

CCMB
COVID-19
CHRONICLES

PREFACE

The last four months have been unprecedented at CCMB, much like in most parts of the world. While we all had our own struggles, the sense of community that emerged here will remain a memory to cherish.

During this period, we have worked incessantly in coordination with the state and central government. This has helped us stay relevant with our work in mitigating COVID-19. However, this has also meant for our people to go out of their way to contribute in the cause. Our students guided by a very able team went out of their way to set up quality COVID-19 testing centre. The CCMB community kept itself apprised of the huge infodemic from all over the world. These experiences made our researchers, young and the more experienced, ponder and work on different ways of contributing in every possible way to the COVID-19 fight in India. This included developing newer ways of testing, culturing the virus, minting collaborations to develop and test therapeutics to developing guidelines for other

partners in this crisis.

To be able to do this in a pandemic requires coordination beyond the lab spaces of CCMB. Our IT support built online processes for the institute quickly. The Administration and Purchase teams followed up the procurement of resources. The canteen and housekeeping worked every single day with limited staff to provide for everyone. The security braved reception of testing samples in CCMB every single day. Guest house arrangements were made for those who needed it. Our doctors were available for timely advice. Our research facilities took every care to ensure that the ongoing experiments were least hampered. The list can go on.

Probably what will remain on my mind is the sense of oneness that the crisis has taught many of us. For CCMB, it was a humble reminder that it is all the people here who make who we are.

RAKESH K MISHRA
DIRECTOR, CCMB

OVERVIEW OF CCMB'S ACTIVITIES

APR

TRAINING

Trained more than 200 people from CCMB and other organizations in COVID-19 testing

TESTING

Begins with 25 volunteers with the testing capacity of 100 samples a day

KIT VALIDATION

Recognized as one of the Centres of Excellence to validate testing kits by ICMR

GENOME SEQUENCING

Sequenced more than 300 genome samples of coronavirus so far, analysed the spread of its different populations

VIRUS CULTURING

Coronavirus grown in cell culture are now used for drug testing, developing vaccines and antisera

MAY

PARTNERSHIPS

with VINS BioProducts, INTEL, IIT, Bharat Biotech, Syngene among others

SUPPORT TO MSME

Support to and collaboration with biotech startups to develop indigenous and better ways of COVID-19 testing

Encourages the research groups at CCMB to devise newer strategies of testing

JUNE

MASS SURVEILLANCE

Pilot run of Next Gen Sequencing based testing strategy begins

Development of hybridomas for antibody-based tests begins

IMPROVED TESTING

Testing capacity improved to 450 samples a day

~10,000 samples tested for COVID-19

Simpler and faster testing strategy awaiting ICMR approval

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Looking at
the larger
picture

ARCHANA B SIVA



Being involved in CCMB's efforts in the COVID-19 fight has been a very gratifying journey; from a point where I was only hearing and reading about the pandemic spread in the media to now having a folder named "COVID" right on my desktop!

The COVID-19 chapter of my life started on March 18th, 2020 with the co-ordination of Technical Trainings for Telangana state hospitals staff as well as our own volunteers for COVID-19 diagnostics. Starting with a mere 25 formal numbers but extremely dedicated PhD students, we took the lead on setting up a COVID-19 testing and training centre in an academic research institute. After all, it does meet CCMB's commitment to the nation of creating trained human resources. My profile as the Skill Development coordinator helped here.

We made training material for circulation, which went to near and far off places; educating the testing personnel on the molecular biology and biosafety aspects of COVID-19 Diagnostics. We gave orientation and hands-on training to technical people from multiple hospitals (government & private), research institutes, universities in the following days. We realized the importance of prior assessment of their skill sets to customize their training session. While those from the hospitals needed training on the molecular biology, the ones in research institutes needed a strict orientation on biosafety aspects while working with highly infectious agents. The trainings continue at CCMB as the need for testing has only increased.

With trainings on one side, we started receiving samples for testing, starting on 30th March. The Testing Lab was a reality now – something neither CCMB nor perhaps any of its

members had done before! There was anxiety, patriotism, excitement, duty, among much that the team felt. But it was time to test our limits, like everyone else in the game.

And CCMB rose to the occasion on the strength of its people including their families.

COVID-19 Diagnostics was arguably the most demanding and elaborate of all the activities. It required co-ordination from end-to-end. We needed to apply the golden rules of management, gradually iron out the differences in the team while keeping the big picture in mind. From receiving information and samples from districts to reporting the result in the promised turn-around-time, CCMB achieved it all. Numbers say a lot - from doing 100-120 samples in 24 hours in April, we expanded ourselves beautifully by testing almost 4 times more in same 24 hours in July 2020. The team grew with newer members. Quantity, thankfully, did not compromise the quality. All of us had a singular goal – to focus on improving testing abilities across the country. We are now on a sustained mode to do COVID-19 testing for as long as the nation needs.

This also facilitated my involvement in research on microbiome, in the context of COVID-19 infection. A topic close to my heart, this was an icing on the cake.

Be it testing or training or research or management, I did it all. It has been a great give and take period; give whatever I could to make things work and take whatever I could to sharpen my skills. It has truly been a phase of my spiritual growth that I feel privileged and proud of.



The task looks much bigger but when many people join hands, it is only a matter of implementing. Every day new ideas, new strategies and new lessons, there is no end to the lessons learnt. One of the biggest learning is how science can contribute in a big way to the society and what exactly researchers can do. Being at the thick of the COVID-19 automatically converts anyone into a multi-tasker, which is useful in the long run.

Santosh Kumar Kuncha



This pandemic time taught me that the best way to protect yourself is to protect the people surrounding you. Perhaps this is the way of survival during critical times. I feel extremely lucky to get the opportunity to be part of different SARS-CoV-2 related works at CCMB.

P Sai Uday Kiran

Biosafety in
the COVID-
19
workspace

RAGHUNAND TIRUMALAI

As CCMB began to formulate its response to the COVID-19 pandemic, which included setting up a testing lab and initiating research on the biology of the virus, we were cognizant of the fact that having in place all the elements of biosafety, was going to be critical to this process. The fact that we had an active infectious disease program with fully functional containment laboratories where pathogenic bacteria, viruses and parasites were routinely handled, made this task considerably simpler. Our prior experience in this domain, allowed us to seamlessly incorporate the required safety components into our Standard Operating Protocol (SOP) for receiving, cataloguing, and processing of patient samples for SARS-CoV-2 testing - this document was then shared with several other organisations, as a primer for setting up a COVID-19 testing centre in an academic research laboratory setting.

We delineated the appropriate biosafety practices for COVID-19 research projects, and mandated that all projects being carried out under this umbrella, would need endorsement from by the Institutional Biosafety Committee (and Ethics Committee when appropriate). Their approval could be fast tracked when needed, but with no compromise whatsoever on the rigour of their scrutiny. While preparing these guidelines, we ensured full compliance with the WHO and ICMR recommendations on the containment and operational requirements

for virus testing (BSL2), as well as experiments involving live viral cultures (BSL3).

Prior to their induction into the testing or research programs, all personnel are required to provide written consent for being tested for COVID-19 and agree to be part of the medical surveillance programme for users of our containment facilities. In addition, they sign a declaration to abide strictly by the biosafety regulations designated for the facilities, after which they are comprehensively trained in safety protocols that include proper donning and doffing of personal protective equipment, routes of personnel movement, and the best practices to be adopted while performing procedures in their respective modules. While our facility managers constantly monitor protocol adherence, closed WhatsApp groups allow our coordination teams to keep track of, and respond in real time to any infrastructural, technical or logistics issue that may affect personnel safety.

As we combat this deadly scourge together, our commitment to maintaining a zero-exposure workspace remain unwavering - our mantra of 'Safety First' remains paramount, always.

MAKING CCMB CAMPUS COVID-19 READY

Young and enthusiastic,
old and wise formed

CAMPUS CO-ORDINATION TEAM

COVID-19 TESTING TEAM

COVID-19 LITERATURE
UPDATION TEAM

CAMPUS SURVEILLANCE TEAM

Starting with 25,
now with 100+
volunteers

Trained ~200
COVID-19 testing
personnel across
India

2 suggestions
to state govt
+
multiple
testing
protocols in
development

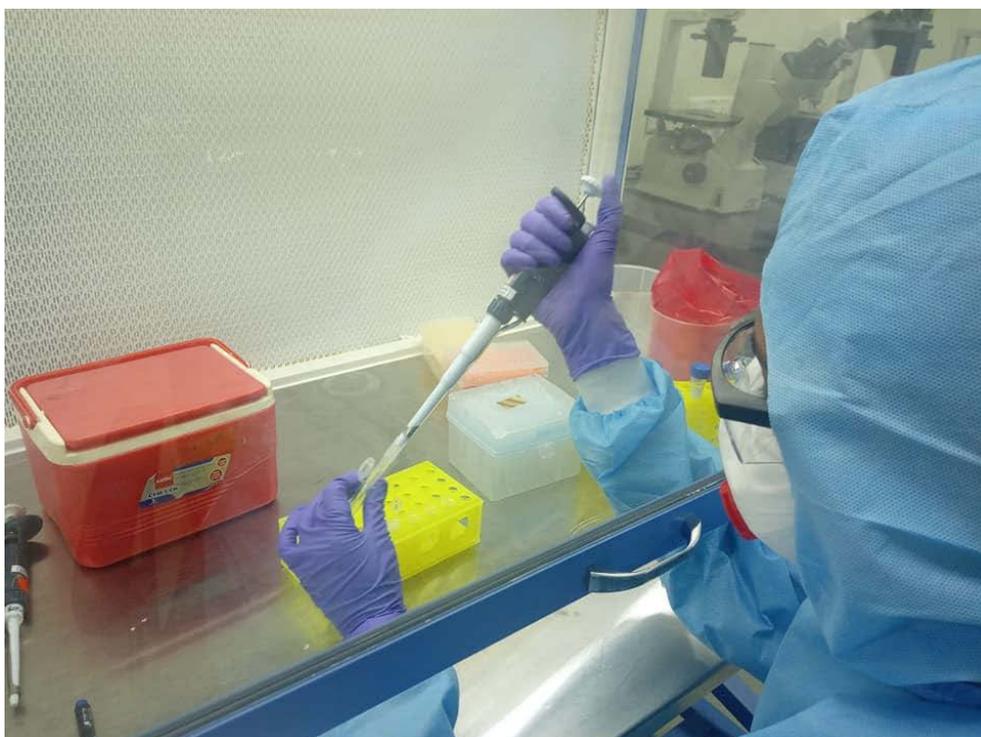
No way
ahead but
testing
more

SANTOSH KUMAR KUNCHA

The country and the world are witnessing an unprecedented time and the normal life of every individual is hampered due to the deadly COVID-19 pandemic caused by the SARS-CoV-2 virus. According to the WHO, the first information of the outbreak was reported to its regional office of China on 31st Dec 2019 and was declared a pandemic on 11th Mar 2020. Unfortunately, the virus spread faster than the measures taken to stop its entry into various countries. India reported its first case of COVID-19 on 30th Jan 2020. As a preventive, the country was forced to take stringent measures of complete lockdown beginning from 24th Mar 2020 to avoid community spread. Given the high population density and the strained medical facilities, the lockdown definitely helped officials and leaders to assess the situation and to prepare the country's medical infrastructure for the surge in COVID-19 cases post-lockdown.

“You can't go back and change the beginning, but you can start where you are and change the ending.” — C.S. Lewis

In the absence of a drug or vaccine against COVID-19, the only way to fight the pandemic is by conducting rigorous diagnosis, followed by containing the positive cases. However, the expertise in handling the patient samples and also performing the technically challenging RT-PCR test was very limited and during initial days all the samples across the country were sent to the National Institute of Virology (NIV), Pune. As the number of samples to be tested was exponentially growing, CSIR-CCMB took up the task of making the state of Telangana self-reliant. To this end, Dr. H H Kirshnan, a virologist at CCMB along with his lab members standardized and established the basic protocols for handling and testing samples for COVID-19. These SOPs (Standard Operating Protocols) were drafted and sent to government hospitals of Telangana. In addition, hands-on training was conducted for technicians from various hospitals and research institutes. This helped increase the overall testing centres in the state from zero to nine. Upon the request of the Chief Minister of Telangana, K. Chandrashekhara Rao, the central government of India has designated CCMB as one of the COVID-19 testing centres. And on 31st March 2020, CCMB started testing for samples received from the government of Telangana.





Recognizes CCMB as

A COVID-19 testing laboratory
for all 33 districts of
Telangana

CCMB with its operational Biosafety Laboratory Level 3 (BSL-3) stepped into the fight against COVID-19 with all its volunteers' strength. These included PhD students, post-doctoral fellows and short-term research fellows. The prior expertise on different techniques of molecular biology helped us train the volunteers quickly. Even before the samples arrived, the volunteers were explained the biosafety precautions and trained for handling the infectious patient samples. Once we started, the whole testing was ramped up by slowly increasing the number of student volunteers, the team was further strengthened by addition of the CCMB technical staff.

The entire testing has been broken down into 5 steps: unpacking and cataloguing of the samples, inactivation (lysis), RNA isolation, RT-PCR and reporting modules. Each module has a dedicated team of volunteers committed to work twice in a week to get the diagnosis running. The untiring efforts of the volunteers of CCMB is what drives the zeal to contribute our bit to the pandemic. As of now CCMB has tested 9000 samples. And the testing capacity of CCMB has been greatly enhanced from 90 samples a day to 500 samples a day. The testing routine has also helped us in fostering a relationship with local hospitals and doctors who provide samples and data for various other

ongoing COVID-19 research projects at CCMB.

One of the biggest advantages of the team is that it includes active researchers who understand the nitty-gritty of each and every step. This allows us to try and test new strategies, to improve the overall testing capacity, and also to reduce the overall cost of testing. To increase the overall testing capacity and to perform community screening, CCMB was the first institute in the country to practice pooling wherein PhD students established the strategy of pooling and testing 5 samples together. The Telangana Government quickly adopted the strategy in testing centres for samples from districts with a low prevalence rates (< 2%). Efforts are also underway to use Next Generation Sequencing for testing thousands of samples a day.

The testing is an ongoing process and CCMB family is fully committed to the cause. This wouldn't have been possible without the excellent support and passion for science and community of all the CCMB researchers. Everyone, right from the coordinators of the program to the student volunteers, the technical staff, HLS staff and others, have contributed immensely and continue to do so.

DIAGNOSTICS

A
scrimmage
with
COVID-19

NIKHIL HAJIRNIS

22 March when the nation is going on a national lockdown, a notification on CCMB student's WhatsApp group reads "Those who want to volunteer for COVID-19 related research, kindly fill this form". In the next 24 hrs, CSIR-Centre for Cellular and Molecular Biology witnessed the stepping up of 109 volunteers, filled with pride, sense of responsibility and diverse expertise.

I am a developmental geneticist and my PhD work revolves around understanding how a developing embryo sets up its body axis. Biology has always startled me, and growing cases of COVID-19 worldwide and now in India were raising my brows. As I filled the volunteer form, I was not sure what was coming my way, but I was very sure of my participation in it.

We were on a war footing 24x7. Our drills, as researchers, were guiding us to fight back with a strong zeal. Similar to the fact that soldiers are trained daily irrespective of a war, our training as researchers would now come into action in situations like these. My PhD project involves tons and tons of screenings to develop transgenic fruitflies. I would also perform micro-injections on these tiny flies' embryos, a process that requires high amounts of patience and agility. I became a part of COVID-19 testing group and was involved in a step called lysis wherein the virus or cells are lysed by adding a suitable solution. My doctoral training helped me in keeping myself stable during the lysis.

Each time you open a vial, it has to be considered a positive sample. It was as if we were diffusing a bomb every time the tip went into the solution. It only reminded me of the patient whose fate is decided by my thumb. It would give me shivers at times to see samples coming from all age groups. I then realized the kind of commitment one needs to show by being one of the frontline warriors, our medical staff. If only research institutes and clinics go hand in hand in India, we would be better equipped and able to bridge the knowledge gap in the medical field, especially with respect to Indian scenario.

