



National Institute of Plant Genome research (NIPGR), New Delhi

DBT- National Institute of Plant Genome Research (NIPGR) effort in fight against COVID-19

The entire world is going through a very challenging time due to the pandemic caused by SARS-CoV-2. To tackle this grave situation there is an immediate need to find therapeutic agents and vaccine against this virus. NIPGR is also contributing in research preparedness in the fight against this virus. Three research groups are rigorously involved in developing plant-based vaccine against SARS-CoV-2 and in exploring plant natural products that are potentially anti-viral in nature. The potential activity of the identified molecule/s against SARS-CoV-2 is under testing in collaboration with International Centre for Genetic Engineering and Biotechnology, New Delhi and Regional Centre for Biotechnology, Faridabad.

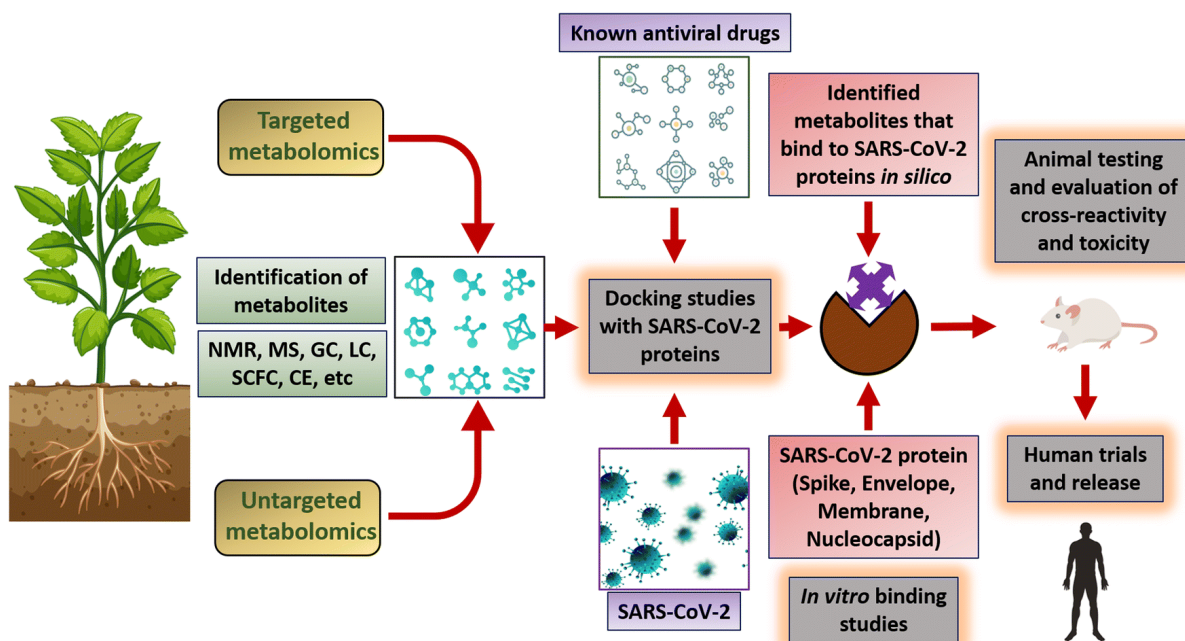


Fig 1: A possible route of identification of antiviral drugs against SARS-CoV-2

A platform for producing COVID related antigens and anti-viral proteins through transient expression in plants

The N-terminal region of SARS-CoV-2 S-glycoprotein consists of receptor-binding domain (RBD) and studies have shown that antibodies against this region can effectively block RBD-ACE2 (host-receptor) interaction. The codon optimized RBD was transiently expressed in *Nicotiana benthamiana* and it was found to be localized in the cytoplasm. The leaf extracts of

plants expressing the RBD and purified protein will be tested and used for immunization of mice (in collaboration with ICGEB, New Delhi) with different doses to trigger a strong immune response against the virus. As plant-based vaccines provide the ease of administration and monitoring, developing such a vaccine for SARS-CoV-2 would assist in executing mass immunization drives.

