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## From the Publisher's Desk

### Welcome to Biotechnology Kiosk!

We wish our readers a very happy New Year 2021! The January'2021 issue of BK is now online for our readers with the regular features. This issue contains a perspective and an opinion piece on cutting edge topics such as rapid point of care diagnostics of COVID-19 and non-invasive next generation biomarkers for early identification and therapeutic intervention in Alzheimer's disease. In addition, this issue contains the regular editor's picks on some exciting developments in brain health in COVID-19 infected patients and salt-tolerant bacteria for sludge.

We hope our readers will enjoy reading these news and views on the current cutting-edge topics that include latest research breakthroughs in different areas of medicine and biotechnology.

We look forward to receiving your feedback. We do hope that you will enjoy reading this issue of Biotechnology Kiosk. Please do write to us with your comments. Your suggestions are always appreciated.  
**Dr. Megha Agrawal & Dr. Shyamasri Biswas.**

*Editors-in-Chief, Biotechnology Kiosk*

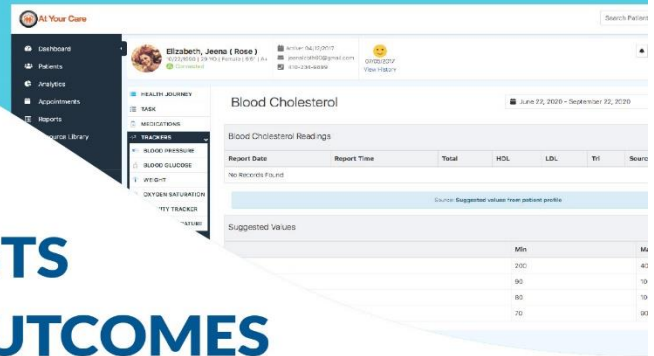


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## **On-Chip PCR Based Plasmonic Microfluidic Platform: Ultrafast Point-of-Care Diagnostics of SARS-CoV-2**

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### **Abstract**

It is critically important to have rapid screening and identification of contagious viral diseases such as the current COVID-19 pandemic that is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Rapid and accurate diagnostic is essential for preventing worldwide spread of virus and ensuring in-time care for patients during the fast spread of pandemic diseases. Nanobiotechnology enabled tools have allowed to develop advanced polymerase chain reaction (PCR) based diagnostics of contagious viral diseases. To this end, microfluidic on-chip PCR platforms have shown huge promise for highly efficient, rapid and small-volume bioassay for point-of-care (POC) diagnostic applications in mitigating the challenges of SARS-CoV-2. Here, we discuss latest advances in ultrafast, real-time, and on-chip nanoplasmonic PCR for rapid and quantitative molecular diagnostics at POC level.

*Keywords: PCR, Plasmonics, SARS-CoV-2, Molecular Diagnostics, Pandemic*

DOI: <https://doi.org/10.37756/bk.21.3.1.1>

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## Introduction

It is widely recognized that rapid diagnosis of COVID-19 and other highly contagious viral diseases is essential to ensure timely medical care, quarantining and contact tracing. Reverse transcription-polymerase chain reaction (RT-PCR) is considered the gold standard worldwide for diagnosis during the COVID-19 pandemic. RT-PCR normally uses enzymes to reverse transcribe tiny amounts of viral RNA to DNA, which is then used to amplify the DNA. This allows detection by a fluorescent probe. RT-PCR is proven to be the most sensitive and reliable diagnostic method. However, bulky and expensive machines are required to complete the PCR portion of the test. Further, the conventional real-time PCR thermal cyclers are based on the Peltier effect that have a long turnaround time of PCR for more than 1 hour. The reason of the lengthy time to complete the PCR portion of the test is due to the fact that it requires 30-40 cycles of heating and cooling in special machines. Moreover, the sample preparation along with false negative results can extend the diagnostic waiting time in multiple PCR tests. Additionally, samples are usually sent out to a laboratory that causes further delays as the patients are required to wait a day or two to receive their diagnosis results. All these procedural and logistic difficulties suggest that time-consuming, bulky, and expensive equipment and analytical steps for real-time PCR based diagnostics have serious limitations that prevent for immediate infection diagnostics at point-of-care (POC) level [1-5].

