

ISSN 2689-0852

APRIL 2020

BIOTECHNOLOGY KIOSK



**THERAPEUTICS TO
CONTROL COVID-19**

VOLUME 2, ISSUE 4
WWW.BIOTECHKIOSK.COM



Executive Publishers

Megha Agrawal, PhD

(Biotechnology)

Publisher and Editor

Expertise:

Neuroscience, Stroke, Pharmacology,
Toxicology, Microbiology and
Molecular Biology

Email: megha@biotechkiosk.com
meghaagra@gmail.com

Shyamasri Biswas, PhD

(Biotechnology)

Publisher and Editor

Expertise:

Structural Biology, Enzyme Technology,
and Protein Crystallography

Email: shyabiswas@biotechkiosk.com
shyabiswas@gmail.com

Editorial, Sales & Circulation Office

160 International Parkway

Suite 100-9, Heathrow

FL-32746, USA

Phone: 386-518-9411

Email: publisher@biotechkiosk.com

www.biotechkiosk.com

ISSN 2689-0852

One stop shop for all things biotech





From the Publisher's Desk



Welcome to Biotechnology Kiosk!

We are pleased to present another interesting issue of Biotechnology Kiosk (BK) to our readers with the regular features that include high-end editorials by experts, biotechnology advances around the world and industry news from pharma and biotech sectors.

This issue contains a number of scholarly editorials and news and views on the current cutting edge topics including diagnostics and surveillance technologies along with innovations in therapeutics for the novel Coronavirus (COVID-19), regenerative

medicine and tissue engineering, neurology, nutritional and environmental biotechnology and bio recycling among other topics and reporting on research break throughs from around the world.

In view of the COVID-19 pandemic, we have extended the deadline for manuscript submission for the special edition of Vacuum Advances in Biotechnology until May 31, 2020. Please check out the call for papers that is posted on BK's website. We are also now open to consider manuscripts in all areas of biotechnology for regular

publication in BK. Please go to the sections 'Aims and Scope' to submit your manuscripts to BK.

We look forward to receiving your contributions. We do hope that you will enjoy reading this issue of Biotechnology Kiosk.

Please do write to us with your comments and feedback. Your suggestions are always appreciated.

Dr. Megha Agrawal and Dr. Shyamasri Biswas

Co Editors-in-Chief, Biotechnology Kiosk





Contents

Volume 2, Issue 4

APRIL 2020

COLUMNS

EPIDEMIOLOGY & THERAPEUTICS5

Innovations in Therapeutics to Control COVID-19

<https://doi.org/10.37756/bk.20.2.4.1>

MEDICAL DIAGNOSTICS FOR COVID-1914

The Need for Next Generation Diagnostic and Surveillance Technologies to Battle SARS-CoV-2 Pandemic

<https://doi.org/10.37756/bk.20.2.4.2>

FOOD & HEALTH SCIENCE23

The tussle between the developing adolescent brain and dietary choices: who's the target who's the trigger?

<https://doi.org/10.37756/bk.20.2.4.3>

OPINION.....29

A Proposed Herbal Formulation: Targeting to Strengthen Inner Immunity to Fight Infectious Diseases

BIOTECH R&D AND INNOVATION NEWS.....33

Editor's PICKS: Biotechnology Advances around the World

Neurology.....34

Regenerative Medicine and Tissue Engineering.....34

Nutritional & Environmental Biotechnology.....35

Biorecycling & Microbiology.....35

BIOTECH AND PHARMA INDUSTRY ROUNDUP.....	37
Dynavax & Sinovac to jointly develop COVID-19 vaccine candidate.....	37
Eagle Pharma to test Ryanodex against COVID-19.....	37
Meningococcal Vaccines	37
AstraZeneca's Imfinzi shows promise in lung cancer.....	37
UroGen's Jelmyto gets expedited approval from FDA.....	37
SMA drug gets a boost.....	38
AstraZeneca to study leukemia drug as COVID-19 treatment.....	38
\$125M donation to speed coronavirus treatments	38
Investments to counter Cancer genes.....	38
Roche presents biomarker for cancer.....	39
French company Stilla raises €20M	39
HALIX B.V. to produce vaccines against COVID-19.....	39
ADVERTISING INFORMATION.....	40
(a) WEB BANNER AND ADVERTISEMENT RATES	
(b) GENERAL AD RATES FOR THE MAGAZINE	





Epidemiology & Therapeutics

By Shyamasri Biswas*, PhD

Co Editor-in-Chief

Biotechnology Kiosk, 2, 4 (2020)

DOI: <https://doi.org/10.37756/bk.20.2.4.1>



Innovations in Therapeutics to Control COVID-19

Abstract

The current COVID-19 pandemic has triggered innovations in therapeutic strategies that are thought to provide viable and faster pathways to cure infected people by the deadly virus, SARS-CoV-2. In this review, we have described the known epidemiology along with the discovered genome structure and viral factors of SARS-CoV-2. Further, the latest innovations in therapeutics including significant breakthroughs in clinical trials on antiviral drugs, remdesivir and chloroquine including the combination drugs have been highlighted. This brief overview on therapeutic strategies should serve a medium to researchers for further innovations in drug discovery and repurposing of anti-viral drugs for SARS-CoV-2.

**Email: shyabiswas@biotechkiosk.com*

SARS-CoV-2: Epidemiology, Genome Structure and Key Viral Factors

The severe acute respiratory syndrome coronavirus (SARS-CoV-2; COVID-19) epidemic broke out first in Wuhan, China in December 2019 that later became a worldwide deadly pandemic. Bat was suggested in earlier studies as the potential reservoir of SARS-CoV-2 [1]. Detailed virus genome sequencing of COVID-19 was conducted throughout the genome to Bat CoV RaTG13 that showed 96.2% overall genome sequence identity of SARS-CoV-2. The virus genome sequencing results and evolutionary analysis suggested that bat CoV and human SARS-CoV-2 might share the same ancestor. Thus, bat was a suspect as natural host of virus origin, and it was thought that SARS-CoV-2 got transmitted from bats via unknown intermediate hosts to infect humans [1, 2]. Further, researchers estimated the basic reproduction number (R_0) of SARS-CoV-2 to be around 2.2, or even more (range from 1.4 to 6.5) in familial clusters of pneumonia outbreaks. This has led to a steady spread of COVID-19 across the globe by human-to-human transmissions taking tens of thousands of lives so far [3, 4].

Researchers have divided coronaviruses (CoV) into four genera that include α - β - γ - δ -CoV. Among these different types of viruses, it has been shown that α - and β -CoV are able to infect mammals, while γ - and δ -CoV tend to infect birds [1]. The SARS-CoV-2 has been identified as a β -coronavirus, which is enveloped in a non-segmented positive-

sense RNA virus (Figure 1) [1]. In previous studies, researchers identified six CoVs as human-susceptible virus. In these six CoVs, the group of α -CoVs - HCoV-229E and HCoV-NL63, and the group of β -CoVs - HCoV-HKU1 and HCoV-OC43 were shown with low pathogenicity causing mild respiratory symptoms similar to a common cold [1]. However, the two other known β -CoVs - SARS-CoV and MERS-CoV have been shown to cause severe and potentially fatal respiratory tract infections [1]. Some of the latest studies have clearly suggested involvement of the receptor angiotensin-converting enzyme 2 (ACE2) that is used by SARS-CoV-2 to infect humans (Figure 1) [1, 2].

Regarding genome structure and key viral factors, Figure 1 schematically illustrates the genome of CoV-2 virus that contains a variable number (6–11) of open reading frames (ORFs) [1]. Researchers have shown that two-thirds of viral RNA, that is mainly located in the first ORF (ORF1a/b) translates two polyproteins, pp1a and pp1ab, and encodes 16 non-structural proteins (NSP) with the remaining ORFs encode accessory and structural proteins (Figure 1) [1]. Further, the rest of the virus genome has been shown to encode four essential structural proteins, including spike (S) glycoprotein, small envelope (E) protein, matrix (M) protein, and nucleocapsid (N) protein. It has also been shown that in addition to structural proteins, several accessory proteins can interfere with the host innate immune response [1].

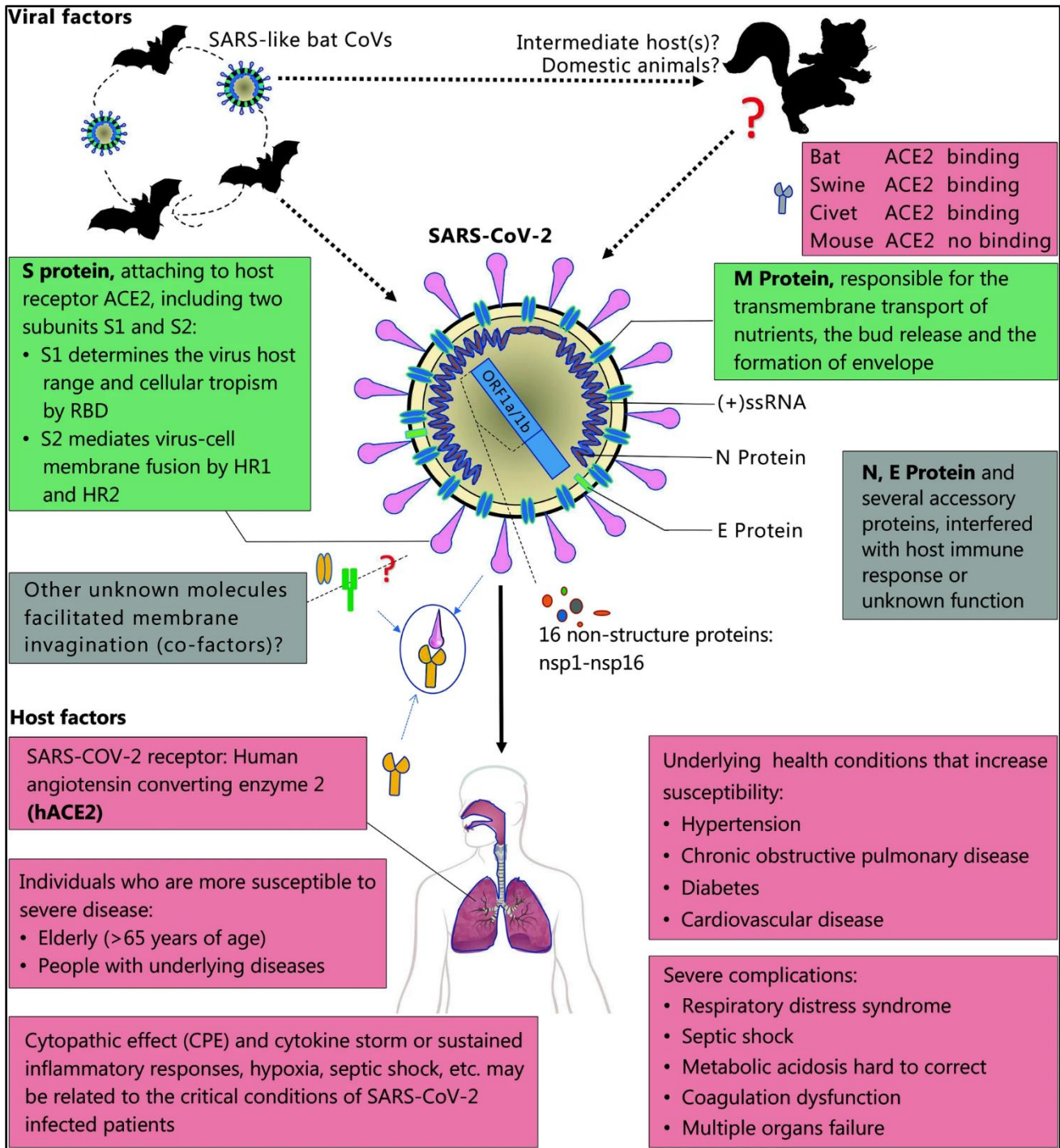


Figure 1: The pathogenesis of SARS-CoV-2 viral that is influenced by host factors. It shows illustration of bats that are considered the reservoir of SARS-CoV-2. The novel virus is thought to have originated from bats or unknown intermediate hosts and subsequently cross the species barrier into humans with virus-host interactions that affect viral entry and replication. The virus genome encodes spike (S) glycoprotein, small envelope (E) protein, matrix (M) protein, and nucleocapsid (N) protein, and also several accessory proteins. Host factors are shown in the lower panel [Source: Military Med Res (2020)].