Examining the potential for the use of the plant natural products, flavonoids, against SARS-CoV-2

Plants produce a variety of natural products in responses to biotic stresses. One major category of plant specialized metabolites are flavonoids. Besides their role in plant biology, flavonoids are reported to have a variety of health benefits. NIPGR laboratory is working with flavonoids to find its applications towards promoting human health. Identifying anti-viral molecules that work against SARS-CoV-2 is of utmost importance in the fight against COVID-19. Keeping this in mind, possible flavonoids which shown to be or predicted to be active against RNA viruses based on literature search have been identified and molecular docking experiments to screen the potential flavonoids against coronavirus proteins such as receptor binding domain (RBD) densely glycosylated spike (S) protein, main protease (M^{pro}), etc. have been done. The promising flavonoids, were purified from banana peel (agro-waste) to perform the *in vitro* binding assay with M^{pro} of SARS-CoV-2 in collaboration with ICGEB, New Delhi. Using *in silico* and *in vitro* binding assay data, the potential flavonoids were screened and tested their anti-viral activity at RCB, Faridabad.

Testing potential of glucosinolate derived isothiocyanate for anti-viral activity against COVID-19

Glucosinolate derived isothiocyanates (ITC) from cruciferous vegetables have been studied extensively in cells and in animals for their disease preventive and therapeutic effects. Sulforaphane (SFN), the major glucosinolate derived ITC present in Broccoli has been well-recognized as an antioxidant, antitumor compound, and potent immune modulator against the attack of microbes. There are also indications that glucosinolate-derived ITCs have anti-viral activity. In another work, the efficacy of various glucosinolates and their isothiocyanates for their anti-viral activity against COVID-19 were tested and to produce it cheaply from plants, in collaboration with RCB, Faridabad. Various potent glucosinolates namely, sinigrin (from *B. nigra*), gluconapin (*B. rapa*) and glucomoringin (*Moringa oleifera*) have been purified in high amounts from seeds and sprouts. Besides, *B. juncea* transgenic lines accumulating high amounts of glucoraphanin (4MSOB) and its isothiocyanate derivative, SFN (4MSOB-ITC) were developed by NIPGR, and used for purification of these precursor glucosinolate at high purity. At least 250 mg of the intact glucosinolates were obtained (1%) and converted enzymatically into their ITC forms (~5 mg) for testing the anti-viral activity. The purity of these compounds were determined by HPLC and LC-MS facility at NIPGR. The determination of cytotoxicity and anti-viral activities of the purified glucosinolates and their ITC forms against COVID-19 infected transformed cell lines has been done at RCB, Faridabad.

Publications:

- Prasad, A., Muthamilarasan, M., & Prasad, M. (2020). Synergistic antiviral effects against SARS-CoV-2 by plant-based molecules. *Plant cell reports*, 39(9), 1109–1114. <https://doi.org/10.1007/s00299-020-02560-w>
- Prasad, A., & Prasad, M. (2020). Single Virus Targeting Multiple Organs: What We Know and Where We Are Heading?. *Frontiers in medicine*, 7, 370. <https://doi.org/10.3389/fmed.2020.00370>
- Prasad, A., & Prasad, M. (2020). SARS-CoV-2: the emergence of a viral pathogen causing havoc on human existence. *Journal of genetics*, 99(1), 37. <https://doi.org/10.1007/s12041-020-01205-x>
- Sharma, N., Muthamilarasan, M., Prasad, A., & Prasad, M. (2020). Genomics approaches to synthesize plant-based biomolecules for therapeutic applications to combat SARS-CoV-2. *Genomics*, 112(6), 4322–4331. <https://doi.org/10.1016/j.ygeno.2020.07.033>
- Prasad, A., Chirom, O., & Prasad, M. (2021). Insights into the biology of SARS-CoV-2. In: Pal, S (eds) COVID-19 Pandemic: A comprehensive understanding. (US ISBN, Under Process)

Notable outcomes and achievements:

- Development of a plant-based platform for producing COVID related antigens and anti-viral proteins
- Molecular docking studies identified anti-viral potential of plant natural products, flavonoids and glucosinolates, against key proteins of SARS-CoV-2
- Purification and testing anti-viral activities of potential flavonoids and glucosinolates, against SARS-CoV-2
- Four high quality publications related to COVID-19 for societal awareness



Institute of Bioresources and Sustainable Development (IBSD), Imphal

Content on COVID-19 efforts of DBT-IBSD for updating COVID-19 Corner of DBT Website