With each sample that I was handling, a sense of teamwork kept escalating. For I trusted my fellow team members, I knew there was no

mistake done by my predecessor while cataloguing the samples and I was very confident that my lysed culture is going to be flawlessly processed for RNA isolation by the next team. We soon turned ourselves into worker bees, with no ifs and buts, no restrictions on work time, and no sheer doubt about an action taken by a colleague. Seeing our colleagues working late till 3:00 am motivated us to go in morning wee hours around 5-6:00 am, a time when my subconscious mind gears me up for the day's activities even though I am in deep slumber. There were a few instances where small logistic scuffles might have arisen. But those were soon cornered by the ardour to work for one common goal.

I soon also got engaged in another direction to know our guest, SARS-CoV2, better. We are all made up of a genetic material that dictates who we are and we are able to transmit this information to our off-springs. A majority of organisms have DNA as their genetic material while only some viruses including SARS-CoV2 have their information coded in the form of ribonucleic acid or RNA. Our aim, as a genomics team, was to understand the sequence or code encrypted by viral RNA in order to trace its lineage. Study from our group could nicely show that there is a distinct clade emerging in India which was called A3i. This clade had parental origins from Philippines and Vietnam, and was also found as an emerging cluster in the Middle East and South Asia. New sets of questions started emerging, a majority of those would be why some patients develop severe symptoms but some recover while being asymptomatic. To understand this, we are trying to understand what are the changes going on in the host system that could correlate with infectivity of this virus.

What I learnt during this whole process and working in multiple projects is beyond expectations. I had never worked in a biosafety laboratory before. A mentor colleague training me gave me a sense of responsibility at multiple levels. a) I had to be very vigilant, and be sure that I take mental note of every small detail that is being told to me. b) I should be able to perform when my mentor is not around me. c) I should be able to mentor the next

mentee for we did not have time to engage a senior official always in the process. This sense of collective responsibility was unparalleled.

While the pandemic had a global impact on several avenues of humanity, it made us rethink our position in nature. It has taught me several life-long lessons at a personal level. After 3

months of continuous scrimmage with COVID-19, I am now better at organizing, quicker with my work, and able to curtail my procrastination, to a large extent. The pandemic united us as a family and propelled us to be better researchers. Life post-COVID won't be the same ever again as it would have had a major impact on everyone for years to come including "washing hands and covering face with masks".





Firstly, I realised science is not just about doing experiments. The actions change as per requirements. For instance, getting an experiment to work 100 percent of the time with 100 % accuracy isn't required during a large scale pandemic; sometimes dirty and quick is necessary.

Secondly, adaptability is key to be able to work in teams of people one barely knows, to follow protocols one has never done before. Thinking out of the box and innovating help along the way.

Thirdly, a fight against a pandemic is a multi-disciplinary task and just reading within the confines of ones research problems is not sufficient. Almost everyone is an infection biologist now and that is (often) impressive.

V Devi Prasad



A few notable ones among several learnings from this experience include realizations that:

- A life in science empowers its practitioners with the mindset, skills and opportunities to contribute to the social framework while enabling individual growth.
- It is always a good idea for a practicing scientist to develop an appreciation for areas of active research other than one's own narrow field of exploration.
- Most individuals rise to the occasion, when an opportunity presents itself.

G Aditya Kumar

Our endeavour
to validate and
standardise
pooled testing

**DEVI PRASAD
VIJAYASHANKAR**

As the COVID-19 outbreak turned into a widespread global pandemic affecting millions, the world needed to test people in large numbers in a short amount of time. Reverse Transcription followed by real-time Polymerase Chain Reaction (RT-PCR) has been the gold standard testing method because of its high sensitivity, and strong concordance with the disease progression. However, the process is elaborate, involving virus inactivation and RNA isolation, followed by detection of SARS-CoV-2 genes using very specific probes. Therefore, the test is expensive, costing a few thousands of rupees for each test. Although testing high-risk subjects (with symptoms, travel history, or known contacts) is definitely worth the resources and effort, screening large numbers of potential contacts and in communities would incur a huge cost per positive case detected. Therefore, many countries, including India, came up with the suggestion of sample pooling/pooled testing, to save on the resources spent on testing negative samples.

Pooled testing involves mixing small portions of multiple patient samples into one tube, and processing them for RT-PCR as a single unit. If and only if a pool tests positive, the individual samples constituting the pool would be re-tested separately (Fig. 1). ICMR has issued an advisory to pool 5 samples per test, in only areas where <2-5% of the population is expected to test positive. Nonetheless, the technical intricacies, modifications in protocols and data interpretation, etc., have been left to the discretion of the testing centres.

At CCMB, prior to and independent of ICMR's advisory, we looked at the global scenario and performed analyses to appreciate the benefits of pooled testing, as well as to identify any limitations to be wary of. Firstly, we estimated that if the frequency of positives was 2-5% in a population, pooled testing would save us 50-70% on the cost of testing and 50% of the time spent per sample. Also, our productivity would increase to 2.5-fold when compared with testing samples individually. These savings are substantial, considering constraints on money and time to be the major reasons for inadequate testing in the country.

We next took to validating several of the technical parameters involved in pooled testing. Since 5 samples were pooled per test, we tested if diluting each sample 5-fold affected the test results. We mixed positive and negative samples in different ratios and found that even a single positive sample could be robustly picked up when pooled with 4 other negative samples. Usually, a sample is considered positive or negative based on a "Ct value" generated after the RT-PCR. Our experiments showed that pooling 5 samples altered the Ct value by 2-3 units, which corroborates with the theoretically predicted value of 2.32 units. For this reason, we recommended that the cut-off Ct value suggested by RT-PCR kits needs to be increased by 3 units while pooling, to not miss out on the borderline values.

Like all techniques, RT-PCR too has a lower-limit of detection. We found that samples with extremely low viral loads had slightly increased chances of going undetected, after pooling, compared to individual testing. However, considering the significant cost-cutting and increase in sample processing power due to pooled testing, we opted to take a chance with getting a few false-negatives.

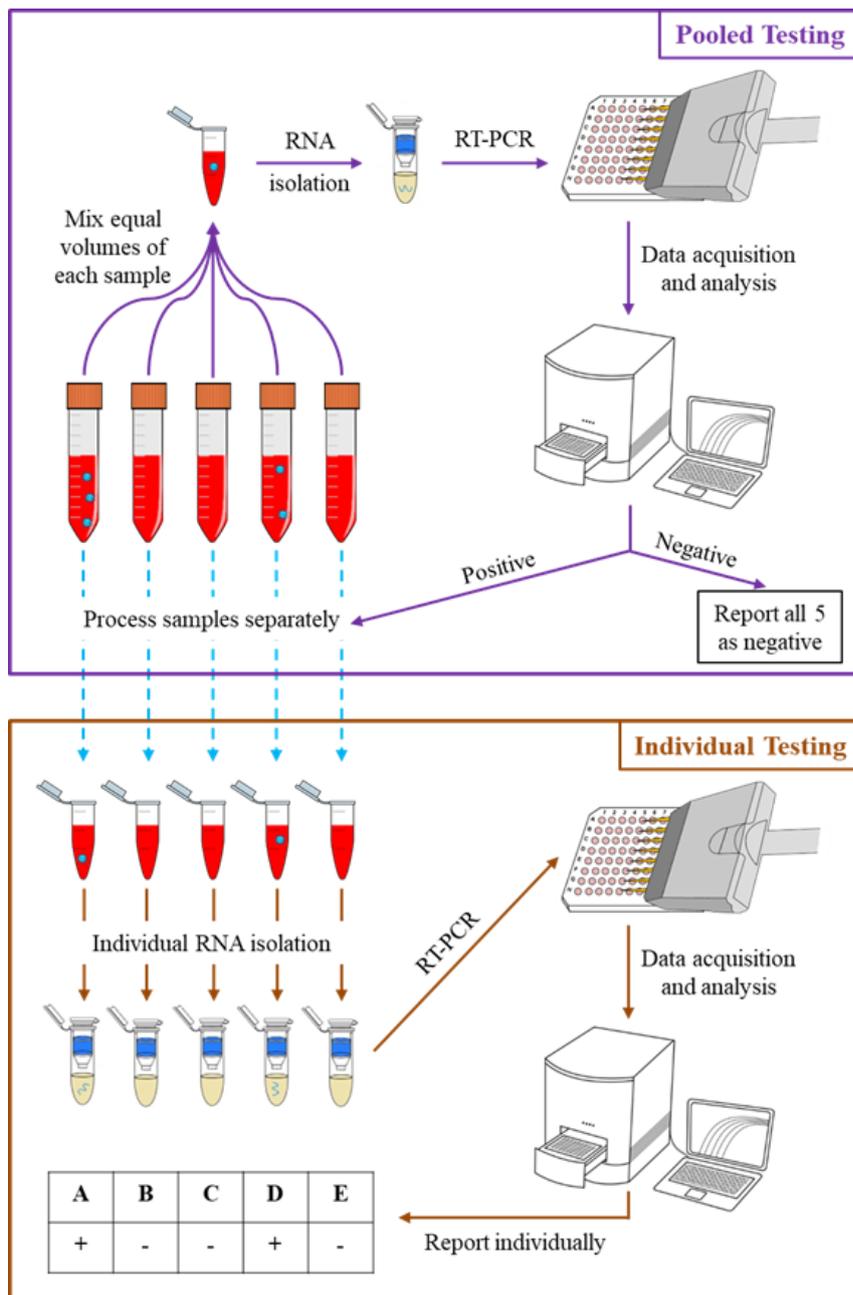
In addition to these technical aspects, we also tweaked some logistics and sample processing protocols to increase efficiency. A large chunk of time (justifiably) goes into cataloguing the patient samples, matching them to the data provided by the collection centres, assigning a local alphanumeric code, and labelling the sample vials manually, to enable accurate reporting of results. However, as with the cost of testing, this step also consumes a lot of unwarranted time and effort for the processing of negative samples. Therefore, we modified the protocol to bypass the cataloguing process and randomly pool 5 samples, as long as they were from the same collection centre. Only the pools that tested positive would be later assigned codes and processed individually, while all the remaining samples would be reported as negative. This would ensure that minimal time is spent on cataloguing negative samples, that form >95% of the population.

We also formulated a set of simple guidelines for the collection centres to ensure uniformity and biosafety in packaging of samples, and to reduce the burden at the testing centres. An elaborate Standard Operating Protocol (SOP) for pooled testing was prepared and shared with the state and central government bodies, to be disseminated to the testing centres.

CCMB has also been involved in evolving the testing process by investigating cheaper and safer alternatives to the current sample collection kits, cheaper and more sensitive methods than RT-PCR, cheaper and quicker processes of RNA extraction, etc. Combining some of these methods can compound the

savings on resources, time, and efforts, and efficiently increase our testing capacity.

All these initiatives have been possible majorly because CCMB has approached COVID-19 diagnostics as a research institute with bright minds, rather than as a testing centre with technicians. We have been encouraged to pitch innovative ideas and also motivated to tirelessly pursue them to fruition. Personally, I feel very humbled to have been a part of this process in a stimulating research atmosphere. It has also been satisfying to contribute to society in my own way and put into practice, what my PhD has taught me.





We have a great potential and very enthusiastic research culture at CCMB and every CCMBian is just a call/message away. Learnt how we can be more resourceful by just introducing small changes in the protocol which will have a huge impact on the society (for example pooling strategy, reduction in the VTM volume).

One of the biggest learning is if you want to do something first set an example. This is because if CCMB had not started testing independently I can't imagine other research institutes taking such steps. Indirectly we have created a positive impact on many research institutions (IMTECH, CDFD, HCU, IICB, IISER Pune, etc.) in the country to start testing.

Santosh Kumar Kuncha

Small tweaks,
big gains

**C. G GOKULAN,
UDAY KIRAN &
SANTOSH KUMAR KUNCHA**

COVID-19 arrived as a setback in all the walks of life. Almost all the currently living humans were unseasoned to live through such a pandemic. The governments and health agencies were advising and executing the most appropriate practices to control the disease spread. As the coronavirus travelled closer, we began to do our best to save ourselves as well as others from becoming a victim. Screening people to identify the infected and isolating them became the key to prevent the pandemic spread. But screening in a population as big as India's needed technical expertise and facilities.

A research institute like CCMB (henceforth 'we') has accessibility to both expertise and facilities. We are equipped with world-class instruments for various scientific pursuits. Without any deferral, we acted and took responsibility in the fight against COVID-19 in multiple ways. We became a testing centre, and started getting samples from Telangana's government hospitals.

A glimpse into the testing process using RT-qPCR: It starts with samples collected from a patient in a liquid Viral Transport Media (VTM) and transported to the testing centre for diagnosis. They are heavily packed to avoid any leakage. Once received at the testing centre the samples are unpacked and catalogued with a unique CCMB-code. Unpacking is an intense process because of the heavy packing. And despite this, sample spillage is a fairly common occurrence.

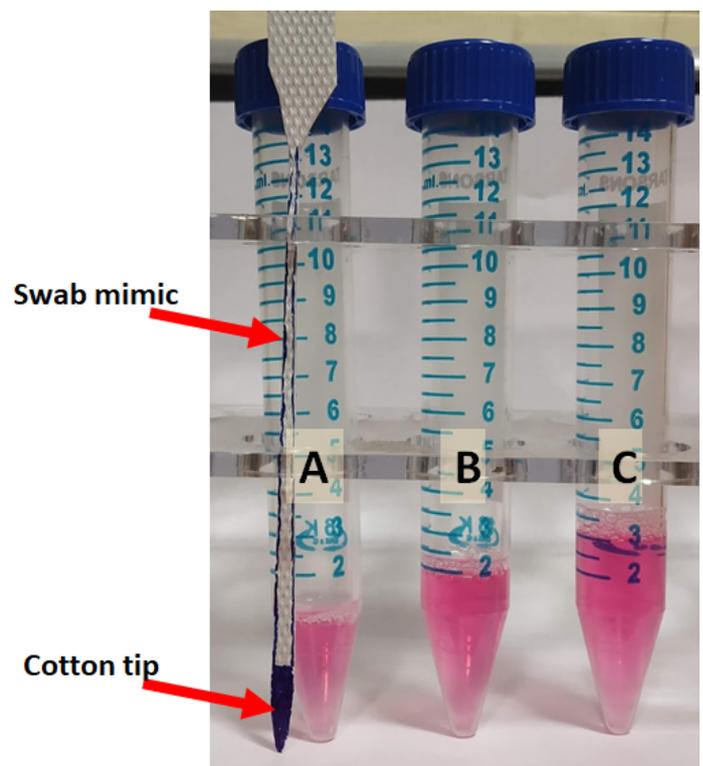
This is followed by inactivating and lysing the virus and RNA isolation, which is the most laborious step. The isolated RNA is then used for setting up RT-qPCR to detect the viral RNA, if any. So typically for 100 samples it takes about 10 hours from cataloguing to test results. One of the first problems encountered by the state government was the shortage in supply in VTM vials. We quickly recommended the use of 1 ml VTM instead of 3 ml, which does not affect the testing outcome and also increases efficient usage of VTM by 3-fold.

As we eased into testing, our minds started performing its usual function, RESEARCH. We brainstormed and listed out the possible ways to make the testing process efficient in as

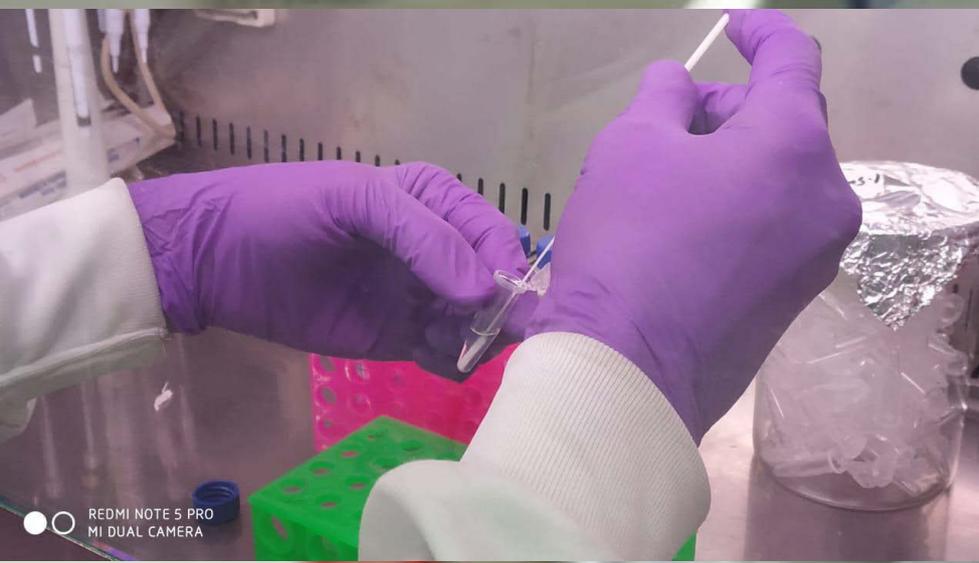
many aspects as possible. With ample support from the director and coordinators, our determined team took the first step towards streamlining the testing process.