Researchers have been actively engaged in the development of PCR cyclers

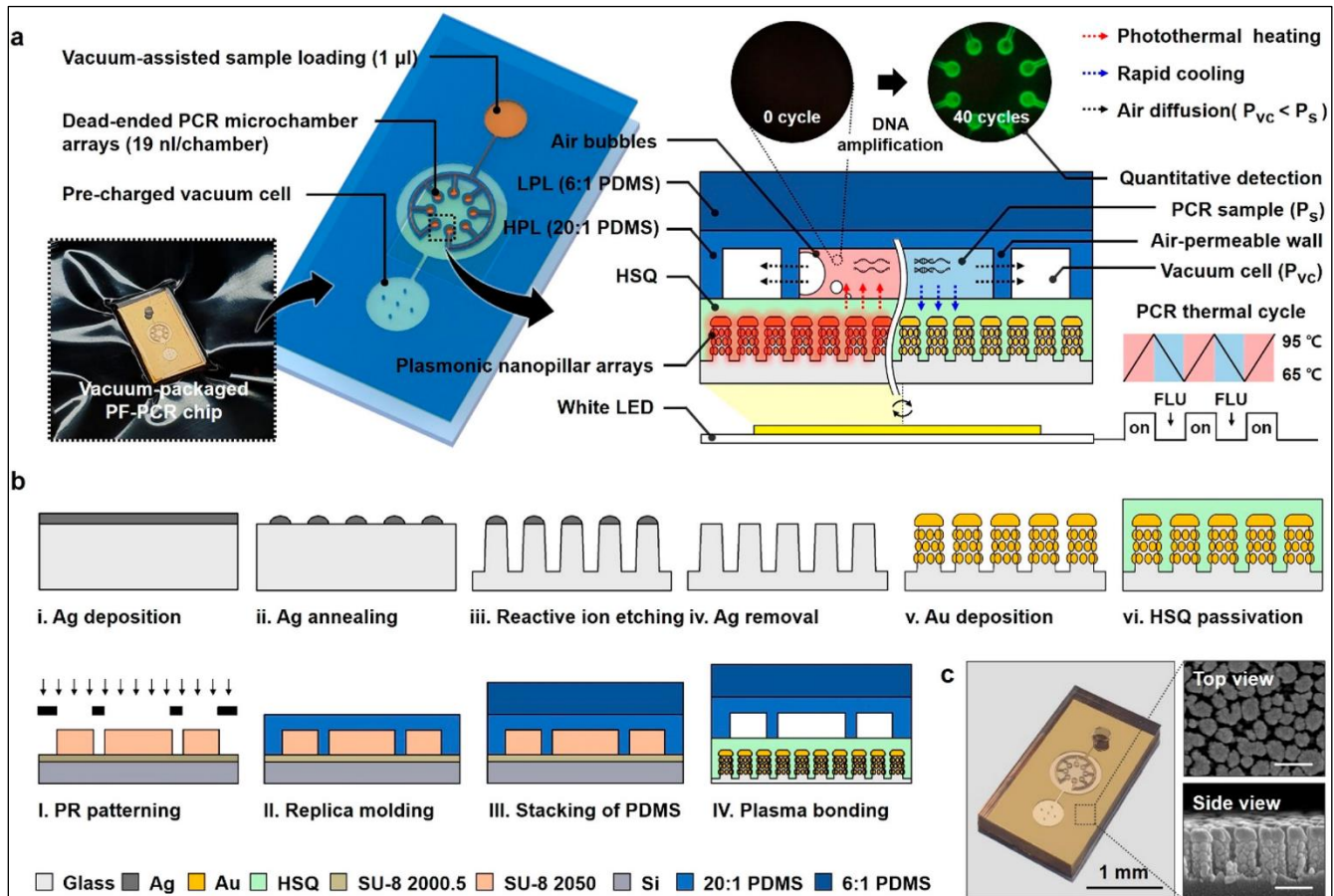
for POC diagnostics that have been demonstrated for accurate and fast thermal cycling to increase heating ramp. To this end, photonic PCR utilizing plasmonic materials has been applied that has shown potentials for substantially reducing the amplification time as a result of the ultrafast and noncontact light-to-heat conversion. In plasmonic principles-based designs, gold nanospheres, nanorods, bipyramids, or nanoshell dispersed in PCR solution have been employed that have been shown to accelerate photothermal heating under laser irradiation. In these systems, light absorption of gold nanoparticles (AuNPs) excites hot electrons that result in strong non-radiative relaxation within tens of femtoseconds. This subsequently produces uniform and volumetric heat of sample solution. Current research has focused on addressing some technical challenges such as temperature gradient, PCR efficiency, and real-time monitoring that are needed to be overcome for rapid and quantitative molecular diagnostics [6-8].

On-chip PCRs are considered one of the best technology options for fast and reliable POC diagnostics [9]. It is believed that such a technology can be leveraged for the miniaturization and integration of POC testing systems. Especially, low thermal capacities are possible to obtain due to small sample volume and high surface-to-volume ratio, which results in fast heating/cooling rates and short reaction time [9]. The advantage is that the technology utilizes spatial and temporal thermal cycling that allows continuous or droplet sample fluid flows along a microfluidic channel with



spatially discrete temperature regions for PCR cycling by using different resistive microheaters. Further, a small volume of sample solution in microchambers can perform rapid PCR using time-variant thermal cycling of Peltier heater, thin film heater, and

infrared laser heater. To make higher-performance on-chip PCRs for practical POC applications, current considerations are to overcome technical challenges such as external pumping or microbubble formation [9].



**Figure 1:** Schematic depiction of a vacuum-enabled nanoplasmonic on-chip platform for polymerase chain reaction. (a) Working principle showing a vacuum-charged plasmofluidic PCR (PF-PCR) chip that allows spontaneous sample loading, ultrafast photothermal heating, microbubble-free reaction, and real-time cyclic fluorescence quantification. (b) Nanofabrication steps of the PF-PCR chip are shown that include plasmonic nanopillar arrays (PNA) that are fabricated by using thermal dewetting, reactive ion etching, and Au thin film deposition on a wafer scale. Subsequently, the HSQ-coated plasmonic nanopillar arrays. (c) A photograph of PF-PCR chip (14 x 26 x 4 mm) with cross-sectional SEM images of PNA [Source: ACS Nano (2021)].