Establishment of INSACOG facility at IBSD, Imphal

The Indian SARS-CoV-2 Genomics Consortium (INSACOG) facility had been established successfully at IBSD, Imphal which is the first time such an effort has been made in this part of the country. The facility was inaugurated by Sri N Biren Singh, Honorable Chief Minister of Manipur in presence of other dignitaries. The sequencing platform/ laboratory within Manipur will be a big leap in our collective fight and understanding of the novel coronavirus. Through this INSACOG network the whole genome sequencing of SARS-CoV-2 virus across the nation can be performed, aiding in the understanding of how the virus spreads and evolves. Any changes to the genetic code, or mutations, can be observed in the samples and provide information to aid public health response to identify the new variants evolving from mutation. INSACOG also aims to focus on sequencing of clinical samples to understand the disease dynamics and severity. IBSD is taking the lead role to establish the facilities with all the instruments required including the sequencing platform for the COVID virus. Now the samples will be tested in the INSACOG sequencing facility at IBSD Campus, Takyelpat, Imphal, where genome sequencing of SARS CoV-2 will be performed for not only Manipur but also for other states of North eastern region of India.

The Indian SARS-CoV-2 Genomics Consortium (INSACOG), jointly initiated by the Union Health Ministry of Health and Department of Biotechnology (DBT) with Council for Scientific & Industrial Research (CSIR) and Indian Council of Medical Research (ICMR) is a consortium of 28 National Laboratories to monitor the genomic variations in the SARS-CoV-2. INSACOG is a multi-laboratory, multi-agency, Pan-India network to monitor genomic variations in the SARS-CoV-2 by a sentinel sequencing effort. The network carries out whole genome sequencing of SARS-CoV-2 virus across the nation, aiding the understanding of how the virus spreads and evolves, and provide information to aid public health response. Initially, ten Regional Genome Sequencing Laboratories (RGSLs) spread across the country were identified to carry out genome sequencing of positive samples from different states which is facilitated by the National Centre for Disease Control (NCDC), Delhi involving the Central Surveillance Unit (CSU) under Integrated Disease Surveillance Programme (IDSP). In view of the increasing realization of disease spread and with the possibility of a third wave, it was decided to increase the sequencing efforts in the country. In addition, as the reported cases of reinfection and vaccine breakthroughs being recorded, including these samples for sequencing assumes importance. INSACOG also aims to focus on sequencing of clinical samples to understand the disease dynamics and severity. Under the Indian SARS-CoV-2 Genomics Consortium (INSACOG), IBSD has taken the initiative for viral genome sequencing-based surveillance of the COVID-19 virus. The INSACOG sequencing facility at IBSD is equipped with modern state of art technologies including the Illumina's MiSeq and NextSeq 550 platforms, Qubit 4.0 from invitrogen and Agilent's Tapstation. Out of samples received from RIMS, Babina and Shija hostpitals, IBSD has completed sequencing of 96 viral genomes on the MiSeq platform. The analysis of these 96 samples is currently underway to determine the variant circulating in the State. Consumables for 3072 viral genome sequencing have already been procured. With the NextSeq 550 platform a total of 384 samples will now be sequenced per run. Currently, IBSD has started sample preparation for the NextSeq 550 run.



Interaction programme on Indian SARS-CoV-2 Genomics Consortium (INSACOG) sequencing facility

An interaction programme in connection with the newly opened Indian SARS-CoV-2 Genomics Consortium (INSACOG) sequencing facility was held at Institute of Bioresources and Sustainable Development (IBSD), Imphal on 14th July 2021. The programme was attended by advisor to Chief Minister (Health) MLA Dr. S. Ranjan Singh, Principal Secretary (Health) Vumlunmang Vualnam, Health Services Director Dr. K Rajo Singh, IBSD Director Pulok Kumar Mukherjee and Babina Diagnostic Centre Managing Director Dr. Th Dhabali Singh. On the occasion, Dr. S. Ranjan Singh, MLA, stated the importance of having such sequencing facility to fight against the pandemic and further delight in having such facility for the first time

in the state. Principal Secretary (Health), FM and AYUSH Vumlungmang Vualnam stated that Indian SARS-CoV-2 Genomics Sequencing equipment and facility has come through the special efforts by the IBSD and expressed his appreciation to IBSD, the entire team and the Department of Biotechnology, Government of India which has facilitated Genomics Sequencing Laboratories for the state of Manipur which would help to get the information about the variant more precisely, quickly and helps to understand the variant of Covid-19. He maintained that the laboratories can receive samples not only from Manipur but also from the other North East states too. He also encouraged IBSD, all members of the scientific community to continue efforts in the fields of Scientific research and knowledge to fight against the pandemic. The officials inspected PCR and Library preparation Laboratory, Sample Processing Laboratory, Delta Analysis Room and Next Generation Sequencing Facility.



