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PERSPECTIVE

Aptamers in the pursuit of COVID-19 management

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As COVID-19, caused by SARS-CoV-2, continues to affect millions of people worldwide, the race to find new tools for diagnostics, treatment, and prevention has become more pertinent than ever to quell its global impact. To date, (June 26, 2020) there have been over 9.6 million cases of COVID-19 across the globe, with nearly 486,000 deaths. Thus, a framework of testing, treatments, and most importantly vaccines is being developed to create a comprehensive management protocol.

While vaccination is the ultimate goal as it would prevent another pandemic, testing and treatment procedures for those currently affected remain the more pressing issue. To address this need, companies worldwide have been coming out with PCR and ELISA based commercial diagnostic kits for the rapid determination of SARS-CoV-2 infection status. Yet, despite these tried and true methods having held their own as reliable analytical tools since the late 20th century, aptamers may be useful in this pandemic as they can be used both to test for and treat COVID-19, especially as traditional methods have proved to be limited by resource and equipment availability. Indeed several members of the aptamer community around the globe are working hard to select new aptamers or develop robust aptamer-based applications in the context of SARS-CoV-2 detection.

In the past, aptamers have been selected against proteins from other members of the coronavirus family, such as SARS-CoV (Ahn et al, 2009), leading to the development of ELONAs (enzyme linked oligonucleotide assays). ELONAs, while similar to ELISAs in principle and application, provide certain advantages including consistent performance, higher sensitivity and specificity, a longer shelf life, lower cost, and smaller size (Aptamer Group, 2020). Thus, aptamers are an attractive alternative to the traditional antibody, particularly because SARS-CoV-2 has several unique proteins that could be used as targets for sensitive detection. Furthermore, because oligonucleotides are more stable and can be produced reproducibly in larger quantities than antibodies, they also offer more leeway in terms of the actual test platform. For example, the Berezovski lab from the University of Ottawa is currently developing a colour changing paper-based assay that would use aptamers to detect both RNA and proteins from SARS-CoV-2 for a comprehensive diagnosis using biological fluid samples (Tunney, 2020). In a more classical sense, other companies such as the Aptamer Group and Pinpoint Science have been leveraging aptamers to create point-of-use ELONA-based diagnostic tools (Aptamer Group, 2020; Pinpoint Science, 2020) which would allow more people access to these definitive tests as they would no longer be reliant on labs for proper handling and storage.

Outside of diagnostics, methods are also needed for surface testing in heavily exposed environments such as hospitals, workplaces, and even households once quarantine measures are lifted. However, as the capacity of SARS-CoV-2 testing is already limited by the availability of supplies, novel methods that do not rely on the same scant diagnostic resources should be explored. In response to this need, the DeRosa lab from Carleton University has a “wipe-test” in the works, which would allow people to detect SARS-CoV-2 using a cloth-based aptamer detection system (Carleton Office for Research Initiatives and Services, 2020); one that would require minimal training and equipment to use, making it much more widely accessible.

The beauty of using aptamers is their applicability to treatment as well as testing. For example, the Bates lab from the University of Louisville has produced an aptamer that, in proof-of-concept experiments, has shown to be effective against SARS-CoV-2 at relatively low doses (Thomas, 2020). This aptamer binds to the nuclear protein nucleolin, shutting down viral replication. Similarly, aptamers have also

been developed by multiple groups for the SARS-CoV-2 spike protein (Liebich, 2020; Rangan et al, 2020) as well as the N-protein (Chen et al, 2020), both of which are involved in the replication cycle of the virus. In all cases, these aptamers could be used simultaneously as both a diagnostic tool and a treatment method. For example, the nucleolin aptamer and the spike protein aptamer could both be tagged with fluorochromes, allowing them to visualize the location of viral attacks within the body while providing treatment. The N-protein aptamer on the other hand was originally developed as a detection method based on previous work done with aptamers selected for the SARS-CoV N-protein. However, it appears that because the N-protein is critical for viral genome assembly, it may also interfere with protein function once bound, making it a serendipitous dual diagnostic and treatment (Chen et al, 2020).

In terms of testing, the greatest strength of aptamers lies in the fact that they are fairly stable and can be used without needing a sophisticated lab set up. As such, they are a much more accessible route, not only for the general public, but also for developing nations where health care infrastructures remain underdeveloped. COVID-19 is a non-discriminatory disease that has affected people worldwide. Thus, the scientific community should expand their considerations when developing testing platforms to ensure they are accessible on a global scale. From a treatment point of view, aptamers provide the unique ability to create a tool that can both detect SARS-CoV-2 and treat COVID-19, allowing for the production of a single biologic with a two-fold application, again leading to increased cost effectiveness and therefore accessibility.

As time passes, the pandemic continues to slow with fewer and fewer cases cropping up. However, those that are affected must be helped if COVID-19 is to be relegated to a relic of the past. While the traditional methods for diagnostics and treatment development have proved to be very successful, the recent boon of aptamer applications make it an important avenue to pursue. With the flexibility that oligonucleotides provide, the aptamer community has good reason to remain hopeful that they can make a difference in the battle against COVID-19.

COMPETING INTERESTS

None declared.

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