### Nanoplasmonic On-Chip PCR: Rapid and Quantitative Molecular Diagnostics

Recently, researchers demonstrated ultrafast and real-time nanoplasmonic on-chip PCR for rapid and quantitative molecular

diagnostics using nanoplasmonics and vacuum-assisted microfluidics (Figure 1) [9]. The so-called plasmofluidic PCR (PF-PCR) chip allowed vacuum-assisted easy sample loading into dead-end reaction microchamber arrays that were enclosed by pre-charged vacuum cell and vapor barrier (Figure 1). They employed vacuum cell with a high gas-permeability layer (HPL) on the wall of microchamber arrays that effectively induced spontaneous loading of sample solution and continuous removal of microbubbles trapped or newly produced during the reaction [9].

In this study, the vapor barrier was shown to have a low gas-permeability layer (LPL) that helped the prevention of solution evaporation during the reaction cycles of high temperature. Glass nanopillar arrays with Au nanoislands were then employed that produced ultrafast nanoplasmonic heating resulting from strong light-to-heat conversion of white light emitting diode 'WLED' as well as rapid cooling due to a large surface-to-volume ratio of nanopillars. This PF-PCR chip provided rapid and spontaneous sample loading, ultrafast thermal cycling, and real-time quantification with bubble-free environment for quantitative POC molecular diagnostic applications [9].

In this design of the on-chip plasmonic PCR, a postage stamp-sized polydimethylsiloxane chip was employed that had a microchamber array for the PCR reactions. Upon adding a drop of sample to the chip, the liquid was pulled into the microchambers by the applied vacuum. It was then positioned above glass nanopillars with gold nanoislands. Further, microbubbles that could interfere with the PCR reaction,

diffused out through an air-permeable wall. Subsequently, by turning a white LED on beneath the chip, the gold nanoislands on the nanopillars quickly converted light to heat that rapidly cooled when the light was turned off (Figure 1) [9].

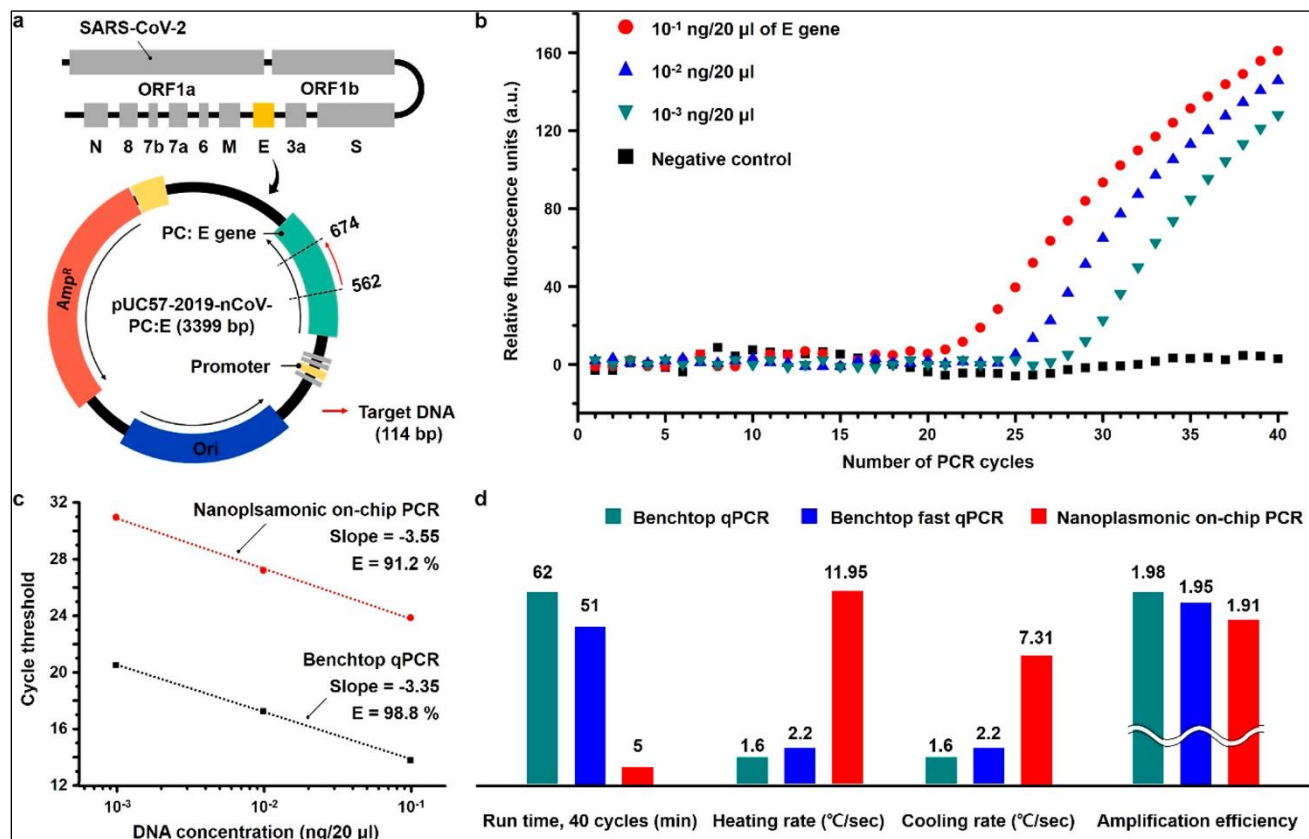
### **On-Chip PCR for the Rapid Diagnostics of SARS-CoV-2**

