

1) Visit of Inter-Ministerial Central Government Team to DBT - CDFD

The Inter-Ministerial Central Government Team visited DBT-CDFD situated in Uppal, Hyderabad, Telangana, on 1st May 2020 afternoon. The five-member team was led by Sri. Arun Baroka, Addl. Secretary, Ministry of Jal Shakti, Govt. of India. Dr Debashis Mitra, Director, DBT-CDFD briefed the team about the actions taken by the institute to combat the ongoing COVID-19 pandemic. Dr. Mitra informed the visitors that CDFD is conducting RT-PCR based diagnostics of nasopharyngeal samples received from different districts in Telangana. Now DBT-CDFD is testing samples for the presence of both the E gene, which is present in all coronaviruses, and the SARS-CoV-2-specific RdRP gene based on the kit made available to us by the state. The Central was also informed that the Telangana government has generously supported this effort with a timely supply of testing kits and PPEs. DBT-CDFD has the capacity to test 150-200 individual samples per day, and is ready to undertake testing of pooled samples as well. Dr M D Bashyam, Dr Ashwin Dalal, Dr Rashna Bhandari, and Dr. R. Harinarayanan are actively involved in the COVID-19 testing activities at CDFD. The inter-ministerial team members visited the COVID-19 diagnostics lab, where Dr. Mitra and the team explained the testing protocols to them.

Link: <http://www.cdfd.org.in/>

Visit of Inter-Ministerial Central Team to DBT-CDFD.



2. Launch of 1000 Genome sequencing of SARS-Cov 2 Virus

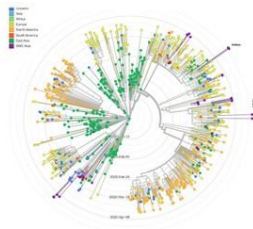
During a review of COVID 19 activities by Hon'ble Minister, the DBT announced Launch of 1000 Genome sequencing of SARS-Cov 2 Virus by DBT Autonomous Institutions consortia to understand viral and host genomics of COVID-19 outbreak. This study will sequence 1000 SARS Cov-2 genomes from the clinical samples to understand the evolving molecular phylogeny of the virus and the emerging mutations in the viral RNA as well as identify the host genetic variations which correlate with transmission, susceptibility and disease severity. This study is being coordinated by NIBMG, Kalyani with active participation from CDFD, Hyderabad; ILS, Bhubaneswar; NCCS, Pune; InStem, Bengaluru along with other DBT Autonomous Institutions. The findings of this study will also assist development of efficient diagnostic assays, vaccine and drug candidates and help formulate policies for containment of the outbreak.

Link: <https://twitter.com/DBTIndia/status/1255366254518509569?s=20>

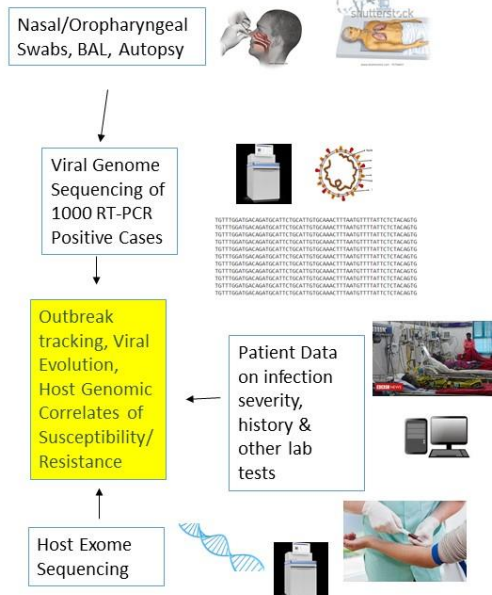
National Consortium for Sequencing 1000 Viral Genomes of SARS CoV2

Participating Institutes:

- West Bengal-NIBMG
- Telengana-CDFD-NIAB
- Odisha-ILS
- Maharashtra- NCCS
- Kamataka- InStem-NCBS
- North-East-IBSD
- Kerala-RGCB
- Delhi-NII-ICGEB-NIPGR
- NCR cluster-THSTI-RCB-NBRC
- Punjab- NABI



Work Plan/Strategy



3. Clustering and supporting NE India Covid-19 Testing Laboratories by DBT-IBSD

DBT- Institute of Bioresources and Sustainable Development (DBT- IBSD), Imphal, Manipur, Sikkim, Mizoram, Meghalaya is supporting COVID-19 testing laboratories in NER using a Clustering approach. The highlights of this support are given below:

Support in the State Meghalaya:

- **Govt Civil Hospital, Tura** –DBT-IBSD is providing Equipment, Equipment Support and consumables
- **Pasteur Institute, Shillong** – DBT –IBSD is Facilitating development of BSL2 facility, Equipment and capacity Building
- **NEIGR Institute of Medical Sciences** : DBT –IBSD is providing-RT PCR Machine