We identified RNA isolation to be the major bottleneck of the RT-qPCR based testing procedure. It is also an expensive procedure. We worked on ways to eliminate this entire step thereby saving money and time. With our collective research experiences and literature survey, we came up with a protocol that was as efficient as the standard method, while it needs only half the time and cost. It eliminates the need for VTM as well. Rather, we use a commonly used, readily-available, and inexpensive elution buffer called Tris-EDTA (TE) buffer to extract the nucleic acid from the swab sample.

For our protocol to be tested, we needed swab samples from hospitalized patients, and CCMB had the processes in place for this.



Recommendation to reduce the VTM volume



Once the samples reached the testing lab, dry swabs were immersed in TE buffer for 30 minutes. A small portion of the TE-extract was then inactivated by heating at 98°C for 6 minutes and was directly used as a template for the RT-qPCR, thereby bypassing the RNA isolation step. Simultaneously, the control samples were processed as required. We were bewildered to see our protocol working its magic. To our surprise the RT-qPCR results of the samples prepared by direct TE-extract were comparable to RNA isolated from VTM (the gold standard method).

This method removes the need of VTM and RNA isolation, making the entire process 2 times faster and inexpensive than the conventional method. On the other hand, this also minimizes the time and consumables required for packing and unpacking the samples, the risk of contamination and infection of the sample handling staff.

In the due course, we inadvertently devised a method to mitigate one of the nightmares of diagnosis - the false negatives in diagnosis.

Contemporary studies reported an alarming increase in the false negative rates in SARS-CoV-2 diagnosis. Depending on the stage of infection the false negative rate ranges from 20 to 40%. We found that the detection efficiency can be increased by 30% when RNA isolated from the TE-extracts. Currently, the entire work is summarized and posted on a preprint server bioRxiv and the proposal for implementing this methodology has been sent to ICMR.

This work would have been impossible without the support from the entire COVID-19 Fighting Force of CCMB, who are working day and night to overcome this pandemic. The work described is just one of the many examples in which CCMB family is contributing to the national/global efforts. We take this opportunity to express our sincere gratitude to the present and past leadership for maintaining a rich CCMB culture of ever encouraging and research oriented atmosphere. This, we believe, is the reason that makes CCMB a premier research institute.



When I joined the testing team I realised how indispensable it is to have more and more well-trained personnel to handle such large scale pandemic. The problem is not only testing kits being less, the number of people able to handle testing kits are way less. India and the world should consider to have taskforce dedicated to such situation as this pandemic seems to be going nowhere in the meantime.

Aritri Dutta

Dealing with
multiple
stakeholders:
A medical
doctor's life at
CCMB

KARTHIK BHARADWAJ

It has been a little more than 3 months since my association with COVID-19 activities at CSIR-CCMB has started. Initially it was just the meetings where I was required to advise as a medical professional on various aspects of COVID-19 management. All that changed on April 1st when I was trusted with the responsibility of coordinating COVID-19 testing activities at CCMB with the state government and its hospitals.

We witnessed a mayhem on the next day as about 900 samples were sent and the system was largely underprepared. The next 4 days were probably some of the toughest days of my life at CCMB as I had to handle samples coming from 33 districts of Telangana, send the reports and also answer all the queries for pending results. The paranoia around COVID-19, and the stress in the administration was all getting transferred to me. With hundreds of calls and messages pouring in my phone had a tough time too.

It is during such times of adversities when you often find your friends. I found a team. A team that was motivated to attend to the crisis and serve the nation. Keeping the team together after a COVID-19 scare in our own campus, was a big challenge which I think has been successfully attended to. After 9000 tests, many sleepless nights and days, this team is what makes me still work long hours.

In addition to this, I had to deal with setting up of collaborations with various hospitals involved in COVID-19 care for facilitating sample collection research work at CCMB. To be part of an institute that had been so proactive in helping the society in the hour of need from doing COVID-19 testing to being one of the few centres where almost all aspects related to COVID-19 biology are being investigated is something that I am really proud of.



The key learning I got that every adversity brings up an opportunity. It is our mindset which decide whether we are going to sit back or going to make maximum out of that opportunity. The gap between "desire of doing something" and "actually doing something" is very small, but the barrier of courage is so huge that only few are able to make it on the other side. In an institutional setup like ours, it's hugely dependent on the person who is leading the bandwagon. The opportunity was open for all research institutes to contribute in this dire situation, but CCMB and few other institute showed a commendable valor to accept the challenge. We not only extended our full support for COVID testing, but are doing everything we can do in our limited capacity. These situations not only reveal the core metal of an organization, but also decide how future generation will look at our institute. I am one of the beneficiary of CCMB efforts and learned numerous things during COVID training, testing and research. These learnings are not only limited to professional level but enriched me at personal level also.

Innovative
approach to
provide mass
screening
solutions

**GUNJAN PUROHIT &
DEBARYA SAHA**



The year 2020 started on a positive note, with our research projects nearing completion. It was time for us to take the next step forward. Unfortunately, a particle 1/1000th the size of a human cell, changed everything: COVID-19 had arrived affecting more than 200 countries/territories, and killing about 4,75,000 people.

By the middle of March, it was clear to us that COVID-19 is here to stay. The entire healthcare system and diagnostic facilities across the country were working beyond their capacity, requiring research institutes and biotech/pharma companies to step-in.

This was the time, researchers like us, working on various fields of life sciences, were called to the front line. Most of us, took a break from our regular research work and became COVID warriors, working on various aspects of the COVID drive. We were involved in training and diagnostics of COVID-19, which involves RT-PCR based detection of COVID-19 genome. Soon, we realized, that the process is extremely time consuming and laborious. Moreover, the tests cannot be done in the absence of elaborate laboratory equipment.

This led us to contemplate different strategies for COVID-19 detection. During this time, AIC-

CCMB/CCAMP called for proposals related to development of ideas/products related to COVID-19. We had an idea, which could detect COVID, much efficiently than RT-qPCR, and that can be performed in rural settings without the need for elaborate equipment. Our application for this project got approved for funding. The excitement was profound, and we were all geared up to do something meaningful.

We have been working on this project for the last one and a half month and have been able to generate basic data to support our idea. However, we hit a roadblock, when, we wanted to perform our experiments with patient samples, because access to those involves elaborate set of rules and regulations. The government in consultation with universities, health care providers and institutes should work on formulating policies, which will simplify the procedures, for young innovators, working on emergency issues to access sensitive materials for their research, while keeping in mind the safety and ethical issues.

However, we are confident that with the support of CCMB and AIC, we would be able to overcome this roadblock and generate results that would simplify the way testing is performed in this country.



A crisis asks the scientific community to change its priorities. It cannot be about competition but rather about transparency, discussions with people with varied expertise and strategically moving ahead - first to address the easily doable tasks, and then to the more difficult ones. This is not only necessary within an institute but the entire community.

Zeba Rizvi

Serological
detection of
SARS-Cov-2
proteins:
Promise for
diagnosis?

RICHA KHANNA

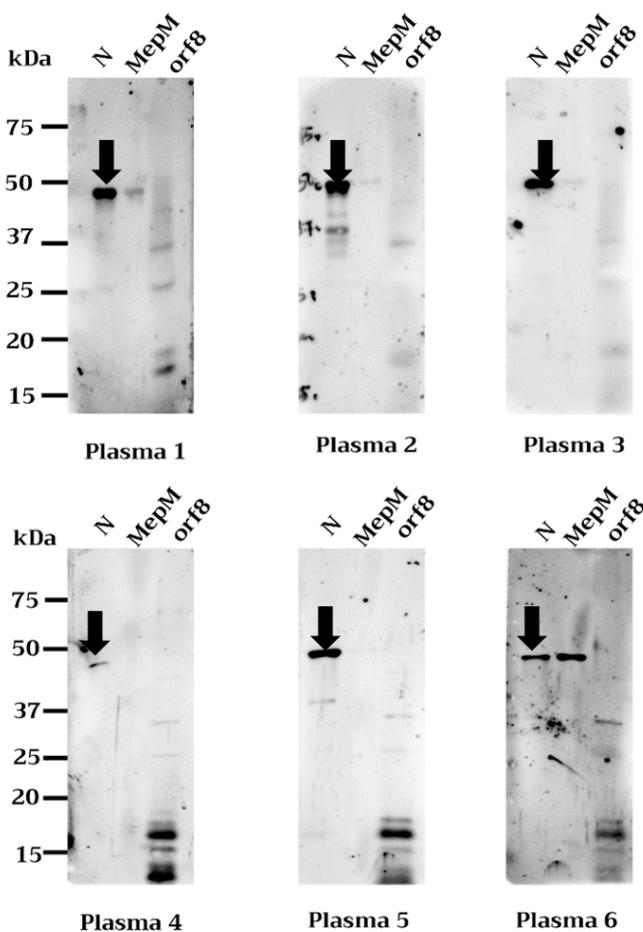
Amidst a surge in the number of COVID-19 patients worldwide and in India, we aim at developing a platform to analyze the potential SARS-CoV-2 proteins responsible for triggering an immune response in the patients. The presence of an immune response is a strong indicator of a current or previous viral infection and hence, holds promise in disease diagnosis. This information, if deciphered, would not only give us an insight into the immunogenicity of the viral proteins, but could also potentially facilitate development of diagnostic techniques to identify the presence of the viral infection by detecting the presence of antibodies against the viral proteins in the patients.

Our lab holds expertise in protein expression and purification in bacterial host, *E. coli*. This time, we wanted to express and purify the structural proteins of coronavirus using *E. coli* overexpression system. The structural proteins of the virus are primarily involved in viral assembly and might therefore, be important in presentation of the same to the immune cells. The nucleocapsid (N) protein, is a major structural protein that binds to the viral genome and is a strong candidate for a potential antigen. A PhD student in the lab, Pavan

Kumar's expertise came in handy in getting good amounts of the purified N protein.

We use the N protein to look for antibodies against it in plasma from patients who have recovered from COVID-19. Although getting plasma from patients was not an easy task, the collaborative efforts from the CCMB team were successful in procuring us a good number to test. This was followed by ensuring that only the infected patients showed the presence of antibodies and not the non-infected ones. It seems we have landed at a good target with N protein. Efforts are also underway to purify other viral proteins and to test them using the same approach.

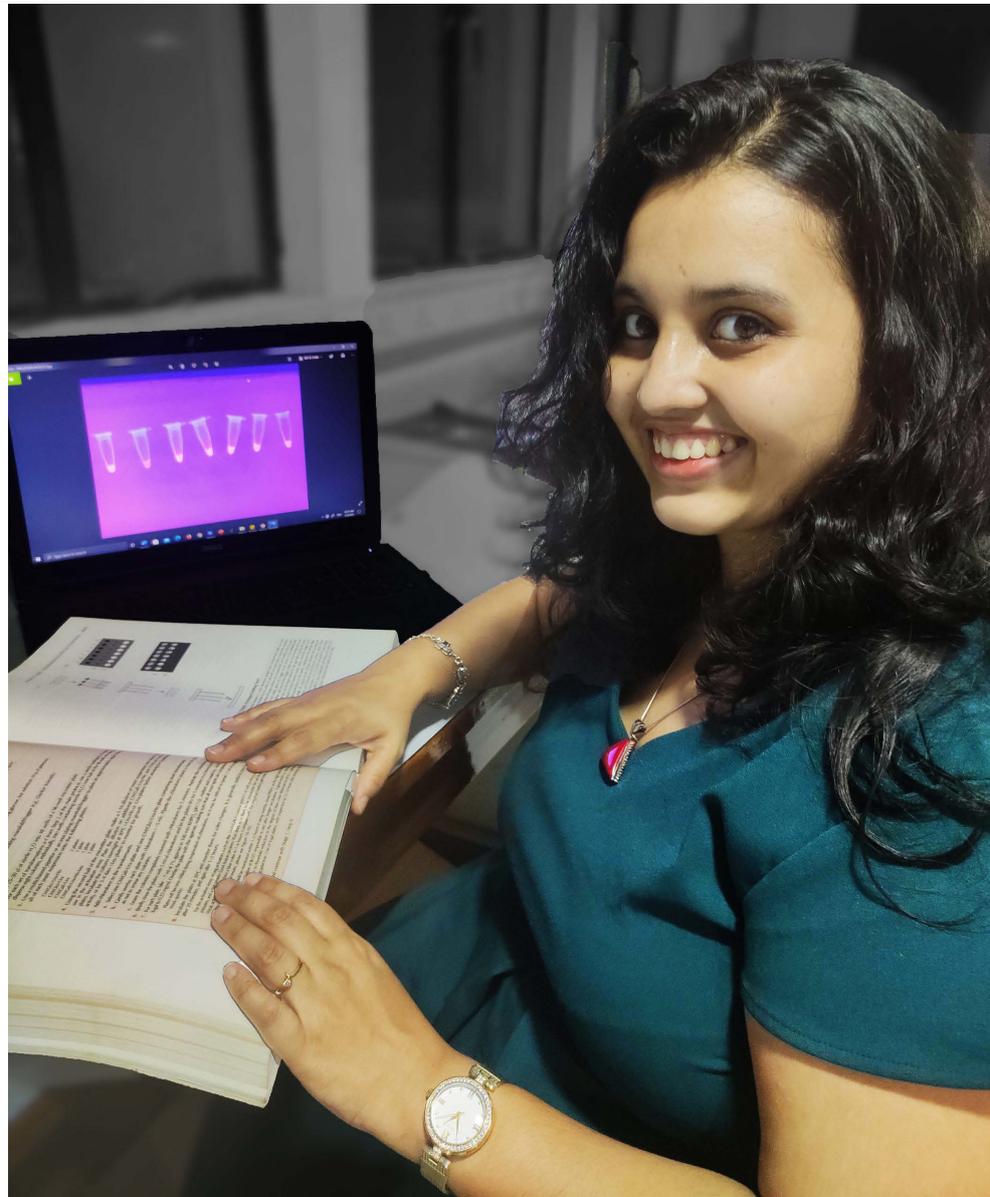
We wish to initiate Enzyme-Linked Immunosorbent Assays (ELISAs) to be able to test the patient samples at a larger scale and validate our hypothesis using more numbers. Also, if the technique shows good specificity, we may have been able to find a good target for a possible diagnostic platform. If successful, this platform could hold promise for rapid testing of the patients with symptoms or even for mass surveillance in COVID-19 hotspots.



Western blots showing presence of Nucleocapsid protein in the plasma of COVID-19 patients. The black arrows indicate the correct molecular weight of the protein.

Back to the
basics- How we
repurposed CCMB
resources to
create a new
diagnostic
technique

SUJOY DEB & DIVYA SRIRAM



As COVID-19 halted the nation, CCMB embarked into serving the country by opening its doors to diagnostic testing for the State of Telangana. Dr Rakesh Mishra, Director, CCMB, quickly put a COVID-19 Response Team together, in addition to other teams. With a dozen PhD students, he constituted this team to analyze 3 main verticals pertaining to the pandemic- Handling and caring for COVID-19 individuals, Emerging diagnostic techniques and Emerging treatment techniques. And that is when our journey started. Both of us, PhD students, were part of a 5-member Diagnostic Response Team. While the CoVID-19 Warriors (RT-PCR diagnostic testing team) were fighting in the battle grounds with testing patient samples, we, the response team, were tailoring strategies to fit the changing dynamics of the CoVID-19 pandemic, to help win the war.

The extensive discussions on the evolving diagnostic techniques, their merits and demerits, and scope of adaptability in developing countries, brought us to a realization that there is a dire need for a diagnostic test kit, that is robust, cheap and scalable, a combination that didn't exist. RT-PCR's sensitivity and specificity has made it a gold standard for COVID-19 testing but the turnaround time, multiple steps involving expertise has testing confined to scientific institutions and high-end diagnostic laboratories only. Moreover, its reagents are expensive, and standalone, this test would not be able to cater to the large population of our country, due to the logistics involved.