Therapeutic Strategies for COVID-19: The Important Roles of Anti-Viral Drugs

Innovations in therapeutic strategies are thought to provide viable pathways to a faster solution to the current COVID-19 pandemic to cure infected people and also to prevent further epidemics. The promising strategies include therapeutic agents targeting

nucleosides, nucleotides, viral nucleic acids and enzymes/proteins involved in the replication and transcription of SARS-CoV-2 [5]. To this end, repurposing some of the existing antiviral agents to treat infection from SARS-CoV-2 are already moving into clinical trials. Figure 2 shows potential drug targets for beta-coronaviruses [6].

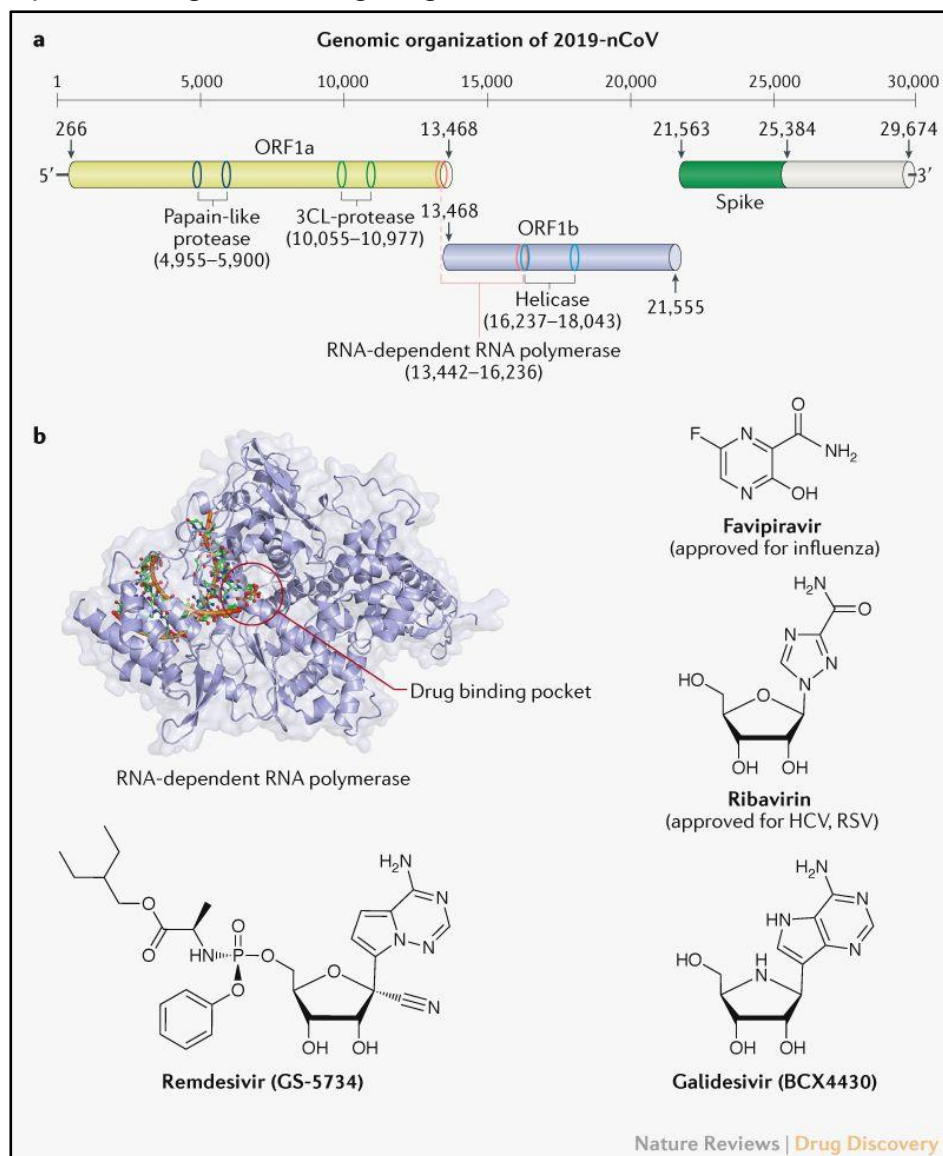


Figure 2: Promising drug targets for beta-coronaviruses. (a) Genomic organization of SARS-CoV-2 (the coding regions for proteins for potential drug targets). (b) A drug binding pocket along with chemical structures of potential inhibitors [Source: Nat Rev Drug Discov. (2020)].

Researchers have shown potentials of approved nucleoside analogues (favipiravir and ribavirin) and experimental nucleoside analogues (remdesivir and galidesivir) against SARS-CoV-2 (Figure 2) [6]. Previous studies have suggested that nucleoside analogues in the form of adenine or guanine derivatives can target the RNA-dependent RNA polymerase and block viral RNA synthesis in a broad spectrum of RNA viruses, including human coronaviruses [5, 6]. For example, researchers have shown Favipiravir (T-705), which is a guanine analogue approved for influenza treatment, can effectively inhibit the RNA-dependent RNA polymerase of a range of RNA viruses including influenza, Ebola, yellow fever, chikungunya, norovirus and enterovirus. In this regard, a recent research reported the promising activity of Favipiravir against COVID-19 ($EC_{50} = 61.88 \mu\text{M}$ in Vero E6 cells) [1, 5-7].

Remdesivir (GS-5734, Figure 2), which is essentially a 1'-cyano-substituted adenosine

nucleotide analog prodrug that inhibits viral RNA polymerases has shown quite a lot of promise. This anti-viral drug has been tested for a wide ranging antiviral activity against several RNA viruses [1]. In a most recent research, *in-vitro* activity of Remdesivir was demonstrated against SARS-CoV-2, and two-thirds of severe COVID-19 cases improved on administering remdesivir (Figure 3) [8]. In this study that employed a cohort of patients hospitalized for severe COVID-19 who were treated with compassionate-use remdesivir, clinical improvement was observed in 36 of 53 patients (68%) in the category of oxygen support, while Improvement was observed in all 12 patients who were breathing ambient air or receiving low-flow supplemental oxygen [8]. Further, 5 of 7 patients (71%) who were receiving noninvasive oxygen support (NIPPV or high-flow supplemental oxygen) also showed improvement. Only 8 of 53 patients (15%) in the oxygen support category showed worsening health conditions (Figure 3) [8].

		No. of Patients in Oxygen-Support Group at Baseline (%)			
		Invasive (N=34)	Noninvasive (N=7)	Low-flow oxygen (N=10)	Ambient air (N=2)
Category on ordinal scale →	5	4	3	2	
Death	6	6 (18)	1 (14)	0	
Invasive	5	9 (26)	1 (14)	0	
Noninvasive	4	3 (9)	0	0	
Low-flow oxygen	3	0	0	0	
Ambient air	2	8 (24)	0	0	
Discharged	1	8 (24)	5 (71)	10 (100)	
Improvement		19 (56)	5 (71)	10 (100)	
Category on ordinal scale ↑					

Figure 3: Improvement levels after treatment with remdesivir in patients in various oxygen support category (improvement: blue cells), no change: beige and worsening: gray) [Source: The New England Journal of Medicine (2020)].

Researchers noted that 17 of 30 patients (57%) who were receiving invasive mechanical ventilation were extubated, while 3 of 4 patients (75%) receiving extracorporeal membrane oxygenation (ECMO), or both ECMO and mechanical ventilation stopped receiving it [8]. While the researchers concluded that further tests were needed, these clinical tests showed encouraging results of the therapeutic power of remdesivir to mitigate COVID-19 [8].

An anti-malaria drug, hydroxychloroquine in combination with azithromycin has been shown very promising for repurposing with great potential to treat COVID-19 [9]. It has been known that chloroquine can inhibit pH-dependent steps of the replication of several viruses that can impart a potent effect on SARS-CoV that can help mitigate the infection and spread [1, 7, 10]. Chloroquine is also known to exhibit immunomodulatory effects that help suppress the production/release of TNF- α and IL-6. In addition, researchers have shown that chloroquine can work as a novel class of autophagy inhibitor. The advantage of such an inhibitor is that it may interfere with viral infection and replication. In previous studies, researchers observed the interference of chloroquine with the glycosylation of cellular receptors of SARS-CoV that functioned at both entry and at post-entry stages of the COVID-19 infection in Vero E6 cells [1, 10, 11]. Chloroquine affects the glycosylation process of angiotensin-converting enzyme 2, known as ACE-2, receptor for binding of viral spike protein, which is essential for interaction with the host

[7, 10]. Thus, it is believed that the proven anti-viral and anti-inflammatory activities of chloroquine can be leveraged for its potent efficacy in treating patients with COVID-19 [7]. For example, in a recent clinical report, chloroquine phosphate was recommended to treat COVID-19 associated pneumonia in larger populations [11].

Innovations in the combination anti-viral drugs seem to hold the key. To this end, a recent work showed the feasibility of the combination of remdesivir and chloroquine that was demonstrated to effectively inhibit the SARS-CoV-2 in-vitro (Figure 4) [10]. Additionally, it was shown that treatment with chloroquine prevents the spread of SARS-CoV infection in the the post-infection period [10]. In this study, researchers employed clinical isolates of SARS-CoV-2, and evaluated the efficacy of seven agents (ribavirin, penciclovir, nitazoxanide, nafamostat, chloroquine, remdesivir [GS5734], and favipiravir (T-705)) in in-vitro conditions (Figure 4) [10]. Cytotoxicity was also evaluated in vero E6 cells, which was followed by infection of the cells with SARS-CoV-2 clinical isolates. The test drug was then evaluated at different doses [10]. Reverse transcription PCR-based quantification was done to get the viral yield, which was later confirmed by immunofluorescence microscopy (nucleocapsid protein visualization) (Figure 4) [10]. The results showed that both chloroquine and remdesivir inhibited virus infection at micromolar level (0.77–1.13 μ M) and with high selectivity [10].