Distribution of institute made face masks along with surgical mask to contain the spread of COVID-19 on 08.07.2021 at IBSD, Shillong

Institute of Bioresources and Sustainable Development (DBT-IBSD), Shillong Node, Meghalaya, handed over institute made face masks along with surgical mask to Mr. Damanstar Syiemlieh, President, Meghalaya State Agricultural Marketing Board, Upper Shillong Farmers Market Sanmer, Upper Shillong, Meghalaya 8th July 2021. The initiative of distribution of face masks was taken up under the guidance of the Director, IBSD, Prof. Pulok K. Mukherjee with an aim to contain the spread of COVID-19 in North-eastern States as number of positive cases is still high in this region. The masks were stitched by the Convent Sisters of St Margaret, Shillong, free of cost as their mission to help the society.

It may be mentioned here that IBSD centres in different parts of North East India are actively participating and serving to protect frontline workers during COVID-19 scenario. Such distributions will be continued to different frontline workers in Shillong area.



Handing over institute made face masks along with surgical mask to Mr. Damanstar Syiemlieh, President, Meghalaya State Agricultural Marketing Board, Upper Shillong Farmers Market Sanmer, Upper Shillong, Meghalaya.



Distributing institute made face masks along with surgical mask to vegetables vendors of Meghalaya State Agricultural Marketing Board, Upper Shillong Farmers Market Sanmer, Upper Shillong, Meghalaya.



Centre for DNA Fingerprinting and Diagnostics

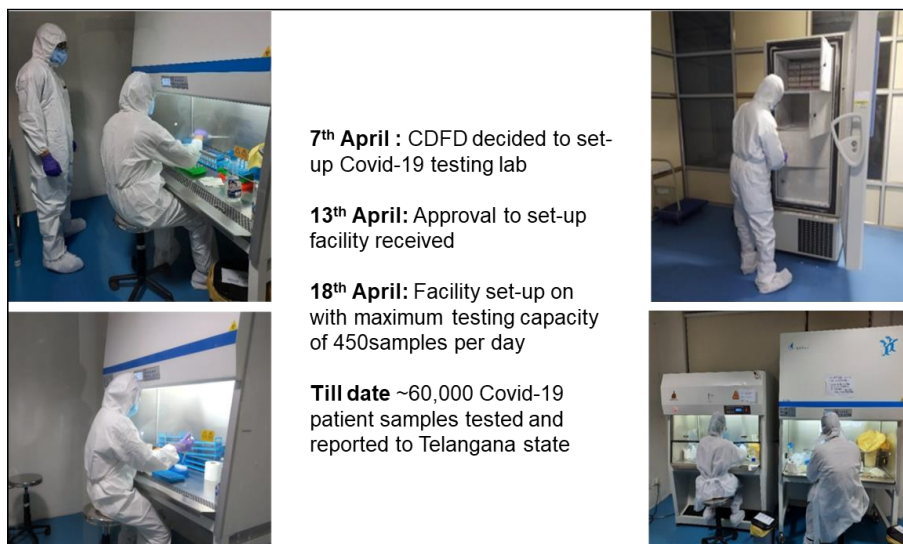
(An autonomous Institute of the Department of Biotechnology, Ministry of Science and Technology, Govt. of India)

Hyderabad

Contributions towards Diagnostics and Genomics research on COVID-19

COVID-19 Diagnostics:

- CDFD initiated RT-PCR based diagnostics of SARS-CoV-2 causing COVID-19 infection from 19th April 2020 by establishing a state of the art laboratory with a maximum testing capacity of 450 samples per day.



