Applications and Successes of RNA-based Testing

In the previous article, we gave an overview of the history of RNA and discussed some of the technologies used to sequence and quantify RNA in different contexts. Now, we turn our attention to specific examples of applications and successes within the RNA testing field.

Viral Diagnostics

Scientists have developed several generations of viral diagnostics for infections such as HIV and hepatitis. Many of these tests look for the presence of viral antigens or antibodies. However, the earliest RNA tools, which have been in existence for over a decade, provide faster and more accurate results than similarly targeted protein-based tests. One example is Quest Diagnostics. Based on data published in 2003, Quest Diagnostics offers an RNA-based test that can indicate the presence of HIV about one week after exposure.

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With hepatitis, clinicians can use RNA as a secondary method of diagnosis and treatment. Antibodies will persist even if the infection is not active. Therefore, clinicians can turn to RNA screening after a positive antibody test to determine if the patient has active disease.

On a more acute level, RNA technologies have been vital for keeping up with the Zika outbreak that has dominated headlines over the past year. Quest Diagnostics received an emergency FDA authorization in spring 2016 for its real-time RT-PCR assay, which can detect positive cases of Zika infection in as little as a week after onset of symptoms.

Cancer Diagnostics

Because analysis of RNA can provide a quantitative readout on the expression levels of genes known to be involved in a given condition, it can be a valuable tool for detecting disease states. Behind viral detection, cancer is arguably one of the most well-established use cases for RNA-based diagnostic testing, although the use of RNA biomarkers in cancer diagnosis and treatment remains a developing field. Analysis of RNA allows clinicians to look beyond the raw sequence and find splice variants, novel transcripts, and then quantify levels of these RNAs in real-time that, in turn, may be used to craft associations with known disease processes.

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An interesting discovery in cancer diagnosis involves analysis of RNA found on platelets. When tumor cells die, their genetic material can make its way into the bloodstream. Living cancer cells may also release some of this material via microvesicles or other means. Platelets, typically thought of as being involved in coagulation, pick up some of the material released or transferred from tumor cells. This behavior, in turn, alters the RNA profile of those platelets. When the platelets are then isolated and analyzed, the tumor-specific RNA sequences can be quantified.

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Last year, a group from Harvard was able to use platelet RNA profiles isolated from tiny quantities of blood to identify cancer types at 90% accuracy. Additionally, the investigators were able to determine the origin of the primary tumor in over 2/3 of cases, which is dramatically better than other blood-based cancer tests (DNA and tumor cell assays). While this particular paper describes an academic investigation that has not been translated into clinical practice, it shows the utility of RNA profiling in diverse cancers.

Research continues to develop additional cancer diagnostics that provide clinically useful information. In 2013, an academic research group described RNA profiling of lung cancer samples that had been preserved and embedded for histological analysis. Now, companies are creating RNA-diagnostics that look at cancer-associated genes in preserved solid tumors. This innovation represents a positive advancement for multiple reasons. First, there is an inherently subjective component to classifying and grading tumor samples by eye through histology and pathology. RNA, on the other hand, is quantitative. Once the algorithms have been validated and the assay protocol standardized, an RNA-based test provides a quantitative readout that can be standardized across clinical practices and labs. Second, the level of detail provided by RNA is a critical component of the recent push towards personalized medicine. RNA from both liquid and solid biopsies can provide information on cellular phenotype, helping clinicians create highly personalized drug regimens for each patient that maximize treatment efficacy. Related to this last point, RNA technologies can be used to monitor treatment efficacy. A company called Rna Diagnostics, featured in several publications, is working to uncover the underlying mechanisms linking chemotherapy efficacy and RNA disruption. Rna Diagnostics looks at the "disruption" of RNA from tumor biopsies to gain real-time information on how effective chemotherapy treats cancer.

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Other Uses

RNA diagnostics are emerging as a stand-alone segment in the diagnostics field. This rise in prominence is the result of recent technological advances and invention of new bioinformatics tools capable of analyzing the data. The relatively long history of viral RNA tests provides a strong foundation for ongoing work to create new tests for indications spanning multiple branches of medicine.

For example, CardioDx provides RNA-based testing for obstructive coronary artery disease (CAD). As the company explains, the Corus CAD test mirrors other RNA diagnostics in that it is non-invasive and has a rapid turnaround time. The test looks at RNA levels (i.e., gene expression) for genes associated with CAD, then combines that data with non-genetic information to determine the likelihood that a symptomatic patient has CAD.

This focus on gene expression by CardioDx parallels the approach that underlies IQuity's technology. We will look at this in more detail in the next white paper, but it is important to note that IQuity is focusing on an untapped area of RNA diagnostics in autoimmunity. Conventional testing in this field often looks at protein biomarkers or indirect measurements of disease activity to facilitate a diagnosis, but the accuracy of these strategies varies widely due to the inherent nature of the reagents used. Thus, there is a significant opening for bringing the accuracy, speed and specificity of RNA sequencing and gene expression analysis to the autoimmune field.

For any questions regarding the IQuity IQIsolate™ tests, please contact us at info@iquity.com or

iquity.com