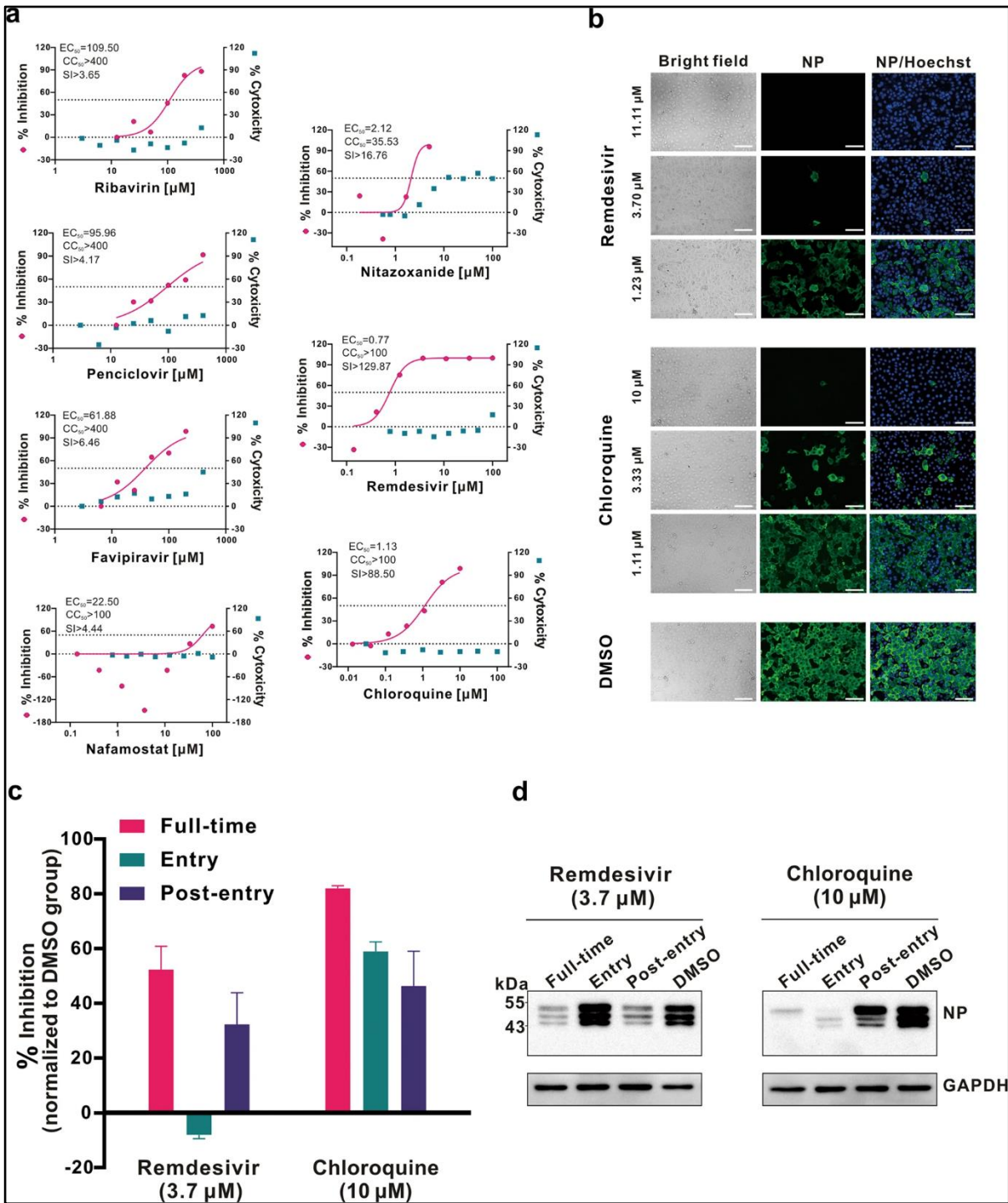


Figure 4: (a) The in-vitro antiviral activities of the test drugs against SARS-CoV-2 with a Vero E6 cells that were infected with SARS-CoV-2. Viral yield in the cell supernatant was then quantified by qRT-PCR. (b) Immunofluorescence microscopy of virus infection upon treatment of remdesivir and chloroquine. (c & d) Time-of-addition of remdesivir and chloroquine showing NP expression in infected cells that was analyzed by Western blot [Source: Cell Res (2020)].

Concluding Remarks

With the rapid spread of COVID-19 pandemic across the globe, it is of immense importance and absolutely essential to focus on the innovations in discovering drugs to mitigate the challenge. This should be done in addition to the ongoing efforts to develop vaccines for COVID-19 and early diagnostics for rapid testing capabilities and having a robust medical systems including sufficient personal protective equipment for front line healthcare professionals. This should help in preparing to combat the future epidemic outbreaks.

References for further reading

1. Guo, Y., Cao, Q., Hong, Z. et al. The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak – an update on the status, *Military Med Res* 7, 11 (2020), DOI:[10.1186/s40779-020-00240-0](https://doi.org/10.1186/s40779-020-00240-0)
2. Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin, *Nature*, (2020), DOI <https://doi.org/10.1038/s41586-020-2012-7>
3. Riou J, Althaus CL. Pattern of early human-to-human transmission of Wuhan 2019 novel coronavirus (2019-nCoV), December 2019 to January 2020. *Euro Surveill.*, 25(4):2000058 (2020), <https://doi.org/10.2807/1560-7917.ES.2020.25.4.2000058>
4. Liu Y, Gayle AA, Wilder-Smith A, Rocklöv J. The reproductive number of COVID-19 is higher compared to SARS coronavirus. *J Travel Med.*, (2020), <https://doi.org/10.1093/jtm/taaa021>
5. Zumla A, Chan JF, Azhar EI, Hui DS, Yuen KY, Coronaviruses - drug discovery and therapeutic options, *Nat Rev Drug Discov*, 15 (5): 327–47 (2016), <https://doi.org/10.1038/nrd.2015.37>
6. Guangdi Li & Erik De Clercq, Therapeutic options for the 2019 novel coronavirus (2019-nCoV), *Nat Rev Drug Discov*, 19, 149-150 (2020), DOI:[10.1038/d41573-020-00016-0](https://doi.org/10.1038/d41573-020-00016-0)
7. Suliman Khan, Rabeea Siddique, Muhammad Adnan Shereen, Ashaq Ali, Jianbo Liu, Qian Bai, Nadia Bashir, Mengzhou Xue, The emergence of a novel coronavirus (SARS -CoV - 2), their biology and therapeutic 2 options, *J. Clin. Microbiol.* (2020), <https://doi.org/10.1128/JCM.00187-20>
8. J. Grein, N. Ohmagari, D. Shin, G. Diaz, E. Asperges, A. Castagna, T. Feldt, G. Green et. al., Compassionate Use of Remdesivir for Patients with Severe Covid-19, *The New England Journal of Medicine*, April 10 (2020), DOI: [10.1056/NEJMoa2007016](https://doi.org/10.1056/NEJMoa2007016)
9. Philippe GautretJean-Christophe Lagier Philippe Parola Van Thuan Hoang Line Meddeb et. al., Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial, *International Journal of Antimicrobial Agents* (2020), <https://doi.org/10.1016/j.ijantimicag.2020.105949>

10. Wang, M., Cao, R., Zhang, L. et al., Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro, *Cell Res.*, 30, 269–271 (2020), <https://doi.org/10.1038/s41422-020-0282-0>
11. Gao J, Tian Z, Yang X, Breakthrough: Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies, *Biosci Trends*. Mar 16;14(1):72-73 (2020), DOI:[10.5582/bst.2020.01047](https://doi.org/10.5582/bst.2020.01047)





Medical Diagnostics (COVID-19)

**By Megha Agrawal*, PhD
Co Editor-in-Chief**

Biotechnology Kiosk, 2, 4 (2020)
DOI: <https://doi.org/10.37756/bk.20.2.4.2>



The Need for Next Generation Diagnostic and Surveillance Technologies to Battle SARS-CoV-2 Pandemic

Abstract

Corona Virus Disease 2019 (COVID-19) has been designated by the World Health Organization as a life-threatening global pandemic caused by severe acute respiratory syndrome coronavirus (SARS-CoV-2). The existing diagnostic practices are mainly based on real-time fluorescent PCR (RT-PCR), which is considered the clinical standard for SARS-CoV-2 nucleic acid detection. The ongoing efforts are focused on to develop new rapid diagnostics including point-of-care diagnostics and surveillance technologies to detect SARS-CoV-2 early in order to control the disease and mitigate it in a timely fashion. Here, we present an overview of the current state-of-the-art of diagnostics of SARS-CoV-2 and the limitations of the existing technologies. We describe the emerging new promising diagnostic technologies that overcome the limitations by offering rapid, point-of-care diagnostic abilities for patients. Finally, we discuss innovative concepts and future directions in developing capabilities on smart surveillance technologies for mitigating the current challenges and also to prevent future global pandemic such as COVID-19

***E-Mail: megha@biotechkiosk.com**

Existing Diagnostic Practices for SARS-CoV-2 Pandemic

The novel severe acute respiratory syndrome coronavirus (SARS-CoV-2, COVID-19) was first detected in December 2019 in the Hubei Province of China. Since the outbreak of this highly infectious disease, the COVID-19 pandemic has brought devastating and life-altering effects across the globe by infecting hundreds of thousands of people, which resulted in tens of thousands of deaths in as many as 182 countries so far [1]. During these difficult times caused by COVID-19 pandemic that has seen a continued spread of the disease, it is critically important that we have effective diagnostic tools and practices in place that can play a key role in the containment of COVID-19. Effective diagnostics can enable the rapid implementation of control measures that can limit the spread through infected patient identification and subsequent isolation. This also enables contact tracing including identifying people that may have come in contact with an infected patient. Figure 1 describes a workflow for the existing diagnostic practices for COVID-19 [2].

Regarding the employed diagnostics of this disease, the computed tomography (CT) images that were obtained earlier during the time of disease breakout suggested pneumonia-like symptoms and abnormal lung in infected people [3]. The negative stained transmission electron microscopy (TEM) was used to identify the morphology of the virus and the images revealed virus with diameter ranging from 60 to 140 nm that comprised an envelope with protein spikes, and genetic material [3, 4].

In addition to CT based diagnostics and TEM based morphological images, a multiplex polymerase chain reaction (PCR) panel of known pathogens was employed to analyze the samples from infected patients. This helped identification of the previously unknown pathogen as an RNA virus through next generation sequencing [3]. The virus was later named SARS-CoV-2 because its genome sequence showed similarity with SARS-CoV, the virus that caused SARS in 2002–2003. Researchers were able to use the whole genome sequence to develop PCR kits to diagnose patients suffering with COVID-19 [3, 4]. PCR/RT-PCR, especially, real-time (RT) PCR/RT-PCR has been employed as a highly sensitive and specific method for detection of infectious diseases such as COVID-19. To this end, PCR/RT-PCR-based methods have been employed to detect nucleic acid (e.g., RNA) of novel coronavirus SARS-CoV-2 for early diagnosis of COVID-19 [2].

RT-PCR is currently used for the diagnosis of COVID-19 along with screening with CT scans. However, PCR/RT-PCR-based methods have limitations due to the fact that they are typically restricted in a centralized clinical laboratory that requires sophisticated equipment and well-trained personnel. Further, the less availability of enough PCR reagent kits is another issue that has been faced to keep up with the high demand. In addition, another challenge is the reliance of RT-PCR on the presence of detectable SARS-CoV-2 in the sample collected [2]. Because of this limitation, it is difficult to identify infection of SARS-CoV-2 in a recovered asymptomatic patient who was infected with the disease before. So, this

does not allow to enforce control measures. On the other hand, CT based imaging procedures are quite expensive and require technical expertise that also cannot

specifically diagnose COVID-19 [2]. Thus, these methods are not considered suitable for simple, rapid, point-of-care diagnostic applications for SARS-CoV-2 [2, 5].