Thus, we fervently began searching for ways to carry out alternate techniques to RT-PCR, that don't rely on expensive machines, specifically, isothermal PCR techniques, like, RPA, LAMP, etc. We presented this idea to the scientists in CCMB. Their constructive feedback urged us to reshape and tweak our think tank in search for a novel and superior technique. The underlying message was that the basic building blocks of the kit should comprise of readily available, inexpensive reagents, finally leading to a test that is easily executable. In a nutshell they wanted us to "innovate more, curate it perfectly and execute it wisely", a daunting task, indeed. Thus, we set foot to develop a PCR-based diagnostic technique or test, which can be

performed isothermally at room temperature (35°C to 42°C), so as to avoid using expensive machines and which could give an end result, visible to naked eye or detected easily through a lateral flow strip.

With this objective, we started looking for resources within CCMB, hitting every other lab, collecting enzymes and buffer components that could make up the building blocks of the kit. The recipe required few additional components (like primers, dyes etc), which were essential but not available. Fortunately, Dr Nalam Madhusudhana Rao, CEO, AIC-CCMB, helped us in getting these reagents and is currently working with us to take the test further. Multiple iterations and repeated failures later, we arrived at the right combination that worked.

During this trial-and-error process, we reaffirmed the importance of appropriate controls which was highly useful in efficient troubleshooting. We also realized how minute concentrations of elements in a PCR reaction, that we take for granted while using commercial kits, can make a huge difference in overall performance of a test. For example, in the middle of the trials, when we thought we had almost captured the candidates, we suffered a major road block, brought about by a cross-contamination, leading to perplexing results. After pain-staking efforts, we dug out age-old literature and came up with a simple but efficient solution, that eliminated the problem, altogether. Additionally, the same solution helped us eliminate false negatives, thus enhancing the sensitivity of the test.

We now have a proof-of-concept for an inexpensive, specific and sensitive isothermal PCR technique that works at room temperature (37°C), for detection of SARS-CoV2 infection. As we are penning down this experience, we are going forward to testing with actual patient samples, with our newly obtained ethical clearance. And the ongoing journey is teaching us that developing a seemingly small idea also requires adept planning, paperwork and efficient management of resources. These facets are as important, if not more, than the idea itself, in order for it to see the light of day.

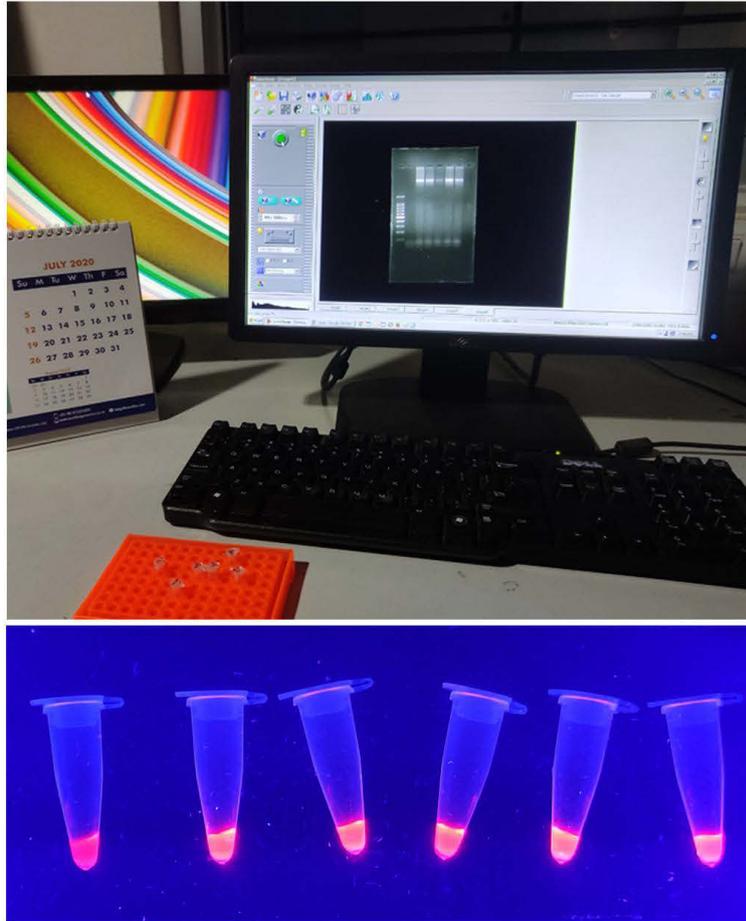
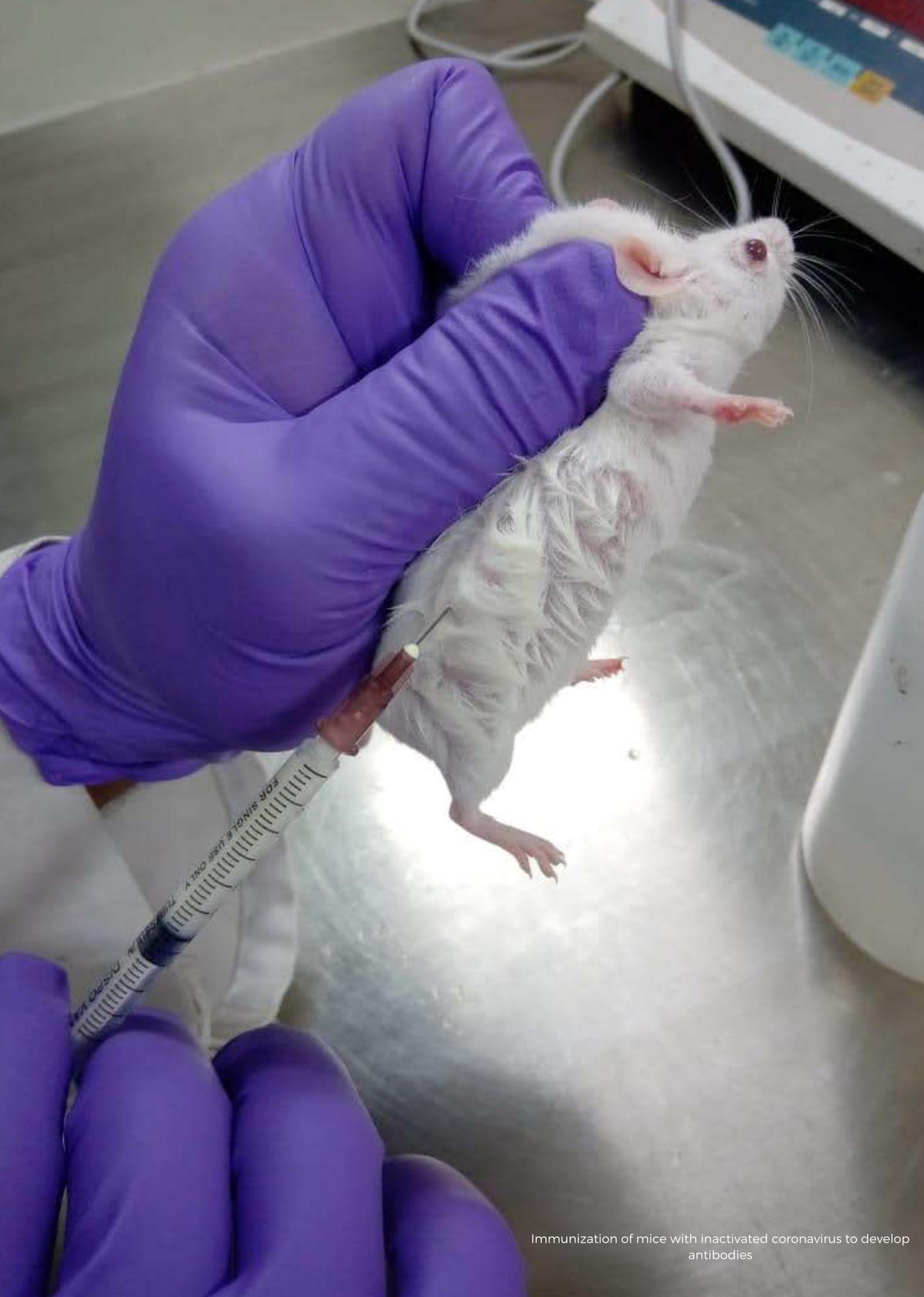


Image of amplified SARS-CoV2 cDNA from patient samples, through specific isothermal PCR at 37 deg.C, Amplified products were seen by gel electrophoresis (upper panel showing gel doc result on screen). Gel shows laddering pattern, typical of LAMP PCR, compared to no amplification in No Template Control or NTC). The result was also visualized by use of a fluorescent DNA-binding dye, under UV light (lower panel).Higher fluorescence, compared to NTC (1st tube from left), indicates positive result.

Mass
surveillance
of COVID-19

**VEGESNA RADHA & P
CHANDRASEKHAR**



Immunization of mice with inactivated coronavirus to develop antibodies

Antibodies produced naturally in our bodies are the best defense mechanisms against environmental pathogens. Monoclonal antibodies that specifically target a single epitope of any biological macromolecule can be produced in unlimited amounts through molecular and cell biological approaches, and have applications in biomedical research, as well as in diagnosis and therapy. While the conventional generation of monoclonals involved immunization of animals followed by hybridoma technology, more recently developed strategies of antibody display and in vitro selection have enabled the generation of monoclonals using recombinant DNA technology, thereby bypassing the use of animals.

The COVID-19 pandemic has been extremely challenging because we lacked simple and effective strategies for diagnosis and therapy. Presently the best and extensively used method of diagnosis is dependent on RT-PCR, and high throughput sequencing, which are multi-step processes, time-consuming, and also expensive. Antibody-based techniques for diagnosis take relatively less time, and can also be modified suitably for point-of-care testing.

Experience from the past 6 months has identified the shortcomings of the currently used diagnostic techniques. Tools that target viral antigens or use antibodies have been recommended for application as soon as possible for mass testing. Monoclonal antibodies generated against viral antigens as well as human antibodies (IgM and IgG) generated in response to viral infection will be extremely useful. However, they are not currently made in India, and we are dependent on imports for carrying out immunological tests. To develop alternate sensitive and specific auxiliary methods for the diagnosis of COVID-19, it is important that we generate our own resources in India, which will greatly cut down on costs.

With CCMB's expertise in hybridoma technology, molecular biology, and NGS

techniques we initiated a project to generate monoclonal antibodies (hybridomas and recombinant nanobodies) for COVID-19 management. These antibodies can be used for various purposes.

Antibody-based tests enable easier identification of asymptomatic patients, as well as those who have recovered from the infection and cleared the virus. They will give a better idea of the prevalence of the infection in the population. On the contrary, the presently used nucleic acid-based tests are useful only to identify people who are currently infected. It might also help in diagnosis of specific Indian variants of the virus. These tests are blood-based, and hence, more familiar to our healthcare workers. This increases the scope for testing in communities, outside of laboratory settings.

Acute and abnormal host response has primarily been the cause of multiple organ failure, and death due to COVID-19. These responses can be monitored using antibody-based tests, and can be useful to follow progression and decide disease management.

Secondary infections during the hospital stay is an additional risk factor for COVID-19 patients. Studies show measuring procalcitonin helps in identifying COVID-19 patients at risk of bacterial coinfections. As part of an earlier project funded by CSIR, we had initiated development of procalcitonin monoclonal antibodies for diagnosis of COVID-19 symptoms.

Monoclonal antibodies have also been used to block receptor-mediated viral entry, block action of pro-inflammatory cytokines, and homing of therapeutic molecules to target tissues. Recombinant human monoclonal antibody could be used to neutralize SARS-CoV-2, and block its entry into cells.

In addition to their role in diagnosis/therapy, these antibodies will also be important in research on COVID-19.



CCMB, though has a BSL-3 lab, didn't use it often until COVID-19 struck. To suddenly get it up and running full-time in the emergency came with its set of hiccups. I wish we could keep these facilities run more to keep them in usable conditions, whenever needed. If we had a functional BSL-4 lab, it would have allowed us trying out so many more things.

Divya Gupta

COVID-19
surveillance
using sewage
samples

SANTOSH KUMAR KUNCHA

COVID-19 pandemic is rising at an alarming level across the world. While the rigorous testing, contact tracing and treatment is being done on a war footing, estimating the scale of infection is quite important to predict the rate of infection. A strong data on the spread of the SARS-CoV-2 virus is essential; this can be achieved by community or random screening which is quite intense and laborious. Individuals infected with SARS-CoV-2 release traces of the virus particles (fecal-oral route) into the domestic wastewater, which provides an opportunity to study the level of infection in the community. This methodology was earlier employed in

eradicating the polio virus. Therefore, detection of the SARS-CoV-2 traces in the sewage sample can be used as a good indicator of knowing the spread of COVID-19 and appropriate measures can be designed and carried out to limit the spread of the pandemic.

In a highly dense country like India, testing all the individuals is almost impossible and therefore necessitated the need to explore methods for community surveillance. In this direction, sewage/wastewater could be a very useful resource to detect and estimate the quantum of COVID-19 spread. As CCMB was



COVID-19 surveillance through sewage water samples



Collection of sewage water sample for disease surveillance

Testing of collected sewage samples in lab



actively involved in performing COVID-19 tests for the state of Telangana, the experience in detection methodologies (RT-qPCR and RT-nPCR) has enabled CCMB to explore the possibility of detecting SARS-CoV-2 in sewage samples. To this end CCMB collaborated with Dr. S. Venkata Mohan's team from the Department of Energy and Environmental Engineering, IICT. This group has expertise in collecting and handling sewage samples. Therefore, with complementing expertise for carrying out community surveillance using sewage samples, CCMB and IICT have decided to set up COVID-19 in Sewage (CiS) laboratory

for the same in CCMB premises and aimed to work together. In this regard SOPs for sample collection and processing are prepared which will be circulated to different labs across India, which would be essential to carry out wastewater based epidemiological studies (WBE). Even though the current project proposed here is COVID-19-centric, it will be a very useful method to also monitor various infectious organisms' prevalence in a community, which would act as one of the major indicators of health status of a particular community.

Experience
on SARS-
CoV2
isolation

KRISHNAN LABORATORY



The team that keeps the coronavirus growing in lab

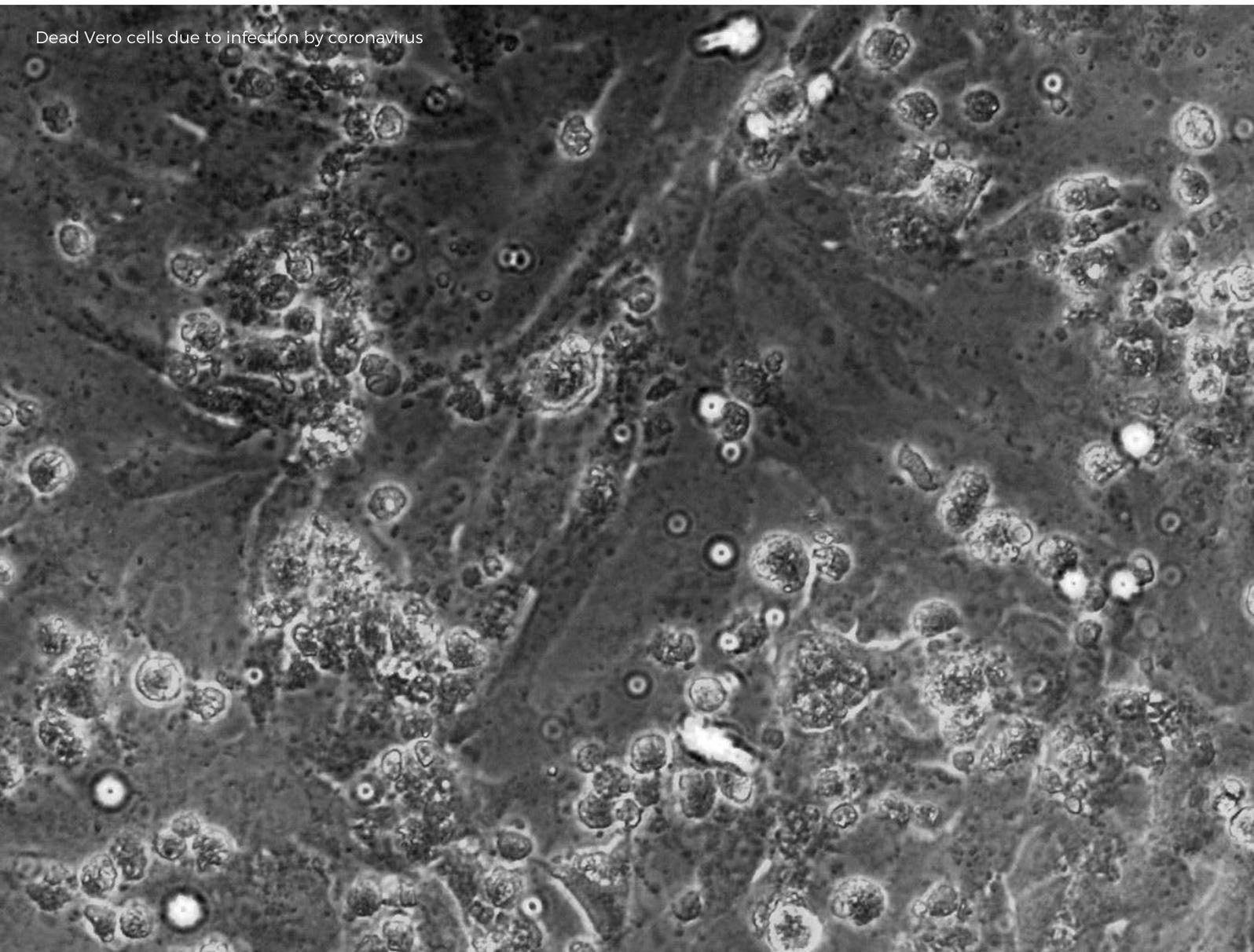
CCMB has a biosafety laboratory 3 that was used in setting up of COVID-19 testing. This allowed us to access the 'precious' patient samples from which viruses could be isolated. The patient samples are typically nasopharyngeal or oropharyngeal swab samples dipped in virus transport medium (VTM). We used VTM samples that were tested positive in diagnostic screening as the source of virus. VTM is supposed to preserve infectious virus particles when stored appropriately. Senior Ph.D. students Dhiviya Vedagiri and Divya Gupta were tasked with this challenging project.