Researchers demonstrated the nanoplasmonic on-chip PCR for ultrafast amplification and *in-situ* cyclic real-time quantification of lambda DNA and E gene as a target for SARS-CoV-2 by alternating the WLED illumination and the fluorescence detection. In this process, nanoplasmonic photothermal modulation of the NPS allowed rapid and efficient thermal cycling inside microfluidic channels of the PF-PCR chip. Further, the researchers tested the device on a piece of DNA containing a SARS-CoV-2 gene, accomplishing 40 heating and cooling cycles and fluorescence detection in only 5 minutes, with an additional 3 minutes for sample loading (Figure 2) [9]. They showed that by adding a step of the reverse transcriptase prior to sample loading, the entire testing time with the new method was drastically reduced to 10-13 minutes compared to about an hour for typical RT-PCR testing [9].

It was shown that both the nanoplasmonic heating and the thin sample confinement resulted in uniform vertical distribution of photothermal heat in a small volume for rapid and efficient thermal cycling. The vacuum-enabled PF-PCR chip of bilayered PDMS configuration not only allowed spontaneous and rapid sample loading without trapped microbubbles but it also helped maintain stable reaction during the full PCR cycles [9]. The real-time on-chip

PCR was shown to exhibit the ultrafast 40 cycle amplification of  $\lambda$ -DNA for 264 s and SARS-CoV-2 for 306 s as well as the *in-situ* quantification of amplicons with high

efficiency over 91% [9]. The new device could pave the way to many opportunities for rapid POC diagnostics during the pandemic [9].



**Figure 2:** A schematic illustration of ultrafast and real-time detection of SARS-CoV-2 envelope protein. (a) Plasmid for the expression of SARS-CoV-2 envelope (E) protein as positive control is shown. (b) Amplification curves of the E gene are shown that use the PF-PCR chip for 40 cycles of two-step PCR (60–95 °C) within 326 s. (c) Standard curves of benchtop qPCR and nanoplasmonic on-chip PCR are shown for the cycle threshold depending on the DNA concentration. (d) Comparative performance factors are illustrated for benchtop qPCR, benchtop fast qPCR, and nanoplasmonic on-chip PCR, based on run time for PCR 40 cycles, heating rate, cooling rate, and amplification efficiency [Source: ACS Nano (2021)].

### Concluding Remarks

The latest advances in rapid diagnostics of COVID-19 offer new frontiers to mitigate the challenges posed by the pandemic.

Especially, the technology that involves on-chip PCR for POC diagnostics is anticipated to impact the field of diagnostics of highly contagious viral diseases in the near future.

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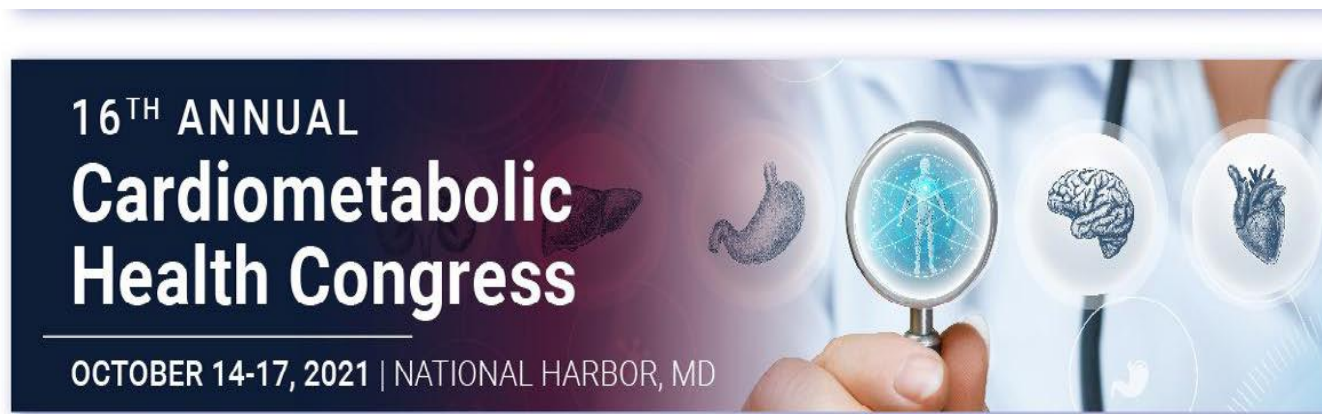
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## Non-Invasive Diagnostic Biomarkers for Alzheimer's Disease

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### **Abstract**

The emergence of biomarkers in biologic fluids is considered an important milestone in the field of Alzheimer's disease (AD) research. Biomarkers are widely considered critically important for the diagnosis and therapeutic intervention of the disease. It is believed that an early diagnosis of AD at a presymptomatic stage could provide the key for a successful intervention and treatment of AD. It is due to the reason that preventative and therapeutic strategies that are known to be AD stage-dependent can have a better chance of clinical success at a very early stage of the disease when critical neurons are not lost. To this end, current clinical trials are extensively being employed by taking advantage of different diagnostic biomarkers. While there has been notable progress in biomarkers for AD, the current research emphasis has been on exploring non-invasive biomarkers due to the advantages of cost-effectiveness, rapid diagnosis and significantly less medical procedural complexities that make these biomarkers potential game changer in AD diagnostics. Here, we present a bird eye view on the subject and discuss the progress made in important non-invasive biomarkers for AD.