7th April : CDFD decided to set-up Covid-19 testing lab

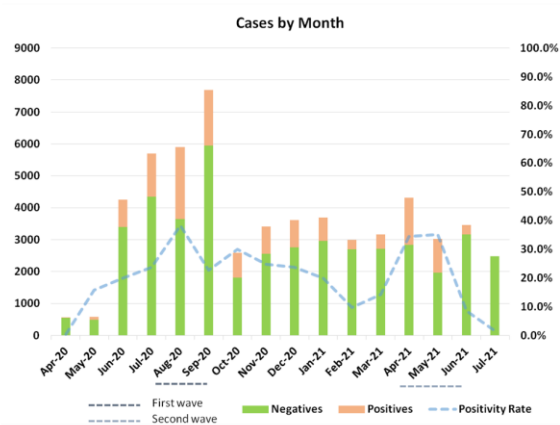
13th April: Approval to set-up facility received

18th April: Facility set-up on with maximum testing capacity of 450samples per day

Till date ~60,000 Covid-19 patient samples tested and reported to Telangana state

- Almost 60,000 suspected patient samples obtained from various districts of Telangana have been analyzed so far. Identification of positive samples has helped the State Govt. in contact tracing and containment measures.

Month	#Cases	Negatives	Positives	Positivity Rate
Apr-20	557	555	2	0.4%
May-20	587	494	93	15.8%
Jun-20	4245	3398	847	20.0%
Jul-20	5706	4350	1354	23.7%
Aug-20	5895	3641	2254	38.2%
Sep-20	7692	5948	1744	22.7%
Oct-20	2590	1812	778	30.0%
Nov-20	3404	2560	844	24.8%
Dec-20	3607	2753	854	23.7%
Jan-21	3696	2962	734	19.9%
Feb-21	2995	2702	293	9.8%
Mar-21	3180	2706	450	14.3%
Apr-21	4433	2834	1484	34.4%
May-21	3183	1965	1062	35.1%
Jun-21	1868	1363	229	14.4%
Jul-21 (till Jul 25)	2874	2477	42	1.7%
Total	59043	44317	13132	22.9%



Covid testing at CDFD: Month-wise distribution of samples received at CDFD from Telangana State followed by positivity rate distribution curve over the months and across age groups.

COVID-19 Genomics Research:

- We performed the first comprehensive study from the state of Telangana on the dynamics of SARS-Cov-2 genomic evolution observed during the period of early March to July, 2020.
- The complete genome sequence of >200 SARS-CoV-2 RNA samples was determined with the overarching objective of identifying unique mutations, in addition to determining the dominant viral lineages circulating in the population.
- The phylodynamic analysis of the sequences revealed a singularly high preponderance of the 20B clade (also called as G/GR clade or B.1 lineage).
- A comprehensive analysis of the mutational landscape including high and low frequency variants revealed the presence of frequently mutated regions.
- Two distinct mutational clusters were detected within the 20B clade. Unique missense mutations were identified in nsp3, nsp4, nsp5 and ORF3a, not identified elsewhere.
- The nsp3 region was found to harbor multiple synonymous and missense mutations, targeting the viral protease domain and nucleic acid binding region (NAR) domain.
- As part of the Indian SARS-CoV-2 genomics consortium (INSACOG) initiative, CDFD has sequenced 1750 SARS-CoV-2 genomes, collected from the states of Rajasthan, Himachal Pradesh, Punjab, Andhra Pradesh, Telangana and Manipur. These sequences have been submitted to the national data hub maintained at NIBMG, Kalyani, WB as well as to the GISAID international data base.
- CDFD has also been actively involved in sentinel SARS-CoV-2 genomic surveillance, towards which routine sample collection is performed from Telangana state designated sentinel laboratories including RT-PCR based testing labs and hospitals. These samples are then subjected to sequencing and subsequent lineage and variant analysis. The results of these analyses are shared with the State as well as with INSACOG.
- The analysis performed on Telangana SARS-CoV-2 samples collected by CDFD internally has revealed a consistent increase in the B.1.617 lineage since March 2021 onwards. Especially the B.1.617.2 (Delta) lineage has risen sharply since April 2021.
- As part of the internal sample collection strategy, special efforts have been undertaken to meticulously monitor and collect samples which are suspected and/or confirmed to be vaccination breakthroughs and reinfection cases in addition to sourcing samples from sudden surge events. The genomic analysis of such samples are expected to shed light into possible mechanisms of viral immune escape.