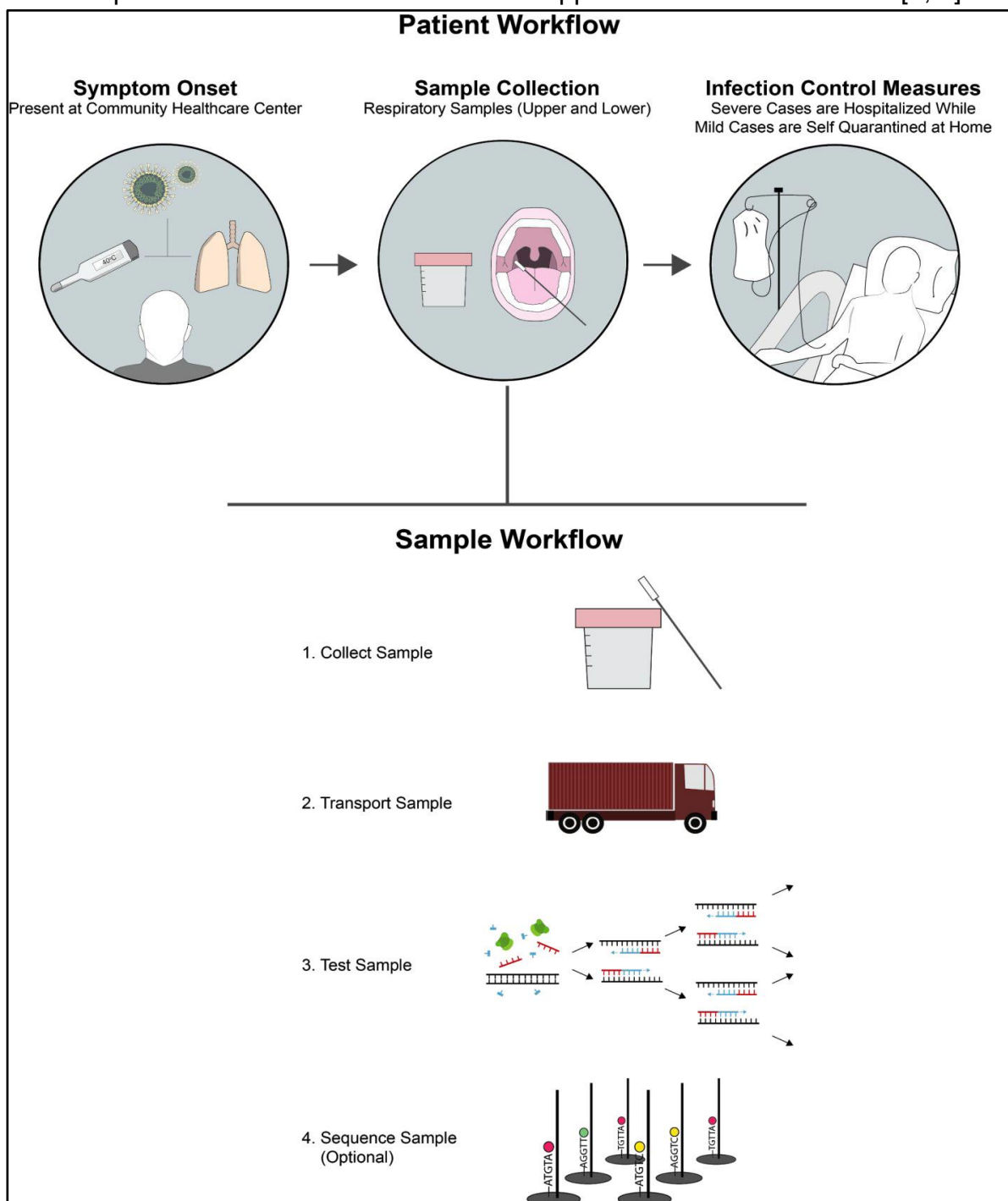


Figure 1: A typical workflow showing the steps of diagnostic practices for COVID-19 [Source: ACS Nano (2020)].

Need for New Diagnostic and Surveillance Strategies

It is of great concern worldwide that COVID-19 might persist well beyond 2020. This places a significant stress on the global healthcare systems. In view of this, it is believed that new innovations in research to develop next generation diagnostics and surveillance technologies are needed to combat the disease. The World Health Organization (WHO) has therefore, recommended for an immediate priority for COVID-19 diagnostics research for the development of point-of-care nucleic acid and protein tests and detection. Point-of-care tests are advantageous as they are cost-effective, handheld devices that can be leveraged to diagnose patients outside of centralized facilities including community centers that can reduce the burden on clinical laboratories. The goal is to integrate these tests into multiplex panels in future [2-4].

As for improving efforts on surveillance technologies, in addition to nucleic acid based tests, serological tests using proteins are being considered. These tests are considered superior than nucleic acid tests taken alone due to the reason that they have the benefits of detection after recovery. This can be leveraged to help clinicians to track both sick and recovered patients, which can provide a better statistics of total SARS-CoV-2 infections [2]. Therefore, it is of immense importance from a healthcare point of view to develop novel diagnostic technologies enabling rapid and simple identification of people infected with SARS-CoV-2. This could potentially enable appropriate isolation measures and contact

tracing that would be helpful to reduce the transmission of SARS-CoV-2 [2].

Rapid Diagnostic Technologies: Looking Beyond the Current State-of-the-Art

COVID-19 pandemic has created a global healthcare crisis that has called for urgent development of point-of-care tests and multiplex assays beyond the available technologies. To this end, the identification and sequencing of SARS-CoV-2 has enabled current research and developments to focus on nucleic acids and viral proteins, antigens and antibody based rapid diagnostics. These diagnostics are supposed to act as a first line of defense against an outbreak of a disease. More advanced diagnostics are believed to include serological tests (i.e., blood tests for specific antibodies) based technologies. These technologies are thought to be easier to administer that may complement nucleic acid tests for diagnosing COVID-19 infection [2]. Researchers are paying a lot of attention to nucleic acid tests using isothermal amplification that are currently in development for SARS-CoV-2 detection [2]. Isothermal amplification techniques include recombinase polymerase amplification, helicase-dependent amplification, and loop-mediated isothermal amplification (LAMP). They can be conducted at a single temperature without requiring specialized laboratory equipment that can provide high analytical sensitivities to PCR [6]. RT-LAMP employs DNA polymerase with four to six primers to bind to six distinct regions on the target genome [2]. Researchers have developed and clinically tested reverse transcription LAMP (RT-LAMP) tests for SARS-CoV-2 [7].

Current research has also focused on viral protein antigens and antibodies that can be used for diagnosing COVID-19 [8]. Among currently considered point-of-care approaches in diagnostics for COVID-19, lateral flow antigen based point-of-care detection for SARS-CoV-2 is under development for diagnosing COVID-19 [9]. Another point-of-care approach based on microfluidic devices is being considered. Microfluidic devices are essentially based on palm-sized chip etched with micrometer-sized channels and reaction chambers [2]. The function of chip is to mix and separate liquid samples using electro kinetic, capillary, vacuum, and/or other forces. Microfluidics based diagnostics for SARS-CoV-2 offer a number of advantages that include miniaturization, small sample volume, rapid detection times, and portability. All these point-of-care diagnostic technologies are envisioned to be adapted to detect SARS-CoV-2 RNA or proteins [2].

CRISPR-Cas12a Assay for Rapid, Ultrasensitive and Visual Detection of SARS-CoV-2

RNA-guided CRISPR/Cas nuclease-based nucleic acid detection has been shown very promising for next-generation molecular diagnostics technology. This is due to the reason for its high sensitivity, specificity and reliability [5]. To this end, important Cas nucleases (e.g., Cas12a, Cas12b and Cas13a) have been shown by the researchers to perform strong collateral cleavage activities. These include a crRNA-target-binding activated Cas that can indiscriminately cleave surrounding non-target single-stranded nucleic acids [5].

Researchers employed CRISPR-Cas12a (termed "AIOD-CRISPR") assay for rapid, ultrasensitive, specific and visual detection of nucleic acid for visual real time SARS-CoV-2 diagnostics (Figure 2) [5]. Dual crRNAs were introduced to initiate highly efficient CRISPR-based nucleic acid detection. In their AIOD-CRISPR assay, researchers all components for nucleic acid amplification and CRISPR detection that were mixed in a single, one-pot reaction system and incubated at a single temperature. This eliminated the requirement for separate pre-amplification and amplified product transferring. Researchers then engineered the AIOD-CRISPR assay to detect severe SARS-CoV-2 (Figure 2) [5]. The advantage of the test results of the AIOD-CRISPR assay was the direct visualization by the naked eye. Therefore, this diagnostic technology was envisioned by the researchers as CRISPR-based next-generation molecular diagnostics towards point-of-care applications for COVID-19 [5].

Figure 2A shows a pUCIDT-AMP plasmid containing 384 nt SARS-CoV-2 N gene cDNA (N plasmid) that was first prepared as the target to develop the AIOD-CRISPR assay. Researchers demonstrated that AIOD-CRISPR assay could detect 1.3 copies of SARS-CoV-2 N plasmids in both real-time and visual detections within 40 min. This offers a rapid and nearly single-molecule level sensitive detection (Figure 2B) [5]. The reaction with SARS-CoV-2_PC showed the positive signal in both real-time and visual detections, which demonstrated the high specificity without cross reactions for non-SARS-CoV-2 targets by the developed AIOD-CRISPR assay (Figure 2C) [5].

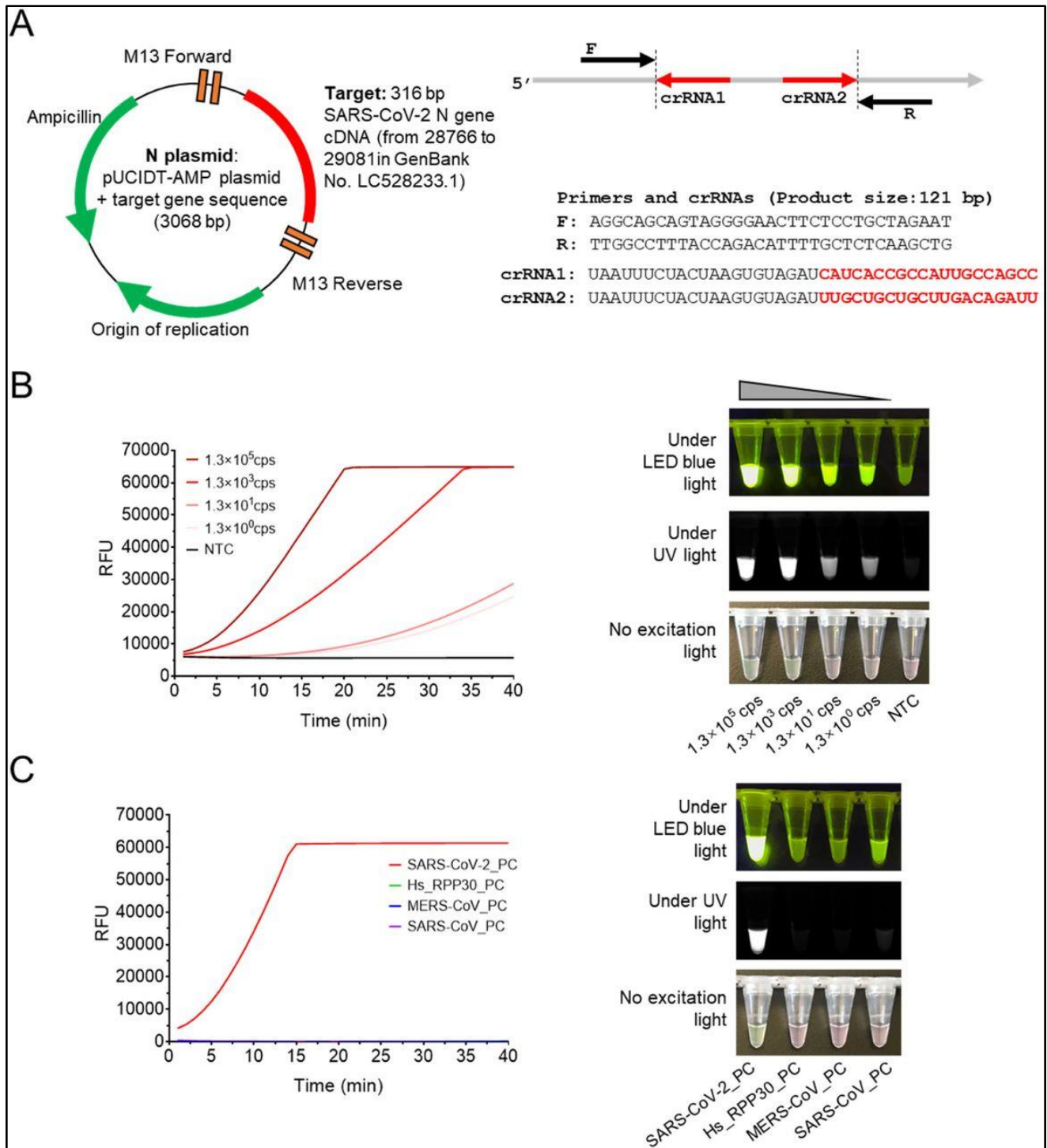


Figure 2: The AIOD-CRISPR assay for SARS-CoV-2 N DNA detection. (A) The pUCIDT-AMP plasmid is shown that contains 316 bp SARS-CoV-2 N gene cDNA (N plasmid) and the primers and crRNAs. (B) Real-time AIOD-CRISPR detection is shown with various copies of SARS-CoV-2 N DNA. (C) Specificity assay of the AIOD-CRISPR assay on SARS-CoV-2 N detection is shown [Source: bioRxiv (2020)].