One of the key resources for isolating any virus strain is the right cell culture. Various reports had demonstrated that Vero, kidney epithelial cell lines derived from African Green monkey, are good permissive hosts for SARS-CoV-2. We identified certain VTM samples with higher viral

load. These VTMs mixed with media were incubated with Vero cells to initiate infection. One of the key indications of infection is the development of cytopathic effects (CPE) in infected Vero cells. At the peak of infection, a large majority of the cells are killed by virus. Dead cells round up and float in the media.

However, our initial experience with CPE was disappointing. In spite of incubating for about a week, the 'infected' cells did not develop any CPE. However, we could still detect SARS-CoV-2 RNA, albeit at low titre, in the culture. This demanded certain tweaks in the infection approach. A large-scale infection study was initiated based on our own experience and adapted from many other reports. We infected Vero cells under various conditions of media, inoculum amount and infection intervals.

Dead Vero cells due to infection by coronavirus



Quite encouragingly, a few wells of infected cells started to show CPE after a few days of infection. These cells along with their supernatants were used to infect fresh naïve cells. Several of them showed consistent CPE indicating robust production of infectious virions. These were further assayed by RT-PCR to confirm the presence of viral RNA. Supernatants from some of these samples were used to set up plaque assay to quantify infectious viral particles in the supernatant. It was very satisfying to note viral titres in the range of 10^7 mL⁻¹, an order of magnitude higher than suggested by various reports. This indicated a very robust production of infectious virions by the cultures. Once these were established, Vishal Sah, a young member of the lab followed up and established a few

more isolates. We are currently performing several optimization studies several of which are significant in improving the culture and virus both in quantity and quality.

Currently we have several isolates of SARS-CoV-2 in CCMB. They are being used for several purposes including drug-screening, vaccines and antibody productions. It has been a great journey that has only started. But establishing this culture has been a critical part. Every virologist dream to be part of an epidemic, and to be able to isolate viral strains from field samples. It feels very rewarding to be able to live up to the expectations, and contribute to the cause of eradicating or overcoming this pandemic.

COVID-19
vaccine
technologies

PURAN SINGH SIJWALI



The team working on the COVID-19 vaccine project

The ongoing coronavirus disease (COVID-19) is caused by the newly emerged severe acute respiratory syndrome corona virus 2 (SARS-CoV2). It causes mild to moderate respiratory illness, resulting in the high fatality in older people and individuals with existing respiratory and cardiac illnesses. Despite all out efforts to contain COVID-19 pandemic, it is rapidly spreading.

Few drugs have been repurposed for COVID-19, but appear to have a limited effect on the disease and an effective treatment appears to be far away. SARS-CoV2 is an enveloped virus with a single stranded RNA genome of about 30 kb. About 1/3rd of the genome codes for structural proteins (spike, envelope, membrane and nucleocapsid), which form the infectious virus together with its genome. As these proteins are essential for infection and encounter the host at the time of virus entry, the presence of antibodies to these proteins in the host can block the virus entry. This can be utilized for development of a vaccine.

Genomes of SARS-CoV2 isolates exhibit >99% identity, indicating that a vaccine will likely offer long-term protection. Most of the COVID-19 patients recover without any clinical intervention, and the recovered individuals develop high titers of virus neutralizing antibodies, which supports a case for vaccine. The Spike protein of SARS-CoV2 has been demonstrated to be the major target of protective immune response and several efforts are underway to develop a vaccine using the Spike protein. Ongoing efforts towards a COVID-19 vaccine include live attenuated/inactivated whole virus vaccine, subunit vaccine and nucleic acid vaccines. With its strength in modern biology research, CCMB is working on two vaccine development approaches: inactivated virus-based and recombinant protein-based.

Immunization of humans with inactivated/attenuated pathogens, particularly for viral diseases, has been an effective approach to develop vaccines. A number of vaccines in use are based on inactivated whole viruses like those against Hepatitis A, Flu, Polio, and Rabies.

CCMB has succeeded in isolating and setting up a large-scale culture of SARS-CoV2.

Although inactivated virus as a vaccine candidate is the simplest and straight forward approach, it has its own limitations. The most important is the possible loss of conformation of proteins, which could render the vaccine ineffective to prevent infection. This varies with the inactivation agent used. The second challenge is to scale-up virus production, which varies with cell culture procedures and safety level of the virus. Hence, optimization of procedures to purify and inactivate the virus are critical, and these are underway at CCMB.

We plan to assess immunogenicity of inactivated viruses in laboratory animals. The immune sera from the immunized animals will be assessed and compared for ability to neutralize virus, thereby preventing infection of cells in cell culture models. Once an optimum inactivated virus formulation is demonstrated to elicit potent neutralization antibodies, this technology can be given to a company for human trials and commercialization.

Initial work for a recombinant vaccine can be done in most of the laboratories, these are safer than inactivated virus-based vaccines and are easy to scale up. Towards a recombinant protein-based COVID-19 vaccine, we are producing structural proteins and their fragments using bacterial, yeast and mammalian expression systems. As in the case of inactivated virus-based vaccine, laboratory animals will be used to immunize with these proteins, and immune sera will be assessed for neutralization of virus in cell culture models. Inactivated virus formulation and recombinant protein(s) producing potent neutralizing antibodies will be taken forward for their ability to protect from infection in appropriate animal models.

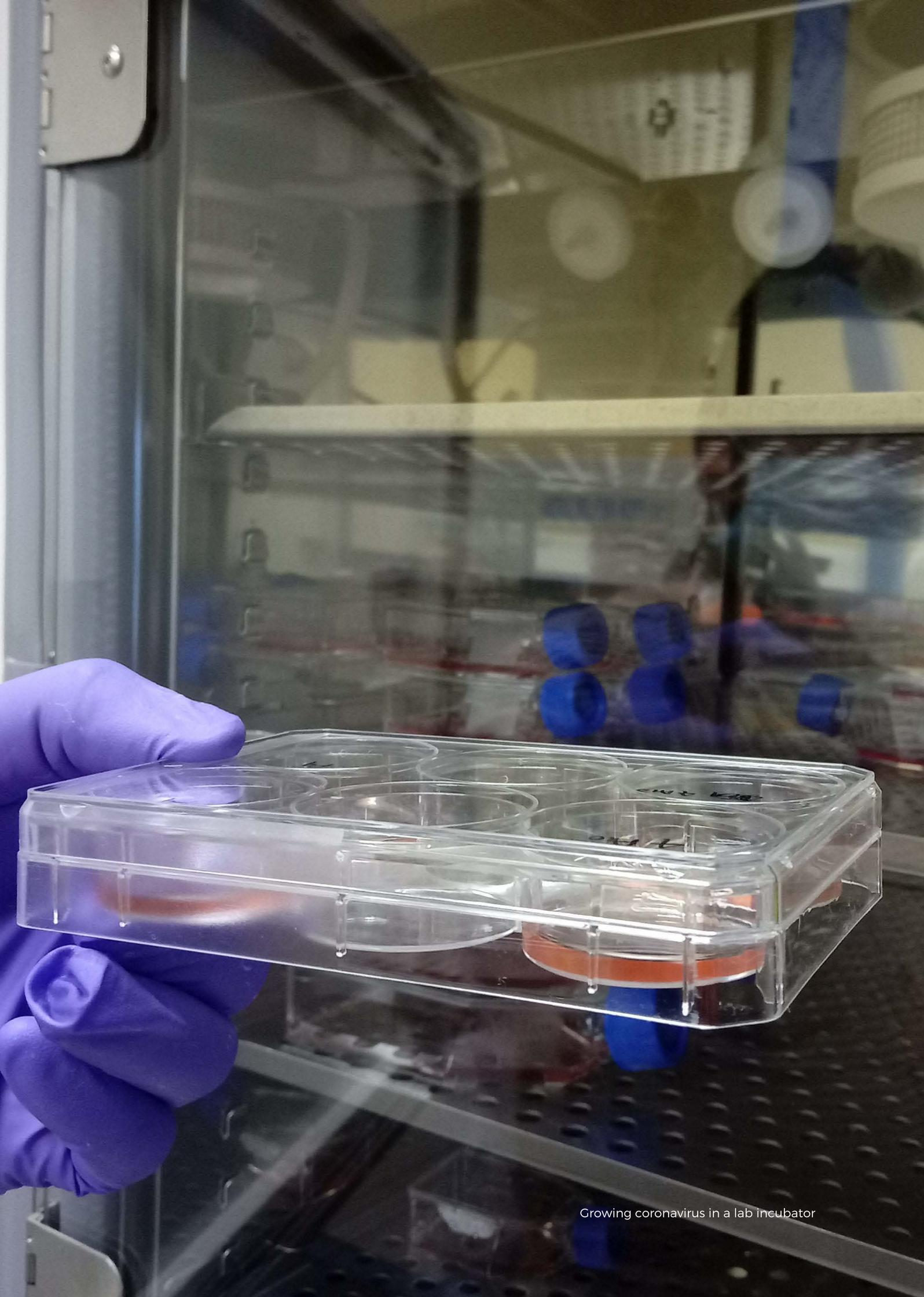
Given the global extent of COVID-19 and possible demand, the world needs several vaccine development efforts in parallel. We believe that CCMB's efforts to develop a COVID-vaccine are timely, and will most likely lead to a technology.

REQUESTS FOR COLLABORATIONS & SERVICES AT CCMB



Collaborating
for anti-
SARS-CoV-2
antisera

KRISHNAN H HARSHAN



Growing coronavirus in a lab incubator

It is quite interesting to note the power of infrastructure facilities. It is even more interesting what the domain expertise can bring to the table. Having a functional BSL3 was a great boon to CCMB around the time Covid-19 was declared as pandemic. Number of Covid-19 positive cases was rising and ICMR was no longer able to test the samples from across the country. Regional labs with testing capabilities were very few. Finding trained people to set up testing facilities was even harder. With both infrastructure and trained human resources, CCMB was able to set up the testing. With the help of trained research scholars who were more than excited to participate, the testing activities took off.

One of the exclusive outcomes of this testing was the access to patients' samples. These samples are brought in a Virus Transport Medium (VTM) that can preserve the infectious virus particles in them if present. They are treasure mines for virologists. Using such precious virus samples, we isolated SARS-CoV-2 virus strains and established culture systems where they can produce over millions of virus particles per milliliter of the medium. Successfully establishing this was very crucial for various reasons, particularly for using them for vaccines, anti-sera and for drug-screening.

VINS Bioproducts Ltd, a biotechnology company located in Hyderabad has been manufacturing anti-sera for various purposes

including against rabies and snake venom and selling them across the world. They approached CCMB to collaborate and generate anti-sera against SARS-CoV-2 in horses. UoH is also collaborating in this effort. This approach is very similar to plasma therapy where anti-serum is obtained from recovered patients. In this case, inactivated virus particles would be injected into horses, and antibodies generated would be purified, proteolytically cleaved to generate Fab' (antigen binding fragment). This can be introduced into patients suffering from COVID-19. This is not a vaccine, but can cure infected patients, and hence, has immense therapeutic potential.

Since SARS-CoV-2 can potentially cause infection in horses, it is very important to ensure that the live virus particles are not injected into them. We inactivate the virus chemically, test total inactivation by virus amplification assays and provide these cultures to VINS Bio for injection into horses. Anti-sera from immunized horses will be tested subsequently for their ability to neutralize virus infection in cell cultures. A few horses have already been injected on an experimental basis and we are eagerly awaiting the results. At CCMB, our lab is currently generating large volumes of SARS-CoV-2 supernatants to be followed up by inactivation and further readying for injection. This could not have been possible without the help of the enthusiastic, skilled and diligent research scholars in the lab.



Recognizes CCMB as

A national repository for
collecting, storing and
maintaining COVID-19 clinical
samples

Coronavirus genomics

**SHAGUFTA KHAN &
LAMUK ZAVERI**

Coronavirus' genomes sequenced at CCMB NGS facility



**~400 coronavirus
genomes sequenced
at CCMB**

We had been hearing about the coronavirus outbreak for quite some time on the news, but initially it felt like a problem in a far-off place and didn't concern us too much. Then WHO changed the status of the outbreak, terming it a pandemic and cases in India were spreading like wildfire. That's when the Government of India initiated a country wide lockdown which showed how serious the situation was. Amidst this lockdown, CSIR-CCMB initiated its coronavirus effort and called for volunteers from within its research community. One such endeavour was the "COVID-19 genomics" group.

The "COVID-19 genomics" team was led by Dr. Divya Tej Sowpati and had a motley crew trained in very diverse backgrounds of epigenetics, cell biology, structural biology, and plant biology. Most of us were clueless about genomics but we all knew that we had to step up and put our skills to work, to help out in these challenging times. In our first meeting, after a customary round of introductions, we got down to business, which was the what, why, and how of COVID-19 genomics. We were quite excited about how we could contribute to CCMB's effort in helping society battle SARS-CoV-2. Our goal was to sequence various Indian isolates of SARS-CoV-2 to better understand the virus, determine its spread, severity, and any other aspect of its infection through genomics. Simultaneously we also decided to try and develop a method for large scale COVID-19 screening by employing the power of high throughput sequencing.

It was during our second brainstorming session that we realised that our biggest hurdle was reagents, or rather the lack of them. As this was happening in the backdrop of the lockdown, there were many restrictions in terms of ordering reagents, disruptions in supply chains, and stock availability. But we had an advantage that we were embedded in an institute with research groups working on diverse biological questions. That's when we started calling our friends, friends of friends and in the process made lots of new friends. It was like a treasure hunt, we begged, borrowed and so far haven't

stolen anything, as yet. We finally managed to gather all the reagents we require and were all set to sequence the first batch of viral samples. Thanks to the great efforts of the CCMB diagnostics team, we were able to get viral RNA samples whenever needed.

The first step was to convert the viral RNA to DNA for which we used an enzyme that was ironically isolated from a virus itself – an excellent example of how we were using examples from nature for the betterment of humanity. The viral DNA could then be treated as any other normal DNA. We amplified the whole viral genome using primers specific to SARS-CoV-2 as there was so little DNA to start with. This was then used to prepare libraries for sequencing. During analysis of the sequences, we realised that some regions of the viral genome weren't getting amplified efficiently. Strangely, this was a problem seen not just by us but also by other labs that were sequencing the viral genome across the globe.