Science Outreach and Popularisation:

Dr. K Thangaraj, Director, CDFD has delivered webinars on Covid-19 at the following events:

- DBT's third Webinar on COVID-19 - Response of the DBT's Autonomous Institutes to COVID-19 (Part-1) on 21st August 2020
- Webinar on Genomics in Environmental Management organised by National Environmental Engineering Research Institute (NEERI), Hyderabad on 30th September 2020
- Two Day Science Academies Virtual Workshop by Department of Zoology-PSGR Krishnammal College for Women, Tamil Nadu on 2nd October 2020

Dr. Ashwin Dalal, Head, Diagnostics Division, CDFD, has delivered webinars for educating students regarding COVID-19 on topic "Molecular Diagnostics and COVID-19 Testing":

- 400 Students at Loyola Academy, Hyderabad on 9th June 2020
- 40 students of Kendriya Vidyalaya No 2, Uppal, Hyderabad on 8th July 2020
- 60 Girl students of Jawahar Navodaya Vidyalaya, Gachibowli, Hyderabad under Vigyan Jyoti scheme on 25th July 2020
- 60 Girl students of Jawahar Navodaya Vidyalaya, Canacona, Goa under Vigyan Jyoti scheme on 28th June 2021

Dr. Murali Dharan Bashyam, Staff Scientist, CDFD, has delivered a webinar on Genomic Sequencing of SARS CoV-2:

- Webinar titled the 'Why, What and How of SARS CoV-2 Genome Sequencing: An Indian Perspective' in association with Premas Biosciences 7th July, 2021.

Dr. Rashna Bhandari, Staff Scientist, CDFD, had delivered a webinar on women scientists' role in Covid-19 fight

- Webinar titled 'Women Scientists at the forefront of the fight against COVID-19' in association with Visvesvaraya Industrial & Technological Museum, Bangalore to celebrate the occasion of International Day of Women and Girls in Science on 11th Feb 2021.

Publications:

- A Gupta, R Sabarinathan, P Bala, V Donipadi, D Vashisht, MR Katika, M Kandakatla, D Mitra, A Dalal, MD Bashyam. A comprehensive profile of genomic variations in the SARS-CoV-2 isolates from the state of Telangana, India. *J Gen Virol*; 2021; 102:001562.
- Singh PP, Srivastava A, Sultana GNN, Khanam N, Pathak A, Suravajhala P, Singh R, Shrivastava P, van Driem G, Thangaraj K, Chaubey G. The major genetic risk factor for severe COVID-19 does not show any association among South Asian populations. *Sci Rep*. 2021; 11: 12346



Center of Innovative and Applied Bioprocessing (CIAB), Mohali

Activity 1: Studies on potential of natural garlic essential oil as a potential inhibitor of ACE 2 protein and the main protease PDB6LU7 of SARS-CoV2

Inputs: Garlic (*Allium sativum* L.), a common spice for Indian family meals has been considered significant in folk-medicine prescriptions against common colds, influenza, and other kinds of infections. The essential oil of garlic is known to possess numerous organosulfur compounds exhibiting strong antioxidant, antibacterial, antifungal, anticancer, and antimicrobial properties. The oil is also proven to be conducive to hypoglycemia, hypotension, antithrombotic, immunomodulatory, and prebiotic therapy. Therefore, a full investigation on garlic essential oil with respect to its qualitative compositional analysis and its biological activity (in vitro and in vivo assay) was targeted. Characterization of garlic essential oil including its component, refractive index, viscosity and density was studied. End use related studies for its educative use/consumption in management of Covid-19 patients is under way in collaboration with Regional Centre for Biotechnology, Faridabad, India. This study may open the door toward the use of the garlic essential oil in discovering and treating SARS-CoV-2 to prevent the current pandemic.