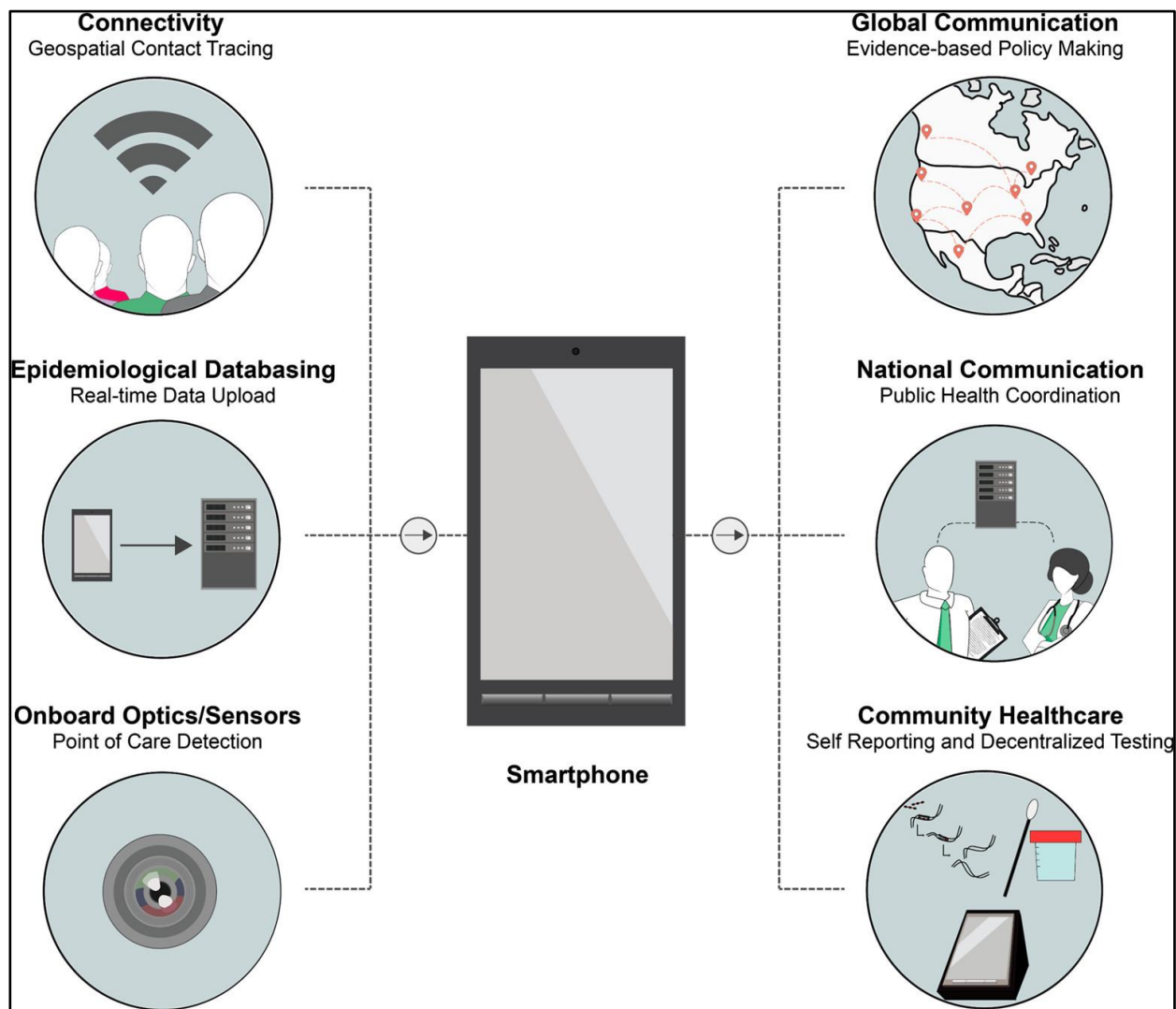


Figure 3: Schematic presentation showing the envisioned role of smartphones in diagnostics for COVID-19 [Source: ACS Nano (2020)].

Innovative Mass Surveillance and Monitoring Technology to Prevent Future Outbreaks

Studies have strongly suggested that insufficient communication and underreporting have been important factors that have contributed to some extent the global spread of COVID-19 [10]. It is believed that a robust system of networks consisting of mass surveillance with rapid diagnostics can help public health officials monitor virus spread and proactively identify areas with increasing infections. Such a system in place

can also be leveraged to anticipate surge capacity needs, and deploy needed resources to the appropriate areas accordingly. However, the functioning of such a system will be impaired in absence of clear and transparent collaboration and communications between nations at the international level, and between federal and state/principal public health laboratories, hospitals, government agencies, and communities at the domestic level [2].

Researchers are considering to employ the innovative combination of diagnostics and smartphones that is believed to provide greater communication and surveillance (Figure 3) [2]. Smartphones are considered attractive choice because they possess the connectivity, computational power, and hardware that can be facilitated for electronic reporting, epidemiological data basing, and point-of-care testing [11]. It is believed that smartphones can be made a widely accessible technology to coordinate responses that include real-time geospatial information empowering national and global health agencies to implement coordinated control strategies during large outbreaks like COVID-19 [11].

Concluding Remarks

Rapid diagnostics, surveillance and monitoring are critically important components in medical practices to deal with COVID-19 pandemic. A robust containment and mitigation system including smart, accurate and rapid diagnostics would curb the spread of highly infectious SARS-CoV-2 disease, while providing healthcare workers the necessary resources that protect the frontline workers fighting the pandemic.

References for further reading

1. World Health Organization: Coronavirus Disease (COVID-19) Pandemic, <https://www.who.int/emergencies/diseases/novelcoronavirus-2019>.
2. Buddhisha Udagama, Pranav Kadhiresan, Hannah N. Kozlowski, Ayden Malekjahani, Matthew Osborne, Vanessa Y.C. Li, Hongmin Chen, Samira Mubareka, Jonathan Gubbay, and Warren C.W. Chan, Diagnosing COVID-19: The Disease and Tools for Detection, ACS Nano, (2020), DOI: <https://doi.org/10.1021/acsnano.0c02624>
3. Li, Q.; Guan, X.; Wu, P.; Wang, X.; Zhou, L.; Tong, Y.; Ren, R.; Leung, K. S. M.; Lau, E. H. Y.; Wong, J. Y.; Xing, X.; Xiang, N.; Wu, Y.; Li, C.; Chen, Q.; Li, D.; Liu, T.; Zhao, J.; Liu, M.; Tu, W.; Chen, C. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus Infected Pneumonia. N. Engl. J. Med. (2020), DOI: [10.1056/NEJMoa2001316](https://doi.org/10.1056/NEJMoa2001316)
4. Zhu, N.; Zhang, D.; Wang, W.; Li, X.; Yang, B.; Song, J.; Zhao, X.; Huang, B.; Shi, W.; Lu, R.; et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N. Engl. J. Med. (2020), 382 (8), 727–733, DOI: [10.1056/NEJMoa2001017](https://doi.org/10.1056/NEJMoa2001017)
5. Xiong Ding, Kun Yin, Ziyue Li, Changchun Liu, All-in-One Dual CRISPR-Cas12a (AIOD-CRISPR) Assay: A Case for Rapid, Ultrasensitive and Visual Detection of Novel Coronavirus SARS-CoV-2 and HIV virus, bioRxiv (2020), doi: <https://doi.org/10.1101/2020.03.19.998724>
6. Craw, P.; Balachandran, W, Isothermal Nucleic Acid Amplification Technologies for Point-of-Care Diagnostics: A Critical Review, Lab Chip, 12, 2469 (2012), DOI: [10.1039/c2lc40100b](https://doi.org/10.1039/c2lc40100b)
7. Yang, W.; Dang, X. et. al., Rapid Detection of SARS-CoV-2 Using Reverse Transcription RT-LAMP Method., medRxiv, March 3, (2020), DOI: [10.1101/2020.03.02.20030130](https://doi.org/10.1101/2020.03.02.20030130)
8. To, K. K.-W.; Tsang, O. T.-Y.; Leung, W.-S.; Tam, A. R.; Wu, T.-C.; Lung, D. C.; Yip, C. C.-Y.; Cai, J.-P.; Chan, J. M.-C.; Chik, T. S.-H., Temporal Profiles of

- Viral Load in Posterior Oropharyngeal Saliva Samples and Serum Antibody Responses during Infection by SARS-CoV-2: An Observational Cohort Study. *Lancet Infect. Dis.* (2020), DOI: [10.1016/S1473-3099\(20\)30196-1](https://doi.org/10.1016/S1473-3099(20)30196-1)
9. Xiang, J.; Yan, M.; Evaluation of Enzyme-Linked Immunoassay and Colloidal Gold-Immunochemical Assay Kit for Detection of Novel Coronavirus (SARS-Cov-2) Causing an Outbreak of Pneumonia (COVID-19), *medRxiv*, March 1, (2020), DOI: [10.1101/2020.02.27.20028787](https://doi.org/10.1101/2020.02.27.20028787)
10. Sun, H.; Dickens, B. L. et. al., Estimating Number of Global Importations of COVID-19 from Wuhan, Risk of Transmission Outside Mainland China and COVID-19 Introduction Index between Countries Outside Mainland China, *medRxiv*, February 20, (2020), DOI: [10.1101/2020.02.17.20024075](https://doi.org/10.1101/2020.02.17.20024075)
11. Wood, C. S.; Thomas, M. R.; Budd, J.; Mashamba-Thompson, T. P.; Herbst, K.; Pillay, D.; Peeling, R. W.; Johnson, A. M.; McKendry, R. A.; Stevens, M. M. Taking Connected Mobile-Health Diagnostics of Infectious Diseases to the Field, *Nature*, 566 (7745), 467– 474, (2019), <https://doi.org/10.1038/s41586-019-0956-2>





Food & Health Science

By Shripriya Singh, PhD

Contributing Editor

Biotechnology Kiosk, 2, 4 (2020)

DOI: <https://doi.org/10.37756/bk.20.2.4.3>



The tussle between the developing adolescent brain and dietary choices: who's the target who's the trigger?

Abstract

Teen brain health and dietary choices comprise an interesting read for all. The adolescent brain is not completely developed and these underdeveloped structures largely influence behavior, cognition and dietary controls. The current article describes the unique complimentary relation between teen brain development and dietary choices. The developing teen brain is characterized by underdeveloped decision-making capabilities, heightened reward system and limited restraint which compels them to eat poorly and in turn negatively impacts the normal functioning of the neurological processes. Immature regulatory processes and underdeveloped prefrontal cortex trigger an urge to consume a calorie rich diet. In turn diet is a crucial environmental factor that affects the overall brain development. A calorie rich diet has a negative impact on the structure and function of the prefrontal cortex leading to altered signaling and neurotransmitter systems. Thus it is important to understand the neuroscience underlying the erratic and impulsive eating behavior prevalent in teenagers all across the world. Obesity is only one of the obvious external indicators of poor health observed in adolescents however, the damage is much deeper. If not corrected timely, unhealthy dietary choices can have a long lasting and irreversible negative impact on the overall brain health.

Key words: adolescent brain, dietary choices, prefrontal cortex, teen brain health.

Introduction:

"I am a grown now and can take my own decisions", well if you have heard this statement before you have definitely encountered the teenage or a teenager. A simple phrase that reflects the crucial phase of adolescence when kids are no longer behaving like kids and adulating is still far away. Parenting a teenager is a herculean task because this transition phase is marked by impulsive behavior, hormonal changes, mood swings and most importantly eating disorders. Fast food joints and cafes have thrived at the expense of the ever hungry teenagers who are constantly binging on burger, pizzazz, pasta, fries, aerated drinks and all things conventionally deemed unhealthy. Working mothers who have teenage kids are constantly worried when their children are at home in close proximity to the refrigerator. It is often said in good humor, 'protect your kitchen from the teen locusts' that shall eat away all the cake and goodies to satisfy their never ending food cravings. These cravings and dietary habits are associated with adolescence which is broadly termed as the developmental period that begins with the onset of puberty and ends with the onset of adulthood.