*Keywords: Alzheimer's disease, Biomarkers, Non-Invasive, Mild Cognitive Impairment, Neuron*

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It is estimated that Alzheimer's disease (AD) could affect 75 million people in 2030 with the current trend of rapidly increasing aging population across the world with much of the increase expected to happen in developing countries [1]. Studies have strongly suggested that in AD, pathologic changes in the brain start well before any obvious symptoms of memory loss with amyloid beta ( $A\beta$ ) pathology are noticed. This is thought to be a key initial step in the progression of AD, which is followed by the development of neurofibrillary tau pathology (Figure 1) [2]. For the characterization of the disease, three different stages are suggested that include preclinical (or asymptomatic) AD, mild cognitive impairment (MCI) due to AD and dementia due to AD. However, it is still a challenge to do an accurate premorbid diagnosis of the disease, which is currently based upon clinical presentations and other imaging and biofluid biomarkers [1]. With respect to the current state-of-the-art of AD diagnostics, positron emission tomography (PET) scans are known to be effective to reveal  $A\beta$  or tau accumulation in the brain. Further, magnetic resonance imaging (MRI) has also been employed to measure function and reveal brain atrophy. Excellent diagnostic accuracy can be achieved with specific cerebrospinal (CSF) biofluid constituents, such as amyloid beta 42 ( $A\beta_{42}$ ) that correlates with extracellular senile plaques. Such studies can be extended to total tau (T-tau) that reflects the intensity of neuronal damage and phosphorylated tau (P-tau) and correlates with tangle pathology. However, in all of these cases, the relatively invasive nature of CSF collection poses challenge. The widespread use in routine

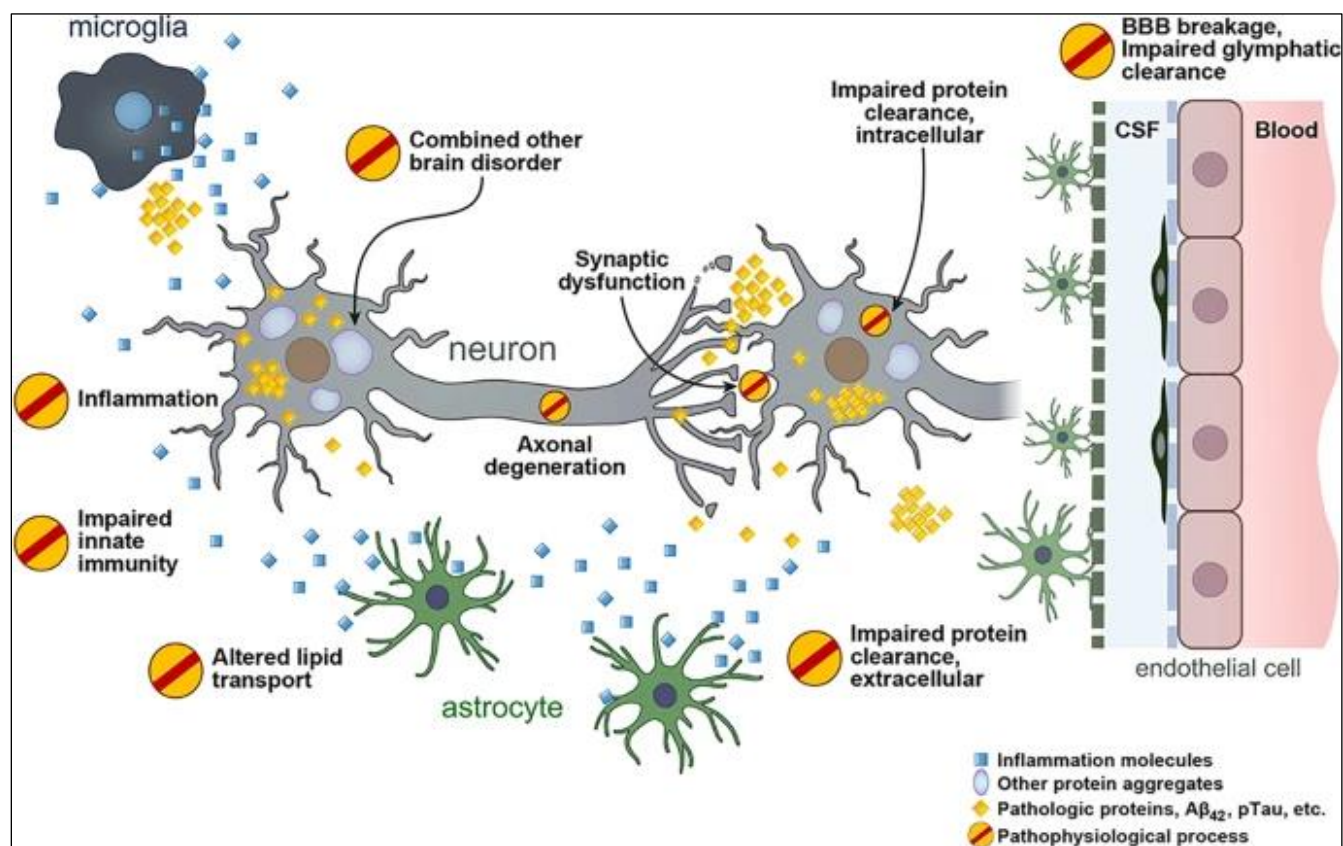
primary care practice is limited due to the complex procedure. Further, in CSF collection process, a lumbar is punctured that can be unpleasant to the patient involved [1-4].