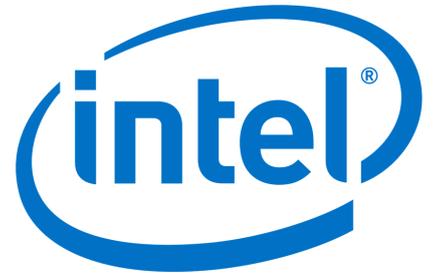
It was during one of our socially distanced coffee sessions where we had one of our 'Eureka!' moments. We tweaked our sequencing protocol here and there and lo! and behold, it worked! Since then, we have been consistently submitting high-quality genome sequences (198 and counting) to GISAID, the worldwide database for SARS-Cov-2 genomes.

With viral genome sequencing in hand, we wanted to scale up throughput, expand horizons, and ask more questions. Our small motley crew of five has now grown larger than a football team. We have now moved into host transcriptomics, metagenomics, and host genomics. We are continuously working on ways to improve our sequencing techniques and see what other questions we can answer. But what's really amazing from all of this is thanks to our efforts, CCMB has identified a SARS-CoV-2 strain that is specific to India, which will be very crucial for vaccine development and therapy, a positive impact for society.

PARTNERSHIPS



TATA CONSULTANCY SERVICES



CodeDx



BHARAT
BIOTECH

Syngene

 A **Biocon** company



glenmark
A new way for a new world

Dr.Reddy's 

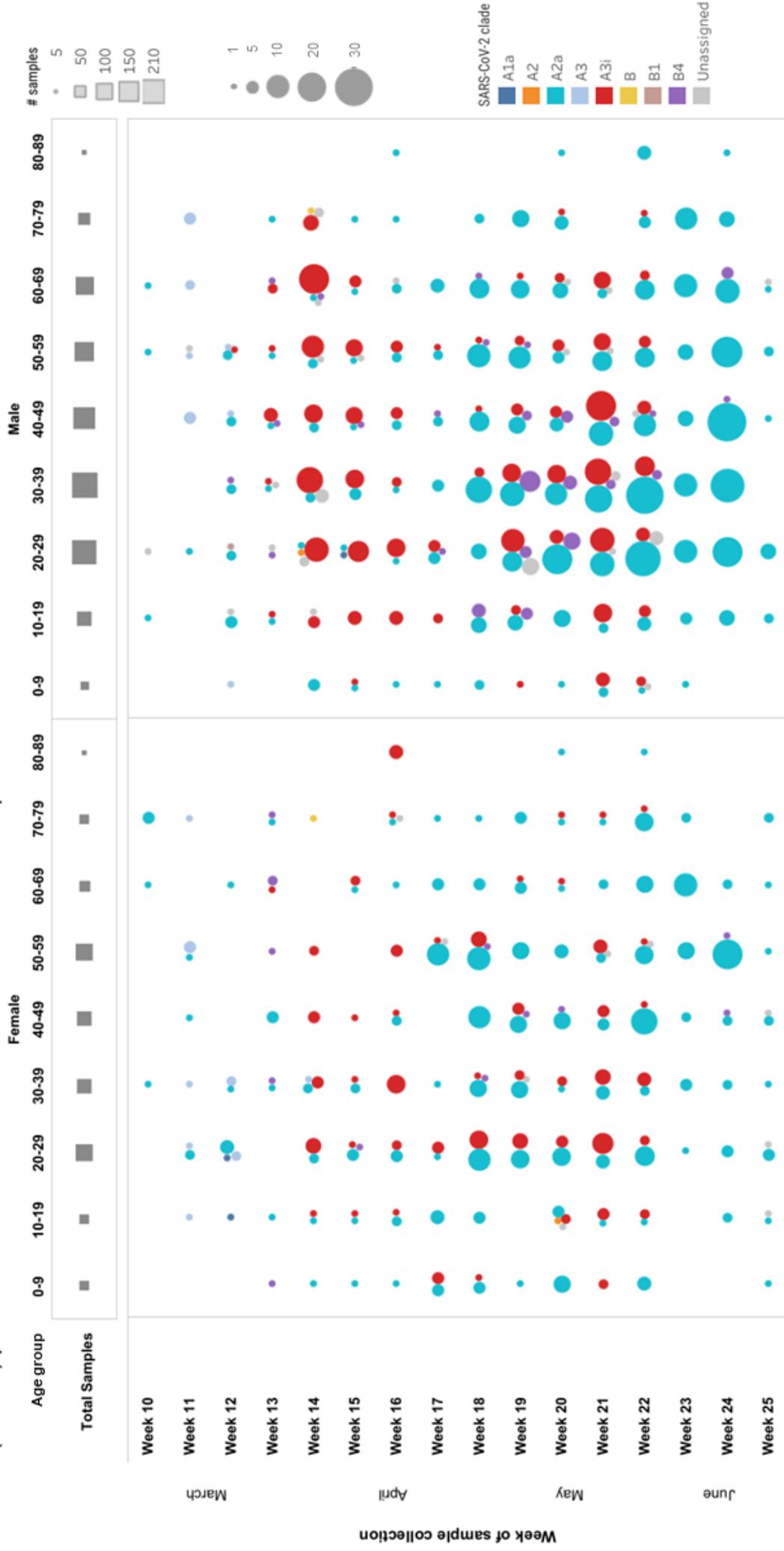
SARS-CoV-2
genome
sequencing
experience

SOFIA BANU

SARS-CoV-2 genomes sequenced from Indian patients

Clade (variant) prevalence from Feb-June 2020 for 1500 viral samples

Data: <https://data.cmb.res.in/gear19/>
 Viz @ <https://www.dataviz.in/>



Clades (color) and number of viral sequences (size of circle) displayed by gender and age group of patient vs. calendar week in which the sample was collected.

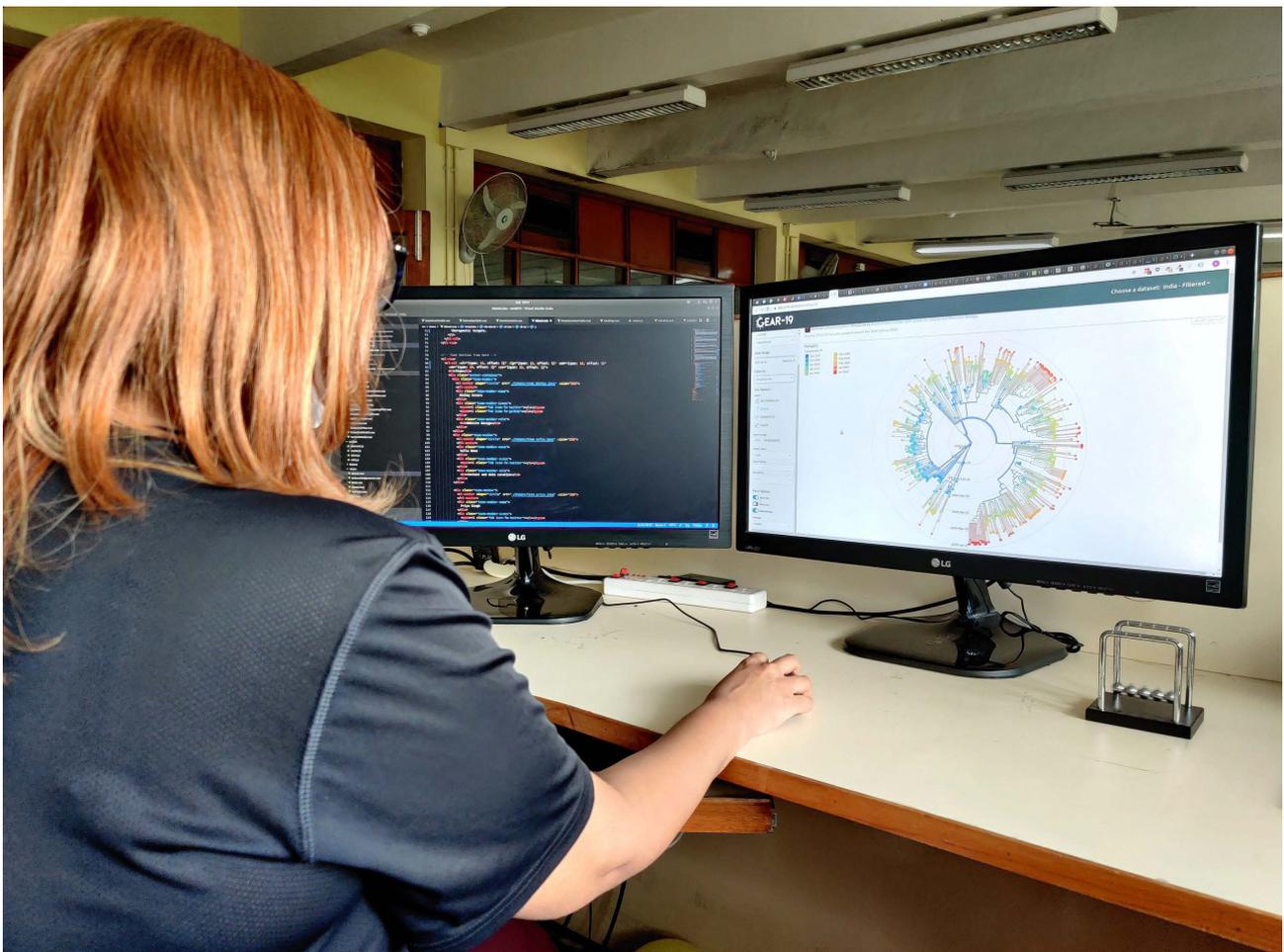
A unique cluster of SARS-CoV-2 genome variants/clades identified from India (Clade A3i), distinct from those currently annotated globally, appeared in March 2020 (Banu et al., 2020; bioRxiv). Over the pandemic's progress this summer, the A2a clade has emerged as the predominantly prevalent strain in the country. This analysis is based on the 1500 patient samples that were obtained and sequenced from March to June.

When one pictures a viral epidemic, visuals of frontline staff in protective suits immediately crosses one's mind. With an upward technology boom in biological sciences in the past few years, one must adapt to emerging resources and applications, look beyond the bench and this is where a small group of us bioinformaticians come into the picture. While the pandemic was gaining momentum in India and lockdowns were being enforced, I watched my peers and colleagues at CCMB engaged in testing of patient samples and racing against time to improve upon existing methodologies to quickly process the ever-increasing influx of samples. I wanted to be able to apply my bioinformatic skills to contribute towards understanding the virus but there was the big question of how.

As patient samples started pouring in and testing was in place, plans were being formulated by our institute to sequence SARS-CoV2 genomes in order to understand its spread geographically and identify any underlying modifications to the genome. Viral genomic

sequencing was new to us and we faced a few roadblocks initially. Failed genome sequencing attempts due to lower viral load in patient samples, sample collection issues, new protocols hindered our progress in the first few days. Eventually, we found our footing and were able to sequence genomes on a large scale.

As a researcher who has been dealing with eukaryotic genomic data for the past couple of years and time being a critical factor, I had very short time to learn viral genomics on the go. My fellow bioinformaticians and I had to work collaboratively from home initially over phone and video calls during the strict phases of lockdown. It was a testing time because we had to prepare ourselves for the new viral genomic data, write and standardize processing pipelines, plan analysis and keep updating ourselves with new findings all at once. Once we had access to the sequences; though we were prepared to a massive extent, we did have a mammoth task of identifying the best protocols to put together the perfect viral genome.



Our work here at the institute transcends beyond just generating genomes. Once we deposit genomes in a global public repository for viral genomes called GISAID, we next wear the hat of an epidemiologist. We use these genomes as well as the ones publicly deposited by other submitters to conduct genomic virus surveillance to monitor the spread across states in India. We track and identify the presence of new strains, monitor the dominance of a particular strain across states and look for possible demographic associations. Apart from this, we also identify single nucleotide changes in the viral genomes as well as their corresponding change in the amino acid sequences and monitor their change over time. We study these changes ie. mutations and computationally predict their possible effect

either on the virus pathogenicity or on the host. Our deductions are based on the number of genomes available to us at a particular time, and we constantly update our inferences. It has been an example of how both in-house and open source data complement each other, and throws light on the importance of data availability in making informed interpretations in pathogenomic studies.

Working on the sequencing front has been a colossal feat held together with pillars of teamwork, outstanding leadership, unparalleled coordination and support. I am fortunate to be involved in such an environment and we shall continue devising ways to mine genomic data for possible leads to overcome the coronavirus pandemic.

Fast-track
deployment:
Advantage
startups

RITIKA MARAMPALLI

COVID-19 came to the Indian shores by 30 January 2020. As the cases began to rise by March 2020, the public healthcare governance was quick to respond. One of the early policies in tackling the then still epidemic was to encourage the participation of the private sector. Unlike pharma giants, startups and MSMEs have a unique advantage of adapting their manufacturing to changing market demands.

CCMB has been actively involved in enabling science-based entrepreneurship through the Atal Incubation Centre (AIC-CCMB) and Common Research, and Technology Development Hub (CRTDH). A number of startups at CRTDH/AIC-CCMB began working on Covid-19 related solutions in the areas of diagnostics, therapeutics as well as disinfectants as early as Jan 2020. As Covid-19 was declared a pandemic and the world came to a screeching halt, CCMB was called to action as one of the primary testing labs in the state for SARS-CoV-2 in Telangana. It is also the only non-ICMR (Indian Council of Medical Research) lab designated to validate the non-US FDA, and non-EUA/CE-IVD approved kits for Covid-19 testing.

Mylab Discovery Solutions, a Pune based molecular diagnostic startup supported by Venture Center, CSIR-NCL the first Indian company to manufacture the Reverse transcriptase - polymerase chain reaction (RT-PCR) diagnostics kit for Covid-19. Another Hyderabad-based company, Huwel Lifesciences Pvt. Ltd. also received ICMR approval for their indigenous Covid-19 diagnostic kit. Huwel Lifesciences, a virtual incubatee of AIC-CCMB was founded by Dr. Rachana Tripathi & Dr. Shesheer Munpally - former research scholars of CCMB and are the promoters of SirfBio Pvt. Ltd., currently incubating in CRTDH/ AIC-CCMB.

Oncosimis Pvt Limited, one of the first companies to incubate in CRTDH/AIC-CCMB has developed a rapid and high-throughput screening of 2019-nCoV infection by bi-layer photo interferometric method. Their method detects anti-2019-nCoV S1-RBD IgG/IgM antibodies in serum/plasma that can give results in less than a minute. This method is capable of screening 100 samples in less than an hour. The

rapid and high-throughput screening is much more affordable with a shorter turnaround time. The kit is under development and CCMB is a partner in the commercialisation.

AIC-CCMB launched the CSIR-CCMB Covid-19 Fast Track Challenge in association with C-CAMP Bangalore's COVID-19 Innovations Deployment Accelerator (CIDA) in April with an objective to identify and support startups in the greater Hyderabad region who had ready to deploy solutions. Under the CIDA initiative, CCMB has pledged funding as well regulatory support in the early deployment and commercialisation of these innovations. By joining this initiative, our startups and researchers are able to leverage the combined support of partners like C-CAMP, UNHIE, Social Alpha, XYNTEO India2022, MedTech Connect, India Health Fund, PATH, and Action COVID-19 Team (ACT).

The CCMB-CCIDA challenge received more than 200 applications, every idea better than the next. Dr. Rakesh Mishra, Director, CCMB, Dr. Madhusudhana Rao, CEO, AIC-CCMB, Dr. Ramjee Pallela, COO, AIC-CCMB as well as external experts were a part of the Technical Advisory Group (TAG) constituted to select the best solutions based on the readiness to deploy and uniqueness of the innovations. Finally, six innovations were selected - four in the area of diagnostics and two in therapeutics. These proposals will be funded (upto INR 2 L per innovator) by CCMB. AIC-CCMB will create a pipeline for commercialization through fundraising, regulatory, facilitation through other agencies.