The World Health Organization defines adolescence as the period spanning between the ages of 10 upto 19 years. However, many argue that this period is prolonged up till early 20s due to continued physical and neurobiological development. This period is marked by heightened psychological plasticity and rapid growth which makes the adolescent susceptible to various health risks and behavioral abnormalities. Healthy dietary practice

requires stringent regulatory processes which help in curbing the urge to consume calorie dense and highly palatable foods. In one of our previous articles entitled 'Over Indulgence in Fast Food Comes with a Price: It Can Cost You Your Vision' we had discussed the relevance of brain development during adolescence and how the prematurely developed prefrontal cortex affects addictions, erratic behavior and dietary habits.

The prefrontal cortex is an area of the brain which is responsible for self-regulation and does not mature until our early 20's. This is directly linked with the underdeveloped regulatory processes which are imperative in governing decision making and dietary behavior. In this article we shall discuss the highlights of an important study by a group of researchers, namely Cassandra Lowe, J. Bruce Morton and Amy Reichelt published in 'The Lancet Child & Adolescent Health'(1). The article traces the dual susceptibility of the developing teen brain with underdeveloped decision-making capabilities, heightened reward system and limited restraint which compels them to eat poorly and in turn negatively impacts the normal functioning of the neurological processes.

Understanding the intricate balance between adolescent brain development and diet

Adolescence is a period marked by continued neuroplasticity and psychological development. The brain undergoes extensive functional and neurobiological remodeling predominantly in regions responsible for reward seeking and behavioral control, namely dopaminergic reward pathways and

the prefrontal cortex. The developing adolescent brain is responsible for facilitating planning, reasoning, impulse control and cognitive flexibility.

Brain development is often influenced by the environment in a process known as experience dependent neuroplasticity that helps in shaping the development of neurocircuits by local remodelling. This involves the dynamic reorganization of brain functions and structures in response to environmental inputs. The presynaptic and postsynaptic neuronal connections are strengthened by environmental stimuli in a process called long-term potentiation. Repetitive exposure to the same environmental stimuli and experience stabilizes the neuronal connections and further influences dendritic and axonal growth patterns. Further neurotransmitters such as dopamine play a role in modulating inter-individual variability in cognitive abilities and functional activation patterns and neuroplasticity (2). Diet is one such crucial environmental factor that affects the developing brain. It is further documented that individual differences in lateral prefrontal

cortex input are responsible for triggering a drive for the over consumption of hyper-palatable calorie-dense foods. This calorie rich diet has a negative impact on the structure and function of the prefrontal cortex leading to altered dopamine signaling and inhibitory neurotransmitter systems within this area of the brain (1). This eventually causes an impaired cognitive control further driving the excessive and persistent intake of hyper-palatable calorie dense foods. Therefore diet and development are linked intricately in such a way that they mutually impact each other. Since developmental studies are ethically challenging to be carried out in human beings majority of the data is generated on the rodent models. Similarly research has shown that when rodents are fed on a calorie dense diet during their developmental stages (equivalent to the adolescent stage in humans) it had a persuasive functional effect on the brain causing severe deficits in learning, memory and cognitive control (3). Figure 1 shows the time lapse images of the cortical development in humans from age 5 up till age 20.

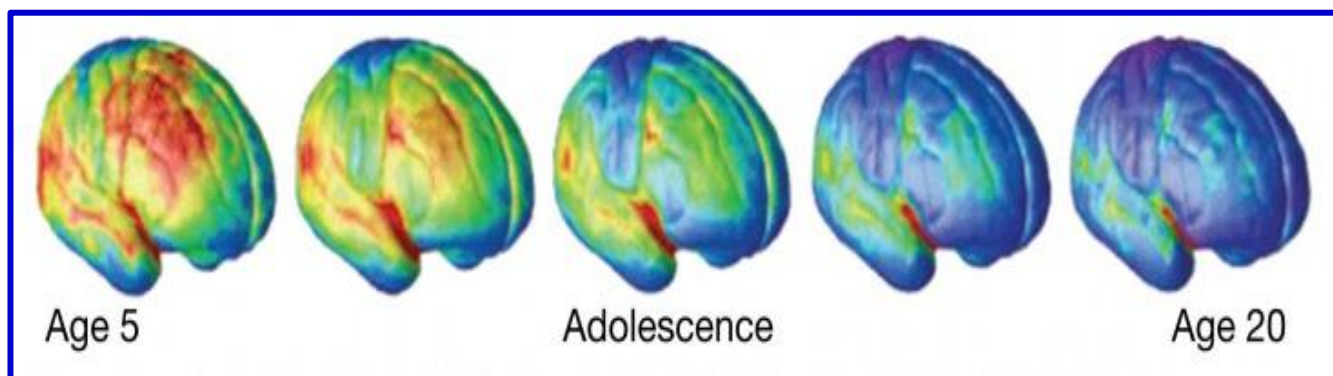


Figure1: Image shows the dynamic mapping of the human cortical development. Source- *Proceedings of the National Academy of Sciences* , 2004 (4)

This period of adolescence is characterized by heightened emotionality where the reward drive is greater as compared to the cognitive control. It is also a stage where the limbic regions reach maturity while the prefrontal cortex is still developing. This difference in the maturation times creates an imbalance between top-down cognitive regulation (from the prefrontal cortex) and the reward-driven behaviors (limbic system), which is manifested as augmented sensitivity to rewards and diminished behavioral

regulation. The underdeveloped connectivity between the amygdale (a key node of the limbic system) and the prefrontal cortex during adolescence is responsible for the low behavioral regulation in rodents and humans (5). This imbalance between top-down regulatory regions and subcortical regions might trigger excessive consumptive behaviors, motivated by food rewards, binge eating and emotional eating which are the major risk factors for obesity.

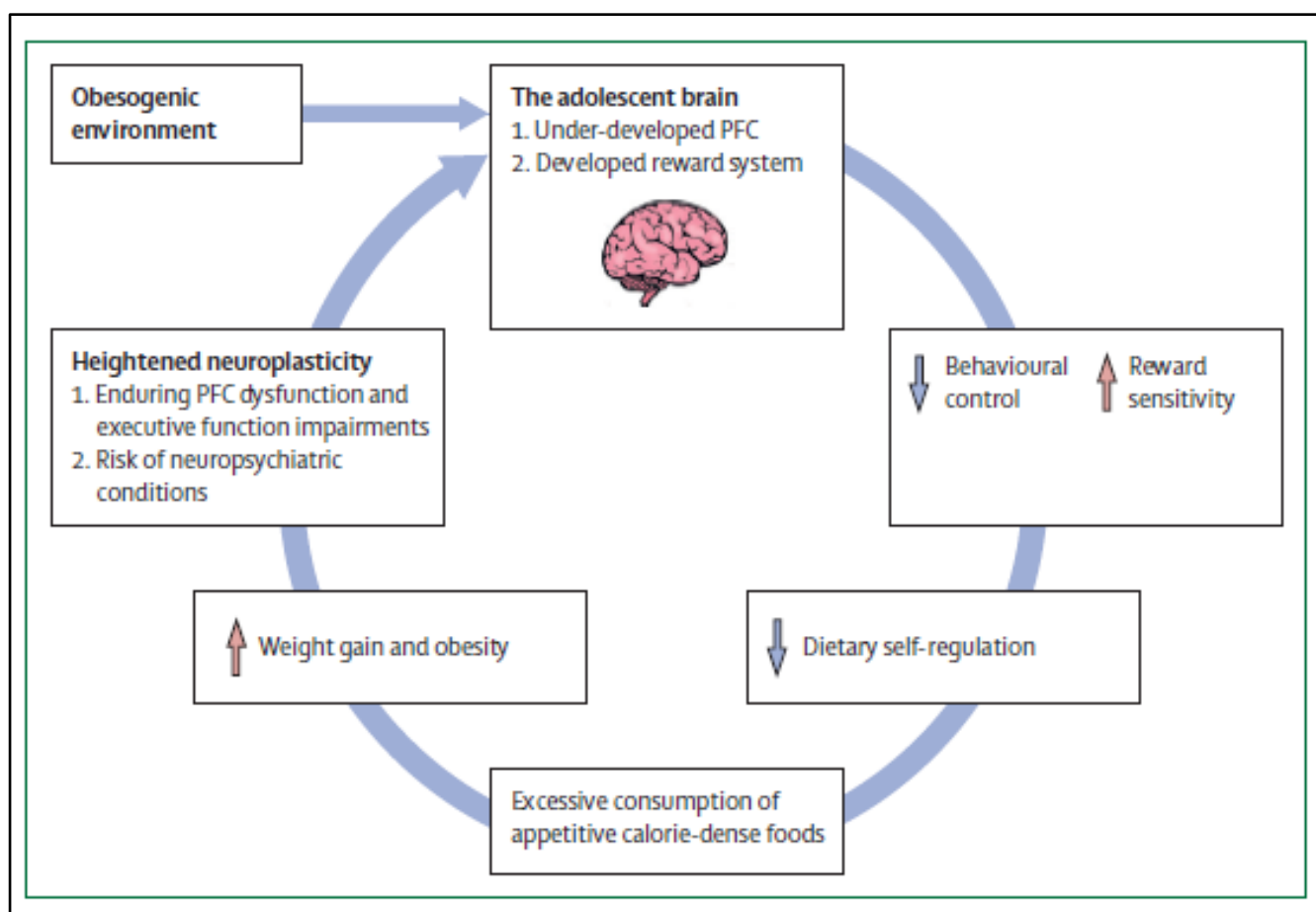


Figure 2: Diagrammatic impact of the obesogenic environment on the developing adolescent brain. Source: *The Lancet Child & Adolescent Health*, 2020 (1)

The increased level of food consumption in teenagers can be attributed to the elevated metabolic activity leading to rapid development and physical growth that comes

with puberty. These developmental changes include gain in fat mass in female adolescents and muscle mass in male adolescents. Rapid growth is observed

across species, whereby adolescent rats have shown the highest caloric intake during this period relative to their bodyweight. It is observed that increased metabolic activity can partially accommodate for excessive caloric load from high fat diets without the considerable weight gain in teenagers, therefore adolescence might provide partial protection against developmental obesity. However, behavioural habits such as diet acquired during adolescence might potentiate overconsumption of calorie-dense foods into adulthood, as the health consequences might not be immediately apparent (1). Thus weight gain alone is not an indicator of bad health instead it's the overall quality of diet that needs to be considered for the development of the teen brains. Figure 2 summarizes the effect of a calorie rich diet on the developing adolescent brain.

Concluding remarks

Discussing teen brain health and the effect of diet is a never ending topic which has intrigued researchers, medical practitioners and health experts. We have made a small effort through this article to highlight the relevance of dietary choices during the growing up years and how they affect the adolescent brain development. Diet and brain development are linked in a way that both influence the effect of the other. Neuroscience has often given us crucial leads in cases where normal medical explanations fail. No doubt brain is one of the most complex organs of our body and will continue to intrigue neuroscientists even in times to come. Every human behavior and action can be explained if we delve at the root cause of the problem and investigate it from

a scientist's perspective. Next time you feel agitated at a teenager for not behaving like a responsible adult do reflect at the possibility of an amateur teen brain that is still developing. It is the responsibility of every parent to understand that adolescents need to be handled with care because they themselves are not completely aware of the biological changes affecting their growth and mental well being. At the same time it is important to ensure that adolescents understand the detrimental effects of calorie dense foods that can harm and even permanently damage their brain growth. Obesity is only a superficial problem that is associated with an unhealthy diet but the problems associated with fat and sugar rich food are deeper and irreversible. Exercise, dietary control and self-discipline are the most effective ways of ensuring a healthy growth during adolescence. Next time your teenage kid insists on gorging his favorite piece of junk food, do not lose your cool instead give him a small dose of neuroscience.

References

1. Lowe CJ, Morton JB, & Reichelt AC. Adolescent obesity and dietary decision making—a brain-health perspective. *The Lancet Child & Adolescent Health*. (2020), [https://doi.org/10.1016/S2352-4642\(19\)30404-3](https://doi.org/10.1016/S2352-4642(19)30404-3)
2. Reichelt AC. Adolescent maturational transitions in the prefrontal cortex and dopamine signaling as a risk factor for the development of obesity and high fat/high sugar diet induced cognitive deficits. *Frontiers in behavioral neuroscience*. Oct

13;10:189. eCollection (2016),
doi: [10.3389/fnbeh.2016.00189](https://doi.org/10.3389/fnbeh.2016.00189)

3. Labouesse MA, et al. Hypervulnerability of the adolescent prefrontal cortex to nutritional stress via reelin deficiency. *Molecular Psychiatry* 22(7):961-971, (2017), doi: <https://doi.org/10.1038/mp.2016.193>
4. Gogtay N, et al. Dynamic mapping of human cortical development during childhood through early adulthood.