It can therefore be stated that diagnosing degenerative diseases of the nervous system such as AD can be a complicated process. Further, the entire method may not be comfortable to patients because of the involvement of expensive procedures such as image the brain, or invasive tests to assess cerebrospinal fluid by lumbar puncture. To overcome these challenges, a new line of thinking has emerged lately among AD researchers that seeks to develop non-invasive early diagnostic biomarkers that can not only be employed to monitor disease progression and manage care, but they will also provide an important and scalable mean of measuring clinical outcomes during AD therapies [1, 2].

One viable non-invasive diagnostic avenue could be blood tests that is believed to have the potential to detect disease before the patient presents with symptoms. This could be immensely helpful in cases where early interventions are deemed necessary to achieve the best treatment success. To this end, the published clinical studies showed measurement of variants of tau in the blood, which is a protein that normally functions to help stabilize microtubules within neurons. These studies demonstrated that a blood test measuring one of two phosphorylated forms of tau (p-tau181 or p-tau217) could effectively differentially diagnose AD from other neurodegenerative diseases with high accuracy and cost-effective manner

compared to more costly and invasive standard diagnostics. These blood tests were also shown to be able to identify the disease at relatively early stage in the course of cognitive decline [5-7]. However, these

blood-based diagnostics are still far from being able to detect the disease at a presymptomatic stage, which is considered the key in AD therapy and its possible cure.



**Figure 1:** Schematic depiction of the pathophysiological process involved in Alzheimer's disease (BBB, blood–brain barrier; CSF, cerebrospinal fluid) [Source: *Exp Mol Med* (2020)].

In addition to the more-widely used blood specimens, saliva based non-invasive diagnostic of AD has gained attention for some unique advantages. These include relative ease of collection that involves no experienced personnel, which essentially offers the exciting possibility for self-collected samples and completely non-invasive and inexpensive sample collection. Such sample collection does not require any anticoagulants along with it provides easier

storage under the human tissue authority guidelines and permissions [1]. However, there are some challenges that include the decreased concentration of analytes. This requires more sensitive analytical approaches. In addition, inability of approximately 1/3 of participants to produce an adequate saliva sample also poses limitation. Salivary based studies have focused on the detection of the amyloid beta 42 (Aβ<sub>42</sub>) peptide by using an enzyme-like



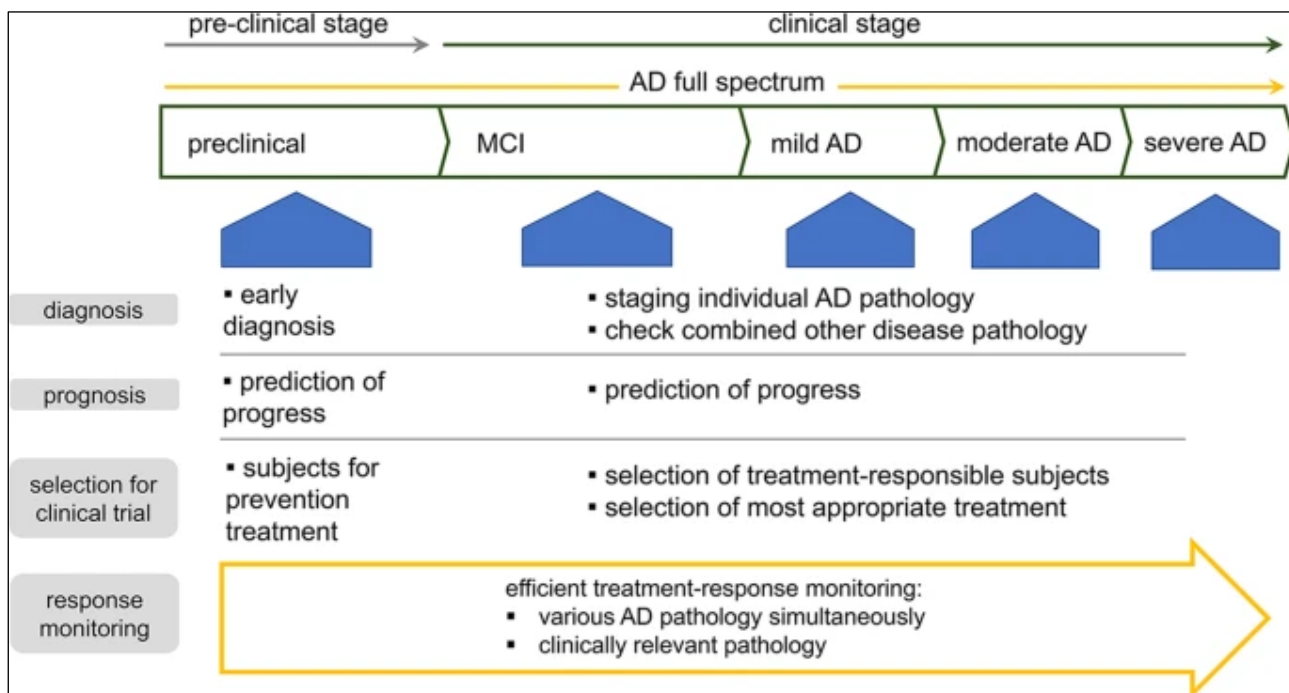
immunosorbent assay (ELISA) as their main experimental approach to detect A $\beta$ . Researchers have suggested some other biomarkers besides A $\beta$  and tau proteins that have shown potential as diagnostic means in saliva specimens. For example, lactoferrin, which is an antimicrobial peptide with a known A $\beta$ -binding ability has been investigated that has shown significantly reduced lactoferrin in AD patients compared to healthy controls [1, 8, 9].