Other notable Covid-19 solutions by CRTDH/AIC-CCMB StartupsRR Animal Healthcare Pvt Ltd - Surface sanitiser RH+ was selected for C-CAMP CIDA. RH+ is a broad spectrum antimicrobial effective against all coated viruses and bacteria. Enhanced with potent sterilizing compounds, the product can be an ideal surface sanitizing solution in infection hotspots, hospitals, etc. as a potent solution for disinfection against coronavirus. The company has developed affordable "SPILD" VTM (viral transport medium) kits with IIT Guwahati. These kits comprise of a CDC recommended and validated transport



Recognizes CCMB as

A Centre of Excellence to
validate COVID-19 kits and
reagents



Deploying Covid -19 Innovations

CSIR-CCMB proudly announces support for startups and innovators in fasttrack deployment of critical technologies to help combat Coronavirus in India.

High Throughput Screening & Rapid Drug Repurposing to Combat SARS-CoV-2



Bi-layer Photo Interferometry based Rapid 2019-nCoV Detection Kit



RT-PCR based Diagnostic Kit for SARS-COV-2



LF based Rapid PoC Testing Device for COVID-19



Platform to Understand Antigenicity Potential & Drug Targeting for SARS-CoV-2



A novel sensitive detection of COVID19



In Association with



ATAL INCUBATION CENTRE
CENTRE FOR CELLULAR
& MOLECULAR BIOLOGY
Supported by Atal Innovation Mission, NITI Aayog



medium that is suitable for preserving the viability of SARS-CoV-2 and other viruses for upto 72 hours at refrigerated conditions. The swabs have a pre-molded breakpoint on their shaft for enabling secure sampling. The VTM kits were recently validated by CCMB as per the ICMR guidelines.

Albot Technologies Pvt Ltd - are working on developing a sensitive & specific immuno-diagnostic test against SARS-COV-2 causing Covid-19 using recombinant antigens. In parallel, they are also screening and characterization of GRAS probiotic strains.

Srikara Biologicals Private Limited & Consytel Life Sciences (Pvt) Ltd. - Both companies have come together for a collaborative study to identify and develop plant based (natural) drugs for SARS-COV-2.

Zedblox Logitech Pvt. Ltd. - ActiPod Smart Active Carrier are developing an intelligent temperature-controlled carrier for last mile cold chain logistics of various biological medicines, vaccines, diagnostics, human cultures and organs. This device uses AI, IoT and geo-sensing



for constant temperature monitoring, live location monitoring and AI based self-diagnostics and can be monitored from a smartphone.

Althion Tech Innovations Pvt. Ltd are developing an emergency pandemic ventilator which is funded by T-Works, Govt. of Telangana (TS). Mr Surya Rao, founder Althion was part of a local impromptu team which included members of T-works and 12 individuals from Hyderabad startups as well as Qualcomm and Honeywell that developed the ventilator. The. The prototype was successfully demonstrated

at NIMS-Hyderabad in the gracious presence of Hon. Shri K.T. Rama Rao, Minister of IT & Industries, Telangana.

In the last few years, CCMB has built an ecosystem to enable biotechnology innovation, engaging academia, industry and investors with entrepreneurs. Together with the passion and drive of our startups, CRTDH/AIC-CCMB is investing its collective knowledge and strengths to build 'Atmanirbhar Bharat' in mitigating Covid-19 while creating wealth and employment at the same time.



I have all praise for CCMB the way they have tackled the situation and changed its course of research in a very short duration. It is understandable that every institute does not have facilities like CCMB, but also reinforces the need of inter-institutional collaborations. The shortage of reagents in India revealed how badly we are dependent on foreign import to do our research- though there is no reason why we can't make them in our country. In my personal experience, for COVID-19 related research project, it took me only one day to get reagent from IICT but I am still waiting for ordered reagents. Institutes like IICT are fully capable of fulfilling the chemical requirements, it is the responsibility of other institutes and government to promote and channeled this process.

In every institute and in every lab, whether it is working on basic or application research, there is a possibility of societal implication of their research. There should be a government or institutional body (consisting of scientific and non-scientific members) to recognize the potential of social implication of scientific research and further role of government would be to provide special fund and encouragement to such projects.

Gunjan Purohit

Good policies
guide best
practices:
Lessons from a
pandemic

SURABHI SRIVASTAVA

Adversity can be a time of learning. The COVID-19 pandemic has upended life as we know it and created panic and uncertainty in communities across the globe. The last six months have caused unfortunate deaths and healthcare misery in almost all countries and India is no exception. The WHO declared COVID-19 a pandemic on 11th March 2020 and India imposed a complete lockdown within a couple of weeks to gain time to marshal healthcare resources. While governance focused on mitigating the impact of the virus, we at CCMB overhauled our research and our thinking to work through the uncertainty and continue contributing to science and to our society. In this article I will focus specifically on some of our work in pandemic preparedness, informing policy, and government and public health stakeholders in what the United Nations has called the 'most challenging global crisis since the second world war'.

As most research work ground to a halt, students and staff at CCMB learnt over the last few months to refocus on tackling multiple aspects of the pandemic instead. For me, and many others, this meant repurposing academic manuscript writing skills into drafting SOPs, white papers and information capsules for researchers and policymakers. A key lesson - sorting through the noise is an exacting and essential requirement for this task, wading through the 'infodemic' that has gone hand in hand, and indeed often surpassed the pandemic. In addition, COVID-19 is pushing scientific research at an unprecedented pace, and data often comes in through pre-prints and hurriedly published articles that need caution and expertise in interpreting results for informing policy. A quick search shows ~27,000 entries listed in Google Scholar on coronavirus in 2020 so far, about 7,500 articles in pre-print archives (arXiv, medRxiv and bioRxiv), and ~16,000 publications on PubMed. Continually tracking the enormous amount of information sources requires effort and team work to identify relevant information for our researchers to work on, and policymakers to be updated about. We therefore constituted an informal team at CCMB for discussions and regular updates.

Some of the key non-research aspects that we undertook, and indeed continue to work on, can

be broadly divided into two categories:

i) Research policies and directions In accordance with the COVID-19 related verticals created by CSIR, CCMB constituted a group of individuals to provide information to the Director for further discussions with CSIR HQ and lab heads. Our task was to keep ourselves updated on relevant information that can guide research directions and to prune away the chaff while providing brief summaries on new publications in peer reviewed journals as well as archived repositories.

One of CCMB's focus areas has been to develop and scale diagnostic testing capacity and accuracy. As a leader of the Rapid and Economical Diagnostics vertical at CSIR, the Director is also involved in the selection of projects that can target quick delivery of test kits and point of care diagnostics. CCMB has developed novel methods to improve testing capacity including an RNA extraction-free approach using dry swab collection method (Kiran et al., 2020), and a nested PCR based approach that does not require expensive real time PCR instruments (Davda et al., 2020). CCMB has also initiated a pilot run using a Next Generation Sequencing (NGS) based approach that can test thousands of samples in a batch. This is expected to bring down the cost under ₹200 per test and enhance throughput to ~50,000 tests/cycle. Apart from the original archival submissions, CCMB has been also developing Standard Operating Procedures (SOPs) and popularizing these research contributions for widespread adoption via technical recommendations, public outreach and journal and popular science articles. These have achieved widespread coverage on television, in print and electronic media.

The recommendations arising from our experiences in diagnostics and testing, sequencing, and culturing the virus are also incorporated into direct scientific consultations with the Principal Scientific Advisor, Director General, CSIR and the All Directors Meets with other CSIR lab heads.

ii) Consultation with government and public health agencies. Due to the nature of this health care emergency, CCMB has also been involved in other roles not traditionally a part of



the mandate of a basic biology research lab. This includes compiling information for guiding healthcare policy in the state and consultation with official stakeholders such as the Hyderabad Governor, Directorate of Medical Education (Telangana), and drawing up surveillance policy recommendations for the government regarding health care workers, patient care and global and India-specific status of vaccine and drug research.

CCMB has been constantly in touch with the Telangana State Government officials, Directorate of Medical Education as well as testing centers across the state. CCMB has been identified as an ICMR Centre of Excellence for validation of non-US FDA and non-European CE/IVD approved Covid-19 qRT-PCR diagnostics. Since mid-April, we have been active in testing kits indigenously developed by companies in India and giving expert recommendations. Handholding industry and start-ups ensures quality and faster delivery of indigenous products that can be cleared through government regulatory approvals.

As a part of the Expert Group for Telangana State for COVID-19, the Director conveys timely

and updated scientific information to the group. Through discussions with the Hon'ble State Minister of Health, Governor, Chief Secretary, Special Chief Secretary and IAS officials, CCMB has consulted with the state at various levels. The five-member inter-ministerial central team (IMCT) constituted by the Ministry of Home Affairs and led by the Additional Secretary, Ministry of Jal Shakti was also apprised during their visit of the new developments and measures at CCMB as early as April 2020.

As the country gears to open up lockdowns and remove restrictions we have also developed policy documents and self-contained notes on measures for scaling up the testing capacity of the country. Global experience shows that, as the nation-wide lockdown ends, tracking and testing infected individuals would need to expand significantly to understand the degree of spread of the virus and to design containment strategies. We at CCMB have worked to compile the best scientific approaches, weighing the economic and technical costs against benefits of scaled-up testing, for policy makers at the highest echelons of governance.



As a personal interest, I understood how mathematical models work in a pandemic like this. It also made me aware of how predictions, assisted by practical measures like testing and quarantine (done in several countries) can actually halt the progression of the disease. On a more human level, I and perhaps everyone, ate the humble pie looking that at even this stage of our modernity and technical progress, we have been shown mirror by a virus. Also, migrant crises gave us an opportunity to look into our own privileged lives.

Mihir Trivedi

New perspectives

COVID-19 has highlighted the importance of maintaining an open dialogue between the administration and the scientific community of a country, and we would do well to retain the dynamic developing in this time of crisis. The way forward lies in recognizing the role academic institutions play in society, not only in carrying out basic research but also in guiding best practices for policymakers. For the learnings of science to translate into benefits for

the people and our nation, a network of our best scientific and policy institutions must come together and create reliable road maps to tackle healthcare issues and promote indigenous solutions. Knowledge - through the evidence-based approach of science - and awareness are the basic pillars to drive away fear and stigma and counter an epidemic. As a premier research institute, we have a major role to play and a long way to go to help the country overcome this crisis.



COVID-19 awareness posters and sanitizers placed across the campus



Communicating the unknown

SOMDATTA KARAK

CCMB to start genome research on samples of Covid-19 patients

Hyderabad: The Centre for Cellular and Molecular Biology (CCMB) will start genomic research on samples of Covid-19 patients in Telangana and other parts of the state. The research is to study why some patients in Telangana are asymptomatic while the rest of the 40 per cent require intensive treatment. It may help in understanding the dynamic nature of the virus and the information may be helpful in developing a vaccine.

Pyt lab offers Covid-19 risk test, CCMB chief sceptical

Hyderabad: If you are worried about Covid-19, then a diagnostic company now promises to provide DNA based risk test to report whether you are asymptomatic or whether you are at risk of getting infected. The test is based on a proprietary algorithm developed by the company. The test is available in Hyderabad and other parts of the state. CCMB chief is sceptical about the test.

CCMB develops Covid-19 tests more samples

Hyderabad: The Centre for Cellular and Molecular Biology (CCMB) has developed a new test for Covid-19. The test is more accurate than the standard RT-PCR test. The test is available in Hyderabad and other parts of the state.

CCMB finds distinct cluster among Indians but made it clear that there is no

Hyderabad: The Centre for Cellular and Molecular Biology (CCMB) has identified a unique cluster of virus among Indians but made it clear that there is no significant difference between the Indian and non-Indian strains.

CCMB tests to detect Covid-19 are fully reliable, says CCMB study

Hyderabad: In a finding that could have widespread ramifications, researchers at the Centre for Cellular and Molecular Biology (CCMB), Hyderabad, have found that about 50% of Covid-19 positive samples tested through the standard RT-PCR may not yield the correct results.

Scientists identify second common coronavirus type

Hyderabad: Scientists have identified a second common coronavirus type. The virus is found in 41% of those analysed. The virus is more efficiently in the lungs.

CCMB DIRECTOR VOUCHES FOR RAPID TESTING

Hyderabad: CCMB Director Rakesh Mishra has vouched for rapid testing. He said that rapid testing is essential for controlling the spread of the virus. He also mentioned that the government should test large number of people quickly, decide whether to lift lockdown, understand which areas are most affected.

CCMB finds cheaper, more effective RT-PCR method to test COVID-19 samples

The procedure would be useful in the face of increasing need for testing across the country.

'Premature to say Indian strain of virus less virulent'

Hyderabad: The Centre for Cellular and Molecular Biology (CCMB) scientists have said it is "scientifically unsound and premature" to speculate that the new coronavirus (SARS-CoV-2) Indian strain is less virulent than the ones circulating in China, Italy and other countries.

CCMB begins research on fast-tracking Covid-19 drug

Hyderabad: The Centre for Cellular and Molecular Biology (CCMB) has started research on fast-tracking a Covid-19 drug. The research is to identify potential drug targets and develop a vaccine.

CCMB gets testing kit to test 60 samples today

Hyderabad: The Centre for Cellular and Molecular Biology (CCMB) has received a testing kit to test 60 samples today. The kit is used for the detection of the virus.

'More testing will help us know COVID-19 spread'

Hyderabad: CCMB Director Rakesh Mishra has said that more testing will help us know the spread of COVID-19. He said that the government should test large number of people quickly.

CCMB to speed up COVID test results

Hyderabad: The Centre for Cellular and Molecular Biology (CCMB) is planning to speed up COVID test results. The test is to be completed within hours.

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CCMB to grow virus

Hyderabad: The Centre for Cellular and Molecular Biology (CCMB) will be growing the virus in human cells. The research is to study the virus's behavior and its interaction with the host cells.

'Earliest anti-corona drug a year away or longer'

Hyderabad: Although research on the Cell Culture system is picking up, and systems are in place to start testing antiviral compounds produced by various institutions, the earliest drug that can come out will take at least a year or longer.

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Coronavirus variant in Telangana linked to Indonesian tested in March

Hyderabad: A coronavirus variant found in Telangana is linked to a variant tested in Indonesia in March. The variant is more virulent than the others.

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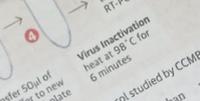
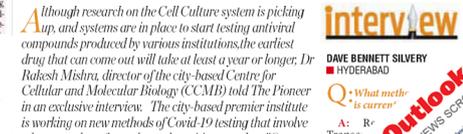
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The fear was setting in the city of Hyderabad in the month of March. Amid this I was travelling to work in a crowded metro, eyeing my co-passengers suspiciously on who might have just returned from a trip abroad. My phone rang, and I was told to make posters on the Do's and Don'ts during COVID-19 within the next two days. It was not the urgency of the matter that concerned me. It was rather the worry of making posters for public consumption on a topic that I as well as the world did not understand enough.

And this was only the beginning. Posters, videos, social media posts from our end, attention from the media have kept us in the limelight throughout. And in these times, being a credible voice meant a lot of responsibility for us to shoulder. It needed the right balance between caution, optimism, information and acceptance of our shortcomings. Over time we have stumbled upon questions that we have not had answers to then. These ranged from preventive measures such as the need for masks, if physical distancing of 6 ft was enough or how long the virus survives or how it spreads to the mortality of COVID-19 among others. Some of these questions have now been answered through COVID-19 research across the world, some not, and some new ones have now been added to the list.

For the first time ever in my term at CCMB, I saw information flowing through only a defined channel within the institute as well as with stakeholders outside. What I would have otherwise called extreme, it was imperative in these times of infodemic. It was absolutely necessary for a defined team to be responsible for the messages that are going out. Not because they had a better authority on the knowledge. But because they knew where

messaging had to be corrected as we understood the virus and the disease better each day.

This was also the first time that the entire current population in the world is living a common and novel uncertainty. While scientists are used to dealing with uncertainties, general public isn't. They expected a miracle drug or an overnight vaccine. Things didn't go that way - because they don't.

It was our responsibility to constantly engage with public on the way science proceeds. CSIR, with its 38 labs, came together to work this out. Blogs, articles in newspapers and magazines, interviews with TV channels are all being used to ensure the messaging goes straight from the resource people to the audience in different parts of India. Regular webinars with various stakeholders have started on social media to look at the problems from multiple perspectives. The heads of organizations and scientists heading the COVID-19 verticals have become accessible. People in different cities and expertise across CSIR has now started collaborating with each other in building, vetting and distributing content. All of this with the aim of helping the public keep pace with us in understanding the new normal.

