, they face their own challenges in reaching the simultaneously high sensitivity and specificity of PCR tests, which requires clever research and engineering to achieve. Further, separate primer design is required to develop these isothermal tests for different diseases and designing primers for these alternatives is generally a more difficult task than doing it for a PCR test.

However, molecular diagnostics at the point of care presents a significant opportunity, not just in the clinical diagnostics industry, but also in allied industries such as livestock- poultry, fish and seafoods as well as in food testing. Isothermal molecular diagnostics solutions which can be done at room temperatures could create opportunities in the POC diagnostics market.

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