Proceedings of the National Academy of Sciences 101(21):8174-8179, (2004), <https://doi.org/10.1073/pnas.0402680101>

5. Gee DG, et al. A developmental shift from positive to negative connectivity in human amygdala–prefrontal circuitry. *Journal of Neuroscience* 33(10):4584-4593. (2013), DOI: [10.1523/JNEUROSCI.3446-12.2013](https://doi.org/10.1523/JNEUROSCI.3446-12.2013)





Opinion

By Balam Mohapatra, PhD
Contributing Editor



A Proposed Herbal Formulation: Targeting to Strengthen Inner Immunity to Fight Infectious Diseases

Rationale of the Herbal Medicine

Use of herbal medicine largely relies on bioactive formulations of medicinal herbs, which can provide a viable alternative for elevating person's targeted immune response and reducing pathophysiology (Samy et al. 2008; Agrawal et al. 2010). Herbal medicines could be beneficial in improving the immune system and stimulating immunomodulatory response of human body to fight against infectious diseases (de Meija et al. 2009; Lee et al. 2015). Especially, in these difficult times of COVID-19 pandemic, use of appropriate herbal formulations could be an advantageous pathway to boost the immune system to mitigate the disease. This could be an alternative form of therapeutics in the absence of any proven therapeutics or vaccines that are not yet available to break the infection chain of Coronavirus.

Proposed Herbal Formulation

We propose most specifically, the combined use of fresh Ginger, basil leaves, black

pepper, and honey, which are considered to be of high medicinal values. Various scientific literatures have proved the antiviral activity of fresh ginger and basil against human respiratory syncytial virus (HRSV), Influenza (Cold/Flu), and others viral infections those affecting human upper and lower respiratory tracts through cell lines (HEp-2, A549) based research (Denyer et al. 1994; Chrubasiket al. 2005; Sookkongwaree et al. 2006; Schnitzler et al. 2007; Koch et al., 2008). The active compounds have shown to stimulate anti-viral cytokines, reducing virus-induced plaque formation, and inhibition of viral attachment to the human receptors (like ACE2 in case of Novel Coronavirus), and internalization as well as excellent antimicrobial against cold causing bacterial pathogens like *Streptococcus* spp. (sore throat) (Wang et al. 2011; Chang et al. 2012). Among several other beneficial traits, reducing anti-inflammatory activities by inhibiting synthesis of prostaglandins and/or cytokines, chemokines, direct and indirect anti-hypertensive effect, gastrointestinal

protection against ulcer and emesis, antioxidant, and radioprotective effects have been proved for bioactive compounds of both ginger and basil (Chrubasiket al. 2005; Ali et al. 2008; Chang et al. 2013). Taking cue from

previous studies, we propose a formulation mix for antiviral herbal decoction. We believe that with prescribed dose that might reduce the chance of viral infection in the respiratory system could be beneficial for strengthening the host immunity.

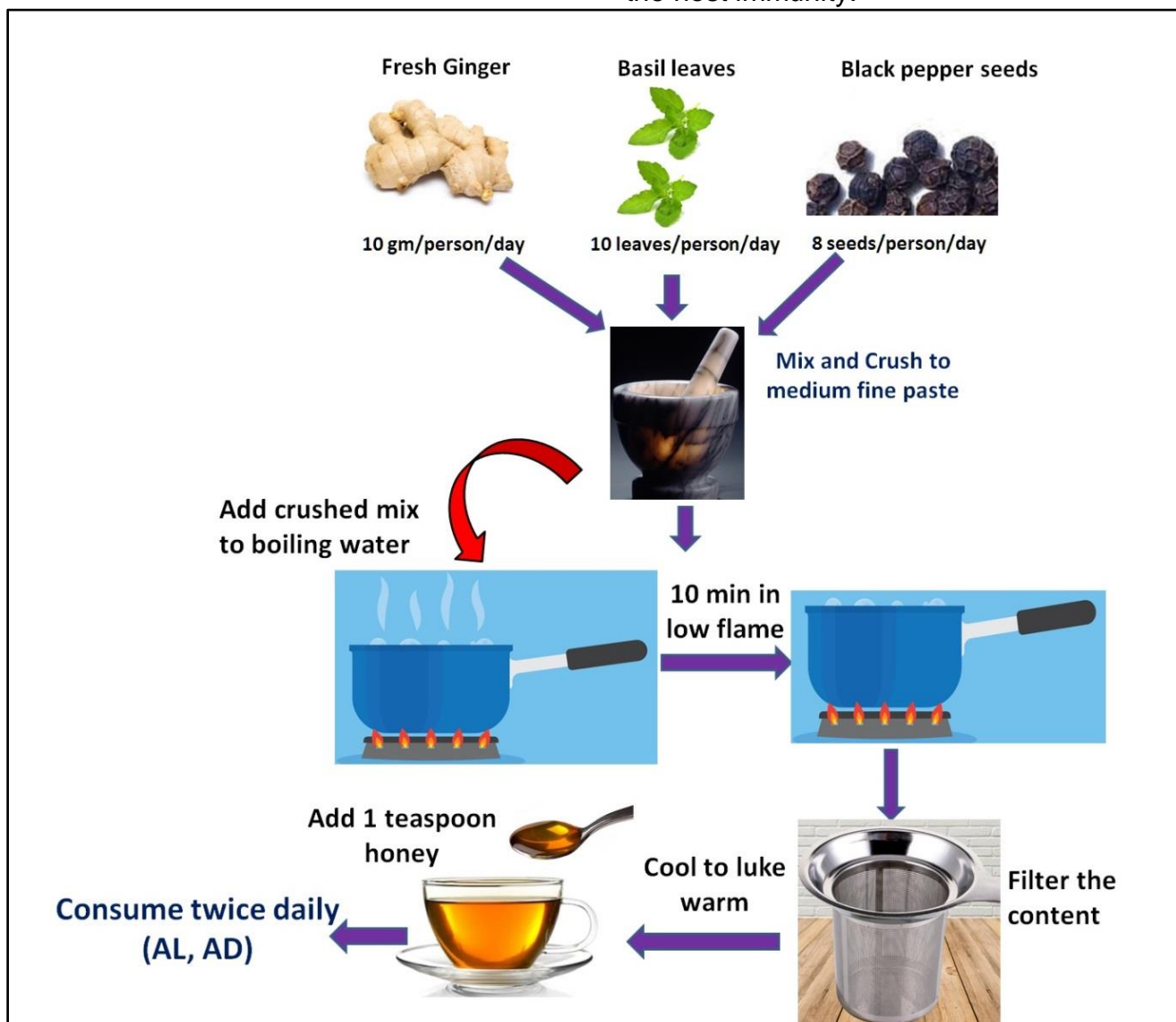


Figure 1. Depicting the easy steps for preparation of herbal immune booster to be taken at home to increase innate immunity to fight against infectious disease including COVID-19. AL: (After Lunch); AD: (After Dinner).

This herbal immune booster could be beneficial in countries such as India, where people are at home following lockdown and those who are prone to respiratory infections.

For average person, a suggested does is about 250 mL of the medicine consisting of, fresh ginger 10 gm, 10 basil leaves and 8 pepper balls. The solution is prepared by

boiling for 15 min after crushing all the components. The prepared liquid is subsequently filtered, which is followed by adding 1 teaspoon honey. The prepared medicine is then mixed and used 2 times in a day. The pictorial (diagrammatic) illustration of the process to make the decoction is presented in Figure 1.

Doses, Age Groups and Potential Side Effects

This decoction is suitable for age group > 15-16 years to an elder population of 65-70 age-group. For adults (> 15- 40 years), half-cup (around 50 mL) of decoction is appropriate, twice a day, after lunch and dinner. For older age group (> 40-70 years), less than a full cup (75 % of a cup, around 70 mL) of decoction is appropriate, once a day. Further,, as the decoction works as a mild laxative, it may stimulate/alter the bowel movement and make it the bowel disturbed , if consumed in excess. For better results, a tiny quantity of lemon juice can be added for supplementing vitamin-C to the body, as vitamin-C is found to be effective during flu/other viral infections. Drinking higher amount of water is also recommended, if this decoction is consumed twice a day.

References for Further Reading

1. Agarwal, S., Khadase, S., Talele, G. Bioactive immunomodulatory fraction from *Tridax procumbens*. *Asian journal of biological sciences*, 3(3), 120-127, (2010).
2. Ali, B.H., Blunden, G., Tanira, M.O., Nemmar, A. Some phytochemical, pharmacological and toxicological properties of ginger (*Zingiber officinale* Roscoe): a review of recent research. *Food and Chemical Toxicology* 46,409–420, (2008).
3. Chang, J.S., Wang, K.C., Shieh, D.E., Hsu, F.F., Chiang, L.C. Ge-Gen-Tang has anti-viral activity against human respiratory syncytial virus in human respiratory tract cell lines. *Journal of Ethnopharmacology* 139, 305–310, (2012).
4. Chrubasik, S., Pittler, M.H., Roufogalis, B.D. *Zingiberis rhizoma*: a comprehensive review on the ginger effect and efficacy profiles. *Phytomedicine* 12,684–701, (2005).
5. de Mejia, E.G., Ramirez-Mares, M.V., Puangpraphant, S. Bioactive components of tea: cancer, inflammation and behavior. *Brain, behavior, and immunity*, 23(6), 721-731, (2009).
6. Denyer, C.V., Jackson, P., Loakes, D.M., Ellis, M.R., Young, D.A. Isolation of anti rhinoviral sesquiterpenes from ginger (*Zingiber officinale*). *Journal of Natural Products* 57, 658–662, (1994).
7. Koch, C., Reichling, J., Schneelee, J., Schnitzler, P. Inhibitory effect of essential oils against herpes simplex virus type 2. *Phytomedicine* 15, 71–78, (2008).
8. Lee, C.C., Chen, Y.T., Chiu, C.C., Liao, W.T., Liu, Y.C., Wang, H.M.D. *Polygonum cuspidatum* extracts as bioactive antioxidant, anti-tyrosinase, immune stimulation and anticancer agents. *Journal of bioscience and bioengineering*, 119(4), 464-469, (2015).
9. Samy, R.P., Pushparaj, P.N., Gopalakrishnakone, P. A compilation of

- bioactive compounds from Ayurveda. *Bioinformation*, 3(3), 100, (2008).
10. San Chang, J., Wang, K. C., Yeh, C. F., Shieh, D. E., & Chiang, L. C. Fresh ginger (*Zingiber officinale*) has anti-viral activity against human respiratory syncytial virus in human respiratory tract cell lines. *Journal of ethnopharmacology*, 145(1), 146-151, (2013).
 11. Schnitzler, P., Koch, C., Reichling, J. Susceptibility of drug-resistant clinical herpes simplex virus type 1 strains to essential oils of ginger, thyme, hyssop, and sandalwood. *Antimicrobial Agents and Chemotherapy* 51, 1859–1862, (2007).
 12. Sookkongwaree, K., Geitmann, M., Roengsumran, S., Petsom, A., Danielson, U.H. Inhibition of viral proteases by Zingiberaceae extracts and flavones isolated from *Kaempferia parviflora*. *Pharmazie* 61, 717–721, (2006).
 13. Wang, K.C., Chang, J.S., Chiang, L.C., Lin, C.C. Sheng-Ma-Ge-Gen-Tang (Shomakakkon-to) inhibited cytopathic effect of human respiratory syncytial virus in cell lines of human respiratory tract. *Journal of Ethnopharmacology* 135, 538–544, (2011).





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 recent biotechnology advances.