NCCS National Centre for Cell Science (NCCS), Pune

1] COVID-19 Biorepositories

S. No.	Institute	Disease Status / Phenotype	No. of Samples Archived	Type of Samples	No. of samples Shared	Shared with
5.	NCCS, Pune	SARS-CoV-2-infected & convalescent patients	127 samples	Plasma & Peripheral blood mononuclear cells (PBMCs)	<p>a) Total number of plasma samples shared so far: 122</p> <p>b) Total number of PBMC samples shared so far: 2</p>	<p>a) Plasma samples were shared with - (i) NCCS faculty: 107 (ii) Gennova Biopharmaceuticals Ltd, Pune: 15</p> <p>b) PBMC samples were shared with - (i) NCCS faculty: 2</p>

2] Other Services provided by NCCS cell repository -

Supply of cell cultures to facilitate COVID research at other organizations: A total of 29 cell cultures have been supplied to 15 organizations so far, which includes national research organizations, a medical college, a university, and a private company.

3] Vaccine Development Efforts

Production of pseudotyped SARS-CoV-2 in BSL-2 setting using VSV platform for candidate vaccine development and biomedical research use (BIRAC-funded): This

project was submitted to BIRAC IIT, Indore, with NCCS as a collaborator. The initial part of the project (pseudovirus generation & neutralization studies) is to be carried out at IIT, and the subsequent part (immune response studies in animal models) at NCCS. SARS-CoV-2 pseudovirus was obtained using two different strategies, and tested for neutralization with patient sera. Pseudovirus production has been established. Mice were immunized with the pseudovirus and their antibody response was tested. A single injection of the pseudovirus induced a strong antibody response. The subsequent booster dose induced a potent IgG response. In addition to IgG, IgM and IgA antibodies were also induced.

4] Development of therapeutics for COVID-19

Generation of virus-neutralizing human monoclonal antibodies (hmABs) against SARS-CoV-2 as potential therapeutics [CSIR-NMITLI funded project, in partnership with IIT Indore, PredOmix Technologies Pvt. Ltd., Bharat Biotech International Ltd. (BBIL) & AFMC, Pune]: Serum samples from patients were screened for the presence of receptor-binding domain (RBD)-specific antibodies. B cells from patients who were positive for RBD-specific antibodies were grown in the laboratory. B cell clones were tested for specific antibodies against the RBD. Selection of positive B cell clones secreting RBD-specific antibodies is being done. Testing of patients' plasma for pseudovirus neutralization has been established at IIT Indore. Neutralization with SARS-COV2 has been tested and protocols have been established.

15 new clones were generated, taking the total number of clones to approximately 150. They are being tested for neutralization of the pseudovirus and the real virus. Two clones were transferred to BBIL earlier, for further development. A provisional patent application for the sequences of these clones has been filed in India. Almost 40 antibody-secreting clones have shown to be specific for the SARS-CoV2 RBD, as tested by ELISA. Their neutralization efficacy is being analyzed at IIT Indore, using a pseudovirus platform. The supernatant from these human mAb clones generated against SARS-Cov2 was transferred to Bharat Biotech International Limited (BBIL) for conducting tests for virus neutralization. Almost 10 clones showed neutralization with the real virus, which are being characterized further. Four more clones were obtained, which yielded antibodies that bind strongly to the RBD. Their supernatants have been sent to BBIL to test for neutralization with SARS-CoV-2.

5] NCCS is in the process of setting up a facility to serve as a Central Drug Laboratory for the testing of COVID-19 vaccines.

6] Genome sequencing of SARS-CoV-2 from clinical samples:

NCCS is a participant in the nationwide consortium to sequence the coronavirus genome, the Indian SARS-CoV-2 Genomics Consortium (INSACOG). As of 20th [April 2021](#), 1058 samples were sequenced and the data for all the samples were submitted to the consortium. The data indicate the presence of a new variant with double mutations, L452R and E484Q, with lineage B.1.617. This lineage seems to be expanding not only in the state but all over the country. RNA was extracted from 1208

more samples and was sent to other labs (CCMB, NIBMG, and ILS) for sequencing. Of these, 834 sequences were received, which have been submitted to the consortium. Around 300 samples were sent to CDFD for sequencing and the sequencing was completed. Following the change in the strategy of sampling by NCDC, NCCS received 75 samples from three sentinel sites in Maharashtra and two from Goa, which were sequenced, and the data were submitted to NCDC. The second batch of samples was received, the sequencing run for these has been completed, and the data were analysed. The samples for the third batch were received. One run was completed, and data for 96 samples were submitted to NCDC. 96 more samples have been sequenced & sequencing of another 96 samples is under process.