As we work our lives out through this crisis, it also brings interesting possibilities for us, the science communicators. This opens up avenues for us to discuss how much of the world around us is unknown to us, pace of technological development, and the country's capabilities and capacities. Will that make for a stronger case for us as a society to dwell on science organizations and understanding their work and methodology better? I want to live through the pandemic to see that.



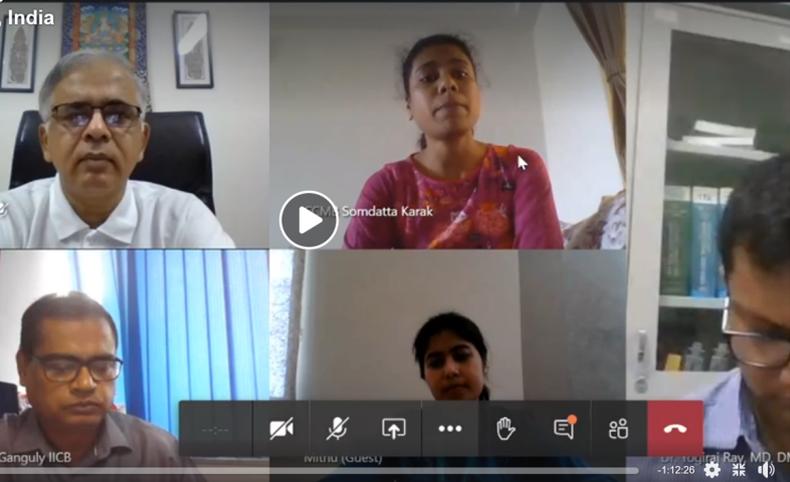
I realized that we are not doing enough to make the society understand the importance of science and scientific methodology. As a researcher, it's pathetic to see people believe that sound and fire can kill the virus.

Santosh Kumar Kuncha

Seeing
CCMB in a
new light

B V RAMAKRISHNA

నం డేంజర్ నుంచి తప్పించుకున్నామా..?



నా మందు తయారీకి కీలకం కానున్న ఫలితాలు



PROF SARMAN SINGH
Director, AIIMS Bhopal



DR RAKESH MISHRA
Director, Centre for Cellular & Molecular Biology



I recall the words of Dr. Jayaprakash Narayan, who graced the dais at CCMB as a chief guest on 26 January 2020 on the eve of Republic Day. He spoke of the repercussions of the virus outbreak at Wuhan, China, and if it occurs in India, it can only be mitigated with the help of research institutes like CCMB. By then, I thought, this seemed like a far-fetched reality.

However, in the coming days when I organized a press meeting at CCMB with the Director, I happened to hear the incidences of COVID-19 in India. More specifically, a case was identified in the old city, alarming the people of Hyderabad. I was at my daughter's place at Anakapalli, Andhra Pradesh, with my family when the Junta Curfew was announced by the Honorable Prime Minister of India, which was followed by the extended lockdown. With an intuition that my services would be required at CCMB during this lockdown, I preponed my traveling to Hyderabad. This gave me an opportunity to be part of the COVID-19 team here, and contribute to the Nation's call.

As a Public Relations Officer, I started receiving a huge number of phone calls and emails, seeking clarifications on COVID-19 related activities at CCMB. I also received an equal number of comments and suggestions to handle the situation at a research level. I could contact the Director and consult scientists who are always available at CCMB to provide appropriate responses. It was a great experience coordinating COVID-19 activities with people within and outside the institute. I must mention that our Director was always available to reach out to people outside. I made several efforts in identifying several important channels for disseminating information on COVID-19 related work being carried out by different groups at CCMB. The interviews of CCMB Director helped in creating awareness on the pandemic and the precautions to be taken to protect people. These interviews in several TVs provided an excellent outreach in creating awareness among the people. This was not missed by the Governor of Telangana who appreciated our efforts in her tweets.

I must also thank the journalist friends who have been always enthusiastic to gather and disseminate information from CCMB.

Until 24 March 2020, I thought CCMB as a Central Government institute focusing on the basic aspects of cell and molecular biology. But now people identify it with human health and disease. In the last two months, the institute has emerged in the areas of advisory, collaborative, diagnostics, and developing basic tools and guidelines for COVID-19. In fact, based on the request of Honorable Chief Minister, Shri K Chandra Shekar Rao to Honorable Prime Minister of India, Shri P Narendra Modi, it took only 48 h for a basic research institute to shape up to COVID-19 testing and research lab. Ever since, the institute hasn't rested for a day or night, and weekday or weekend.

Forgetting holidays and festivals people have worked here round the clock since then on the pandemic in day and night shifts. I am blessed to be in this Institute and happy to be part of the COVID-19 team under the dynamic and able guidance of our Director. Like many of us, I am also looking forward to vaccines/drugs from our institute.



Dr TAMILISAI Soundararajan ✓
@DrTamilisaiGuv

Director Rakesh k Mishra
Director CCMB interview
highlighted world class
facilities in CCMB for validation
of diagnostic kits & training
opportunities .Recall my VC with
him wherein he shared valuable
information on the potential
expertise in @ccmb_csir to take
forward in future





CCMB has people who can educate the ones not so aware of the situation, specially the marginalized class about the issue with pandemic. The problem today is with people becoming more casual about physical distancing protocols as the lockdown lifts. Educated and less educated alike. We, as an institute, may need to put up more societal awareness messages by webinars, videos, flyers

Aritri Dutta

Communication in times of a pandemic

ASHISH BIHANI

A pandemic is a curious sort of calamity. There is nowhere to run. Only way out for a long time is to take precautions. In addition, right when even the scientific community finds itself dumbfounded by the explosion, a variety of pseudo-scientific theories and cures mushroom up on mass media. At that point, we need to explain the problem, recount the basic preventive steps one can take and debunk the most influential or appealing misinformation that is around. This needs to be done via simple messages, necessarily in native languages, in this particular case, without sabotaging social distancing yourselves.

We set about this, heavily utilizing social media tools. First, I wrote a basic script in the language I know best, Hindi. We had it critiqued by people with experience in science communication and biology (mostly fellow researchers in Hyderabad biocluster) through online collaborative document editing. Then, with a normal phone camera and mic, I made a quick recording. We had it looked at by the aforementioned group using WhatsApp and cloud storage.

Simply using our person to person networks, we found people who knew different Indian languages (which is easy because good research institutes are often very diverse). We found people who knew Tamil, Telugu, Malayalam, Punjabi, Marwari, Gujarati, Marathi, Maithili, Bengali, Nepali and Manipuri. Some translated, others made recordings, others found more people who knew other languages. Thus, within days, we had created videos in more than a dozen Indian languages, uploaded them on YouTube and shared across Facebook, Twitter, LinkedIn and Reddit*. Looking at our scale, we got a sizable response – people thanking us and asking further questions.

India hosts incredible linguistic and cultural diversity. We cannot expect this huge number of people to learn one single language. There is a radical need to bolster scientific education and communication in native languages, so that people have to cross only one barrier instead of two (language and subject) to understand scientific information. There really isn't sufficient infrastructure for that right now. I discovered that there were several locally organized, concerted efforts to do this. But these efforts have limited reach.

Scientists are a small minority in the national workforce. They need additional hands and mouths to create an army of science communicators. This could be people like teachers, doctors, engineers, etc. These people would become the channel to reach masses. They can translate and put the scientific discoveries and information in their local context. Needless to say this is important for young minds, especially for those in rural areas where access to other kinds of media can be a challenge. This information can be evaluated and broadcasted on a wide scale (newspapers, TV channels, radio broadcasts, chat groups and sessions in remote areas). Such routes are helpful in continued discussions – an enormous need while dealing with a novel pandemic. In the long term, if we create an extensive translation and emanation machinery, it may bring about scientific research in native languages. Our vibrant culture definitely needs this mechanism to sustain itself.

We have a long way to go towards preparing our people, scientists and communicators to fight such menaces, that we expect, to only become more frequent in near future. A long arduous way to fight with openness, with empathy, with uncluttered communication.

*Link to the videos-

https://www.youtube.com/watch?v=kF4wBQSQxaA&list=UUKm_jr3spl_Y06RYSv6NWWGw

Going
ahead by
oneself

KAMAL MALUKANI

Being someone who has a runny nose once every week, it was hard for me to volunteer for COVID-19 related research and testing. I used a different approach. I started making videos on coronavirus related information and circulated it on social media. Later I also started personal on-call consultancy for people not following lockdown seriously. I asked everyone I know, outside the science community, to take proper precautions and asked them to advise the same to others. If they were not able to convince someone, my friends or relatives made them talk to me and I convinced them in a simple way with scientific facts. Later I also started

answering doubts of people on Quora and removing fake information from the platform

This whole information taught me one thing, in between over-hyped media, right concise important information is fading away. There is no one-stop place with just important information that someone needs in daily life. A simple sober website. So, I started a website for scientific information in simple language*. It's in English and I'm going to soon start one in Hindi as well. I hope our cumulative efforts can increase awareness and save people from COVID-19.

*Link to the website-

<https://www.lifewithcoronavirus.org/>

I have learned new skills and have experienced what it feels to be doing a team work for the society in mid of a pandemic. It makes me believe that we as scientists can and have a lot to do for the wellness of our world.

Pratheusa Machha

As a premier institute in the country, CCMB can make the understanding to crises much more lucid and can allay the unnecessary fears (also, make them cautious, if necessary!) about how the pandemic spreads and how it can be decelerated, though cannot be eradicated. As an institute, I am proud that many of us have contributed immensely for the cause.

Mihir Trivedi

LaCONES
during the
pandemic

KARTHIKEYAN VASUDEVAN



Working with physical distancing protocols at LaCONES-CCMB

SARS-CoV-2 brought most to a standstill in India except poaching, which went on a rise [1]. However, between the last week of March and first week of May we received only six wildlife forensic cases! This might be due to insufficient field staff stationed in the field, at that time to process the cases. Subsequently, from the second week of May, till date, we received 22 cases. Gearing up to the “new normal” we put in place SOPs for receiving and opening cases, to ensure safety of staff handling the cases. This was essential so that the staff handling the cases is not exposed to infection.

It is during this period that the Maharashtra state forest staff rescued an abandoned ~3 months old tiger cub found in an agricultural field in Chandrapur district. They tracked two female tigers with cubs in the vicinity of 5 sq. km. This case was referred to us with a request to identify the mother of the cub based on fecal samples of tigers collected from the forest. Our analysis provided the identity of the tigress, the mother of the rescued cub. The forest department is using this report to reunite the cub with the tigress in Chandrapur forests.

On the other hand, on April 5, 2020, Bronx Zoo, USA, reported that a four-year-old female Malayan tiger had tested positive for COVID-19. They also found three other tigers and three African lions showed similar symptoms, and were later confirmed to be infected. This triggered a concern in India with a possibility of infection spreading in zoo animals and in the wild populations.

SARS-CoV-2 infection in animals meets the criteria of an emerging disease [2]. The World Organisation of Animal Health (OIE) announced that animals infected with SARS-CoV-2 should be reported to the OIE in accordance with the OIE Terrestrial Animal Health Code and include information about the species, diagnostic tests, and relevant epidemiological information. The Central Zoo Authority and Telangana State Forest Department have been in constant touch with LaCONES, to understand the scope of the problem and the way to deal with it. The Nehru Zoological Park consulted us to put preventive measures in place to avoid spread infection from zoo staff to animals. We also house leopards in the animal cages. We put sanitization protocols in place, and monitored the health of our animals.

During this period several news reporters sought information on the possibility of infection spreading from pet animals to humans, from meat shops, and the level of hygiene to be maintained with pets. We provided scientifically valid information to the reporters, so that, well-curated information is disseminated to the public.

Now as facilities are opening up, zoos are no exception. Our role continues with the Central Zoo Authority and the Telangana State to make guidelines and norms for opening up the zoos for the public again.



A white tiger with neoplastic growth treated at LaCONES-CCMB



Temperature checking and hand sanitization at the campus entrance



Proteomics
facility
during
COVID-19

SWASTI RAYCHAUDHARI

We, at the proteomics facility at CCMB, were preparing for the inevitable already 7-10 days before the lockdown was announced. At that time, we were anxiously waiting for the arrival of Zeol engineers from Japan and Singapore to train us on the newly installed MALDI TOF/TOF mass spectrometer. One of the first things we were forced to do was to postpone this training. We also decided to avoid public transport as much as possible and I suggested the staff to coordinate with the users and attend duty as per requirement only.

Then the lockdown was enforced within a week's time and research work was stopped. We also stopped accepting samples from users. None of our staff was considered as essential for

COVID-19 related emergency duties. However, complete shutdown of mass spectrometers is not advised. Therefore, as a local-resident I was managing to attend the mass spectrometers at least on alternative days and kept them functioning for a month. Ultimately, we could arrange a COVID-19 essential service pass for a senior staff around end-April to start analyzing COVID-19 related samples. Guidelines for the new-normal activities were prepared and communicated. Within a week of unlocking we started operating all the mass spectrometers and HPLC instruments to their full capacity. Staff remained flexible in attending daily duties and contributing to COVID-19 testing activities. We are now planning online training for the MALDI TOF/TOF mass spectrometer.





CCMB canteen's kitchen during COVID-19



CCMB canteen has functioned every single day of the pandemic with staff & resource reorganization.



Meals at CCMB during COVID-19



Tissue
culture
facility
during
COVID-19

VEGESNA RADHA



For a setup that caters to over 100 users culturing and experimenting with live cells, the sudden lockdown imposed in the wake of the COVID-19 pandemic came as a major challenge.

The facility normally involves 2 arms of activities; 1) maintenance of nearly 200 cell lines, primary cells, iPSCs, etc, and 2) maintenance of a variety of equipment, and stocks of reagents required by users to culture cells and tissues. At any point in time, the majority of the users are carrying out experiments that require a minimum of a week, to several weeks/months.

Shutting the facility meant loss of effort, time and resources in the case of ongoing expts. Shutting down could not happen as suddenly as an administrative decision was taken, as it involved ensuring that all the incubators were cleaned, and rid of moisture after shutting off. We had to ensure that the facility was shut down in a phased manner to enable some of the users who were generating stable cell lines, to grow them sufficiently to freeze. Because all work on the floor requires to be carried out under sterile conditions, it was important that maintenance staff attended to work daily to keep the place clean. Some users were specially enabled to carry on their experiments required for time bound revision of papers. The other activity that was essential in nature was to

replenish liquid nitrogen in the canisters which store the frozen cell stocks. This had to be done at least twice a week, and required coordination with personnel maintaining the liquid nitrogen plant.

The shutting down of the facility of course caused disappointments because many ongoing expts that were of long term nature like characterizing stable lines, new hybridomas, and organoids had to be stopped abruptly.

I can't but refrain from mentioning that while all citizens were remaining at home to stay safe, the TC staff had to attend to duty by travelling long distances, and putting up with many hurdles on the streets. Infact, few of the staff were even coming through roundabout routes, before they could be issued passes. It was very heartening to see how the staff coordinated among themselves with extra-ordinary responsibility to ensure that the facility did not suffer any setbacks or damages during the lockdown. Their involvement with the facility and the extent to which they are duty bound, stood out starkly during this period, something to be said of the special culture ingrained in all of us at CCMB. This is something that requires to be recognized and applauded.



COVID-19 has also taught all kinds of lessons, irrespective of any field from taking care of planet mother earth to the major GDP of any country, is based on Science, Technology, and its R&D. Every Individual has to contribute their own time and some due respect in not harming any other living being. Should maintain the eating habits, let us and others live happily without disturbing the ecosystem. This crisis has been a test for each individual who wants to survive healthy and happy. It has taught us the importance of life and has given an insight into the future.

Purushotham V

Scientific literature is not something that should be taken for granted. A review published in Clinical Microbiology reviews by Dr. Vincent C., et. al, in Oct 2007, clearly said that there is presence of SARS-CoV like viruses in horseshoe bats and culturing of exotic animals in Southern China for eating would be a time bomb. Despite a published study, we came to a point where there was nothing that could be done to prevent this pandemic. This only tells us how the scientific communities' work shouldn't be taken for granted, studies should receive proper funding in order to ensure generation of effective precautionary measures if not prevention.

Saniya Pamnani

Organization pursuing science at the highest level must take 'proactive' measures to enable the society to adopt a scientific way of life. CCMB has been at the forefront of such efforts. However, the target audience of these initiatives could be expanded to encompass laymen and not just students.

G Aditya Kumar