Dr. Megha Agrawal
Co Editor-in-Chief



Dr. Shyamasri Biswas
Co Editor-in-Chief

Neurology

Klotho-VS heterozygosity protect against Alzheimer Disease (AD)

It has been known for decades that one main contributor to the neurodegenerative disorders is a gene variant apolipoprotein e4 (APOE4) that is found three times higher in patients with Alzheimer's disease (AD) than among people without the disease. This has put research focus on the identification of genetic factors that interact with the APOE4 allele to reduce risk for Alzheimer disease (AD) with goals to accelerate the search for new AD drug targets. Researchers have shown that Klotho-VS heterozygosity (KL-VSHET+ status) can protect against aging-associated phenotypes and cognitive decline. However, it is not yet clear whether it protects individuals who carry APOE4 from AD.

Now investigators in the United States have reported in a new study that people with a high risk gene variant for AD are protected from the debilitating effects of AD, if they also

carry a variant of a completely different gene (klotho variant--a genetic status referred to as heterozygous). Their findings were recently published April 13 in JAMA Neurology (Association of Klotho-VS Heterozygosity With Risk of Alzheimer Disease in Individuals Who Carry APOE4, JAMA Neurology, 2020; DOI: 10.1001/jamaneurol.2020.0414).

Based on their study, researchers suggested that a substantial fraction of the estimated 15% of Americans carrying the high-risk gene variant are protected to some degree from AD by a variant of the other gene. Researchers envision that their study will pave the way for a better understanding on how the protective gene variant works, which may also lead to shed lights on the functions of ApoE4's debilitating effect on cognition. This eventually may help identifying therapeutic targets for the prevention or mitigation of those effects causing AD.

Regenerative Medicine and Tissue Engineering

Fibrous 3D structure of keratin protein scaffolds for advanced tissue engineering

In the field of biomedical science, the regeneration of tissue is an important subject of research in regenerative medicine and tissue engineering. It is highly desired to have the ability to regenerate tissue at the site of injury or wounds caused by burns or diseases such as diabetes. Biomaterials that are employed in such tissue engineering require complementary key ingredients.

These include biologically compatible scaffolds that can be easily adopted by the body system without rejection. Biocompatibility is critically important as it allows suitable cells in the scaffold including various stem cells effectively replace the damaged tissue without adverse consequences. In addition, scaffolds are required to mimic the structure and biological function of the native extracellular matrix especially at the side of injury for effective

regeneration of tissues. These are challenging tasks to achieve.

In a new study, researchers at Mossakowski Medical Research Center of the Polish Academy of Science have reported a simple method for preparing 3D keratin protein scaffold models that can be leveraged for the effective regeneration of tissue. They published their research article in the De Gruyter open access journal Open Medicine (Can keratin scaffolds be used for creating three-dimensional cell cultures? Open Medicine, 2020; 15 (1): 249 DOI: 10.1515/med-2020-0031).

The researchers studied the development of three-dimensional cell cultures derived from fiber keratin scaffolds from rat fur. They demonstrated the ability of cells to grow up and form the 3D colonies on rat F-KAP for several weeks. This was achieved without compromising the morphological changes of the cells and with no observed apoptosis. This study showed the absence of morphological changes in cells and the lack of apoptosis, in addition to the low immunogenicity and biodegradation of KAP scaffolds. This makes the scaffolds made of fiber keratin very promising for tissue engineering in future clinical applications.

Nutritional & Environmental Biotechnology

Climate friendly process of making protein powder using fava beans

People across the globe are increasingly recognizing the important role of plant proteins in human nutrition. This requires more sustainable options to produce plant based proteins that would be able to provide alternative to animal protein.

Soy-based protein is a popular choice in vegetarian cooking. However, the processing of soy to produce protein places great strain on the environment. A collaborative team of Researchers from Denmark, Ireland and Germany recently

demonstrated the utility of fava beans that hold great promise as a non-soy source of plant protein. Moreover, favas are a better alternative for the environment. Researchers showed a method of processing fava beans in such a way that allowed to produce a concentrated protein powder from fava beans. Their research was published in Foods (Comparison of Faba Bean Protein Ingredients Produced Using Dry Fractionation and Isoelectric Precipitation: Techno-Functional, Nutritional and Environmental Performance, Foods, 2020; 9 (3): 322 DOI: 10.3390/foods9030322).

Biorecycling & Microbiology

Microbe helps degrade polyurethane-based plastics

Polyurethane (PU) has a vast array of applications ranging from refrigerators and buildings to footwear and furniture to

numerous other applications due to its attractive properties such as lightweight, insulating and flexibility. However, polyurethane is not biodegradable. It is not energy-intensive to recycle or destroy polyurethane due to the fact that these plastics are thermosetting polymers that do not melt easily when heated. The waste product usually ends up releasing a number of toxic chemicals, some of which are carcinogenic into the landfills. This creates a huge environmental hazard.

A viable solution to this complex environmental problem is leveraging some microorganisms that are capable of metabolizing these hazardous compounds and degrading the plastic waste in the process. Scientists in Germany have identified a useful bacterium that could be used to help break down polyurethane-based plastics for future bio-recycling. German researchers recently reported in the journal *Frontiers in Microbiology* (Toward Biorecycling: Isolation of a Soil Bacterium

That Grows on a Polyurethane Oligomer and Monomer, *Frontiers in Microbiology*, 2020; 11 DOI: 10.3389/fmicb.2020.00404) about their discovery of a strain of bacteria capable of degrading some of the chemical building blocks of polyurethane.

The researchers demonstrated the utility of the bacteria to recycle these compounds as a sole source of carbon, nitrogen and energy, which paved an important way forward to reuse hard-to-recycle PU products. The German team showed the capability to isolate a bacterium, *Pseudomonas* sp. TDA1, from a site rich in brittle plastic waste that was subsequently leveraged to attack some of the chemical bonds that make up polyurethane plastics.

Compiled and Edited by

Dr. Megha Agrawal & Dr. Shyamasri Biswas

Co Editors-in-Chief



Biotech and Pharma Industry Roundup

Dynavax and Sinovac to jointly develop COVID-19 vaccine candidate

In a recent announcement, California-based Dynavax Technologies has partnered with Sinovac Biotech to develop a vaccine candidate against COVID-19. The two companies are supposed to evaluate the combination of Sinovac's chemically inactivated coronavirus vaccine candidate, with Dynavax's advanced adjuvant, CpG 1018 [Source: <https://www.biospace.com/>].

Eagle Pharma to test MH Drug Ryanodex against COVID-19

Eagle Pharmaceutical recently demonstrated in a controlled laboratory test, the efficacy of their malignant hyperthermia treatment Ryanodex (dantrolene sodium) that inhibited the growth of SARS-CoV-2, the virus causing the COVID-19 pandemic. In the in-vitro tests, Ryanodex showed antiviral activity and a lack of cytotoxicity. With this success, the company now hopes to launch a clinical trial testing the efficacy of the drug in patients in the near future [Source: <https://www.biospace.com/>].

Meningococcal Vaccines expected to touch US\$ 9 billion by 2026

Bacteria Neisseria meningitidis causes meningococcal disease. This disease occurs throughout the world especially in the developing world. Typical symptoms include inflammation in the membranes of the brain

and spinal cord which is characteristic of meningitis. The meningococcal vaccines market is pretty vast with a lot of potential to make its footprints even larger in the future that is expected to reach \$9 billion by 2026. This vaccine exists in the market and doing a great business due to its utility and need for preventing the incidence of this deadly disease [Source: <https://www.biospace.com/>].

AstraZeneca's checkpoint inhibitor Imfinzi shows promise in lung cancer

The company recently reported that high-level data analysis from its Phase III CASPIAN trial demonstrated that Imfinzi (durvalumab) in combination with standard-of-care chemotherapies suggested a clinically meaningful and sustained overall survival benefit in patients with extensive-stage small cell lung cancer treated in the first-line setting [Source: <https://www.biospace.com/>].

UroGen's Jelmyto gets expedited approval from FDA for Urothelial Cancer

The U.S. Food and Drug Administration (FDA) recently approved on fast track UroGen Pharma's Jelmyto (mitomycin) for pyelocaliceal solution for adults with low-grade upper tract urothelial cancer (LG UTUC). The fast track approval was granted on the basis of data from the Phase III OLYMPUS trial. Jelmyto is made up of mitomycin, which is a well-known

chemotherapy agent, and sterile hydrogel. The drug is processed using the company's proprietary sustained release RTGel technology. Jelmyto is the first and only non-surgical treatment for patients and is designed to allow longer exposure of urinary tract tissue to mitomycin [Source: <https://www.biospace.com/>].

SMA drug produced by Roche gets a boost with new study data

Roche recently announced that its experimental drug risdiplam helped babies with the severest form of the rare disorder spinal muscular atrophy sit unassisted one year after beginning treatment. This finding should help Roche's case for approval now before the FDA. It is expected that if this drug is finally approved by the FDA, risdiplam will enter a highly competitive field already served by two injectable drugs, Biogen's Spinraza and Novartis' gene therapy Zolgensma [Source: <https://www.biopharmadive.com/>].

AstraZeneca to study leukemia drug as COVID-19 treatment

In an effort to repurpose existing therapies for the fast-spreading disease, AstraZeneca will go into clinical study for a leukemia drug that could help calm the overactive immune response seen in some patients with COVID-19 [Source: <https://www.biopharmadive.com/>].

Gates, Wellcome donate \$125M to speed coronavirus treatments

Three philanthropic foundations The Bill and Melinda Gates Foundation, Wellcome and

the Mastercard Impact announced that they would spend up to \$125 million to help advance treatments for the new coronavirus in a collaborative effort that would engage regulators, non-governmental organizations and the biopharma industry. The joint effort known as the COVID-19 Therapeutics Accelerator is designed to encourage research and development of existing drugs that can be repurposed for the coronavirus as well as new agents not yet authorized for use in humans [Source: <https://www.biopharmadive.com/>].

Investors pouring cash to counter cancer genes

It is known for years that a family of genes that, when mutated, turn regular cells cancerous. There has been recent progress in developing drugs that can effectively silence those genes. This has fueled investor optimism in companies going after these genes that are known as RAS. The most recent example of investments comes from a California based biotech company named Revolution Medicines that has raised \$238 million through an initial public offering. RAS genes are known to make special proteins that regulate how a cell grows, specializes and divides. One of these proteins, K-ras, has drawn a particularly large amount of attention for R&D. and Amgen, the country's largest biotech has released data showing an experimental drug appeared to stabilize disease in a small group of lung cancer patients with KRAS gene mutations. This has further fueled extensive R&D in this area [Source: <https://www.biopharmadive.com/>].

Roche presents biomarker for checkpoint block blockade

Researchers at Swiss pharma giant Roche AG have demonstrated a subpopulation of dendritic cells that determines how cancer patients respond to immune checkpoint inhibitors [Source: <https://european-biotechnology.com/>].

French company Stilla raises €20m in series B financing round

French biotech company Stilla Technologies SA raised €20million in a Series B funding to boost digital PCR-based genetic testing [Source: <https://european-biotechnology.com/>].

Dutch Biotech Company HALIX B.V. to produce vaccines against COVID-19

Dutch CDMO HALIX B.V. has entered in a research consortium coordinated by the University of Oxford, to provide GMP-compliant production of Vaccitech Ltd's COVID-19 vaccine (ChAdOx1 nCoV-19) targeting the viral spike protein [Source: <https://european-biotechnology.com/>].





Advertising rates for the magazine:

Top Banner..... 728 pixels wide x 90 pixels high (includes URL link)

Medium Banner.....400 pixels x 90 pixels (includes URL link)

Please supply animated banners as gifs. Static banners may be supplied as gifs, PNGs or JPEGs. All banner files, static or animated, should be kept to 75k or below.

Top Page Banner Position: \$600 per month

Middle Page Banner Position: \$350 per month

Side and Bottom Page Banner Position: \$250 per month

General AD Rates for the Magazine

	Per month rates
Full Page	\$1000
Half Page	\$700
1/4 th Page	\$500

For all production related questions or sending your ads, please e-mail or call our production department: E-mail: sales@biotechkiosk.com; Phone: 386-518-9411.