Researchers have suggested a number of hypotheses to explain the origin of salivary biomarkers that are indicative of AD. It has been proposed that biomarkers may be secreted by nerves into salivary glands as a result of their close proximity to the central nervous system. This also includes the salivary proteins that originate after transport of molecules from blood to saliva through ultrafiltration and passive diffusion or active transport [1]. Recent studies have shown the potential of oral microbiome as a diagnostic means for AD. A quantitative polymerase chain reaction (qPCR) assay was employed to quantify the load *Porphyromonas gingivalis* (*P. gingivalis*) for the development of chronic periodontitis that was considered as a high-risk factor for AD. It was found that a majority of CSF and all salivary samples were positive for the presence of *P. gingivalis*. These studies suggest potential use of *P. gingivalis* that may serve as a differential non-invasive diagnostic marker for AD [1, 10].

Another potential non-invasive specimen is oral mucosa cytology samples that have been suggested for an almost non-invasive and relatively inexpensive

alternative for AD diagnosis. Researchers have studied buccal cells as biomarkers in different neurological disorders since these cells that are similarly to skin and brain cells can be derived from ectodermal tissue and therefore, they can be embryologically related to the central nervous system and share common AD-specific characteristics [11].

Future studies of AD-related pathophysiology through biomarkers are linked to diverse aspects of AD pathophysiology that include neurodegeneration, synaptic dysfunction, neuroinflammation, lipid dysmetabolism and disturbed protein clearance. It is believed that such biomarkers-based characterization would be immensely helpful for predicting the progression of individual facets of the pathology along with understanding their relative contributions to clinical deterioration [2]. For example, a common perspective among researchers is based on comprehensive understanding of disease status that is expected to aid in the selection of patients who are most likely to have a favorable response to specific disease-modifying therapies [2]. It is believed that such a characterization strategy could pave the way to superior treatment regimens that could allow monitoring of the response to treatment on an individual patient basis. This could be immensely beneficial given the diversity of AD pathology, and the developed precision medicine could increase the efficacy of the therapeutic effect (Figure 2) [2].



**Figure 2:** Future perspectives and clinical trial strategies for the use of new biomarkers (AD, Alzheimer's disease; MCI, mild cognitive impairment) [Source: *Exp Mol Med* (2020)].

In conclusion, several studies have clearly suggested that loss of cognitive or motor capacity can be deeply concerning to those in early stages of neurodegenerative decline in Alzheimer's disease (AD). This situation can get aggravated especially in the event of not being able to identify the cause of the onset of AD symptoms. This can be devastating to patients and their families because of the absence of answers and a clear diagnosis. With respect to blood serum biomarker research, it offers some hope to develop non-invasive accessible and affordable biomarkers with scalable tools to test and improve interventional therapies for AD. Regarding oral samples such as saliva or buccal cells for AD diagnosis, large-cohort studies are required to be conducted to ensure that these non-invasive oral samples

can act as a research and/or clinical tool for AD.

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## *Biotechnology Advances around the World*

### **Editor's Picks**

Every issue of Biotechnology Kiosk presents select latest research news picked by the editors-in-chief on significant research breakthroughs in different areas of biotechnology around the world. The aim is to promote further R&D in all of these cutting-edge areas of biotechnology. The editors have compiled and included the following innovations and breakthroughs to highlight the latest biotechnology advances.



**Dr. Megha Agrawal**  
**Co Editor-in-Chief**



**Dr. Shyamasri Biswas**  
**Co Editor-in-Chief**

## COVID-19 and Brain

### ***The spike protein of SARS-CoV-2 crosses blood brain barrier in a mice model***

It is known that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is responsible for the coronavirus disease 2019 (COVID-19) pandemic in the world. COVID-19 causes pneumonia and acute respiratory distress in addition to a host of other symptoms that relate to the central nervous system 'CNS' that include loss of taste and smell, headaches, twitching, seizures, confusion, vision impairment, nerve pain, dizziness, impaired consciousness, nausea and vomiting, hemiplegia, ataxia, stroke and also cerebral hemorrhage.

It is not completely clear whether SARS-CoV-2 can enter the brain of humans. Studies have shown that SARS-CoV-2 binds to cells via the S1 subunit of its spike protein, often called the S1 protein. This spike protein dictates which cell the virus can enter. It has been observed that the virus does the same thing as its binding protein. Further, S1 proteins can also cause damage as they detach from the virus that results in inflammation. The S1 protein in SARS-CoV2 and the gp 120 protein in HIV-1 function are similar as they are both glycoproteins. These proteins have a lot of sugars on them that are hallmarks of proteins that bind to other receptors. It is known that both these proteins can function as the arms and hand for their viruses by grabbing onto other receptors and both can cross the blood-brain barrier and S1, similar to gp120, is considered toxic to brain tissues.

During COVID-19 infection, the intense inflammation occurs, which is called a cytokine storm. In cytokine storm, the immune system upon seeing the virus and its proteins responds in its attempt to kill the invading virus. As a consequence, the infected person is left with brain fog, fatigue and other cognitive issues. Further, it is thought that during COVID infection, patients have trouble in breathing due to the infection in the lung. However, another explanation for breathing trouble is also given that is based on the virus entering the respiratory centers of the brain and causing problems there as well.

In a new study, researchers in the US reported that the spike protein can cross the blood-brain barrier in mice. They showed that the spike proteins alone can cause brain fog. Since the spike protein enters the brain, the virus also is likely to cross into the brain. Their research was published in Nature Neuroscience (The S1 protein of SARS-CoV-2 crosses the blood-brain barrier in mice. Nature Neuroscience, 2020; DOI: 10.1038/s41593-020-00771-8).

Researchers concluded that the S1 protein can likely cause the brain to release cytokines and inflammatory products. Their study indicated that I-S1 crosses the blood-brain barrier by adsorptive transcytosis and that murine angiotensin-converting enzyme 2 is involved in brain and lung uptake. However, this is not the case in kidney, liver or spleen uptake.

## Bacteria & Biodegradable Plastics

### Salt-tolerant bacteria for sludge to make biodegradable plastics

According to an estimate, the United States generates seven million tons of sewage sludge annually that is considered enough to fill 2,500 Olympic-sized swimming pools. The associated problem is that while a portion of this waste is repurposed for manure and other land applications, a substantial amount is still disposed of in landfills. Further, it has been reported that the price of raw materials to cultivate biopolymer-producing bacteria accounts for 25-45% of the total production cost of manufacturing bioplastics. This implies that the high cost can be greatly reduced if an alternate resource is employed that is cheaper and readily obtainable.

One can take an example of polyhydroxybutyrate, which is an emerging class of bioplastics. This plastic is produced by several bacterial species when they experience an imbalance of nutrients in their environment. This polymer has been shown to be capable to act as the bacteria's supplemental energy reserves, which is similar to fat deposits in animals. Especially, it has been found that in the scenario of abundance of carbon sources and a depletion of either nitrogen, phosphorus or oxygen can cause bacteria to erratically consume their carbon sources and produce polyhydroxybutyrate as a stress response. One such medium that can be considered to force bacteria to make polyhydroxybutyrate is crude glycerol, which is a byproduct of biodiesel manufacturing. It is known that crude glycerol is rich in carbon that has no nitrogen, thus making it a suitable raw material for making bioplastics. However,

one problem is that crude glycerol contains impurities such as fatty acids, salts and methanol, which can prohibit bacterial growth. Similarly, like crude glycerol, sludge from wastewater also has many of the same fatty acids and salts. Because of these problems, the effects of these fatty acids on bacterial growth and, consequently, polyhydroxybutyrate production are quite challenging to achieve.

In a new study, researchers showed an efficient way to use leftover sludge to make biodegradable plastics. Researchers reported their work in the Journal American Chemical Society (ACS) Omega (From Organic Wastes to Bioplastics: Feasibility of Nonsterile Poly(3-hydroxybutyrate) Production by *Zobellella denitrificans* ZD1. ACS Omega, 2020; 5 (38): 24158 DOI: 10.1021/acsomega.9b04002the). They demonstrated that the bacterium *Zobellella denitrificans* ZD1, found in mangroves, can consume sludge and wastewater to produce polyhydroxybutyrate, which is a type of biopolymer that can be used in lieu of petroleum-based plastics. In addition to reducing the burden on landfills and the environment, the researchers showed that *Zobellella denitrificans* ZD1 can offer a way to cut down upstream costs for bioplastics manufacturing. This shows a step toward making them more competitively priced against regular plastics.

This opens up a potential way to use municipal wastewater-activated sludge and agri- and aqua-culture industrial wastewater to make biodegradable plastics. In addition,

since the bacterial strain was shown not requiring elaborate sterilization processes to prevent contamination from other microbes, further cutting down operating and production

costs of bioplastics could be possible to achieve.

**Compiled and Edited by Dr. Megha Agrawal & Dr. Shyamasri Biswas.**







# ISHA Therapeutics

CONTRIBUTING TO THE SPIRIT OF DRUG DEVELOPMENT

## “Contributing to the spirit of translational drug development”

*ISHA Therapeutics, is a unique organization with its primary location based out of New Jersey, exclusively focused on supporting clinical and translational development programs spanning from very early on to late stage developments. We provide consulting services to our esteemed clients who aspire to develop safe and efficacious new drugs, devices and biologicals. We also have our in-house innovative drug development pipeline.*

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