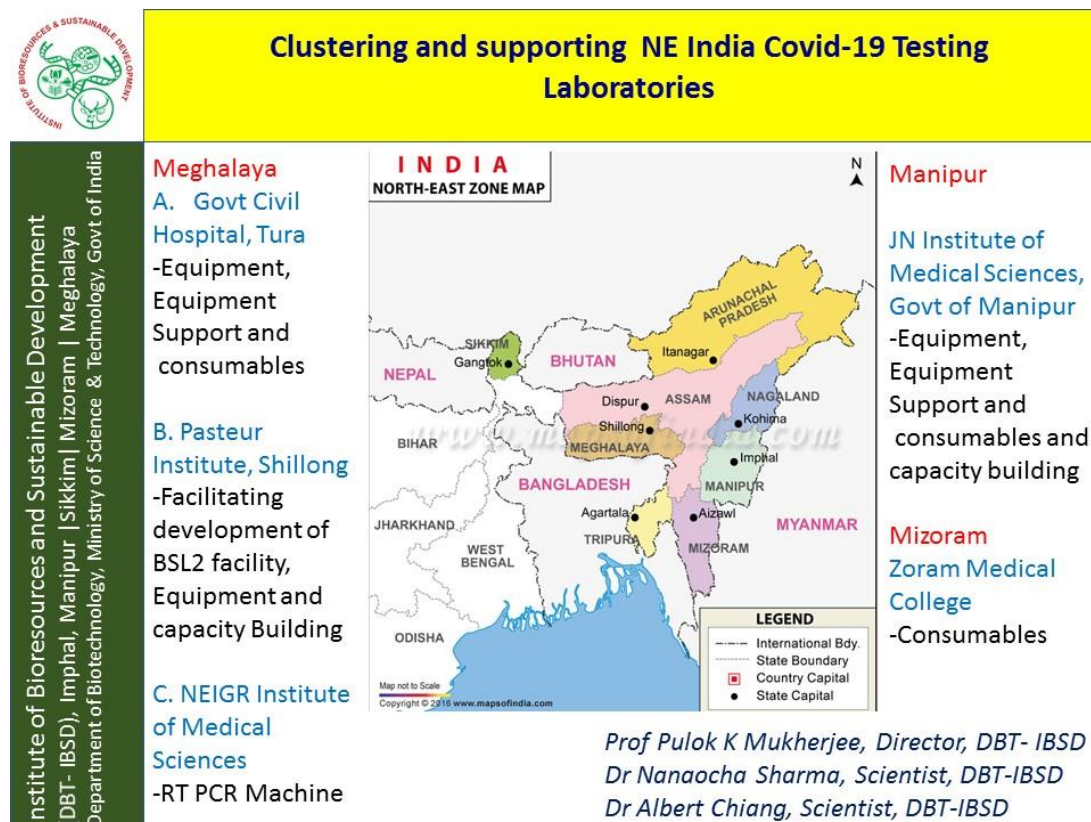
Support in the State of Manipur:

- **JN Institute of Medical Sciences, Govt of Manipur:** DBT-IBSD is providing Equipment, Support and consumables and capacity building

Support in the State of Mizoram:

- **Zoram Medical College** – DBT-IBSD is providing Consumables

<https://ibsd.gov.in/>




4. DBT-IBSD : Traditional Medicine Inspired Development of antivirals and immunomodulators as therapeutics or prophylactics against SARS-CoV-2 from Medicinal and Aromatic Plants (MAPs) of North East India

As on 1st May, 2020, there are more than 33,000 confirmed cases of patients with Covid-19 in India . However, the combined number of cases in the 8 states of NE India is still below 100. Even during the SARS-CoV of 2003, the incidence in NE India was much below the national average, suggesting a higher inherent immunity or anti viral reaction in the residents of NE India. This could be attributed to the high biodiversity of the region and the prevalent daily consumption of local medicinal plants as food, which IBSD is screening for novel anti virals and immunomodulators against SARS-CoV-2.

<https://ibsd.gov.in/>

Institute of Bioresources and Sustainable Development
(DBT- IBSD), Imphal, Manipur | Sikkim | Mizoram | Meghalaya
Department of Biotechnology, Ministry of Science & Technology, Govt of India

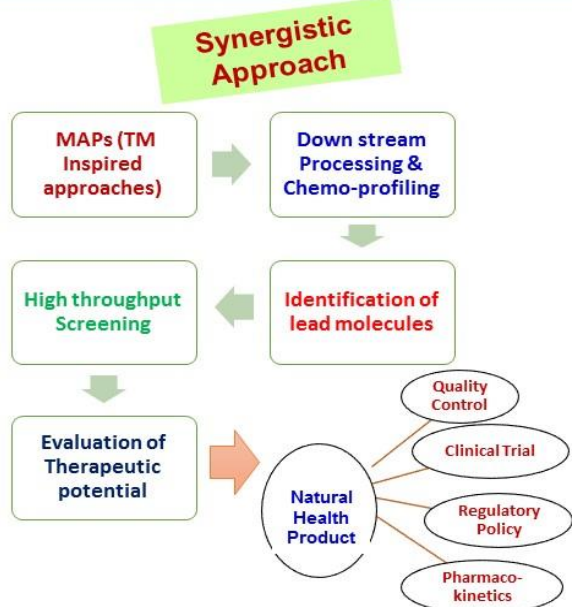


Traditional Medicine Inspired Development of antivirals and immunomodulators as therapeutics or prophylactics against SARS-CoV-2 from Medicinal and Aromatic Plants (MAPs) of North East India

Rationale-

As of today (1 May, 2020), there are more than 33,000 confirmed cases of patients with Covid-19 in India . However, the combined number of cases in the 8 states of NE India is still below 100. Even during the SARS-CoV of 2003, the incidence in NE India was much below the national average, suggesting a higher inherent immunity or anti viral reaction in the residents of NE India. This could be attributed to the high biodiversity of the region and the prevalent daily consumption of local medicinal plants as food, which IBSD is screening for novel anti virals and immunomodulators against SARS-CoV-2

Synergistic Approach

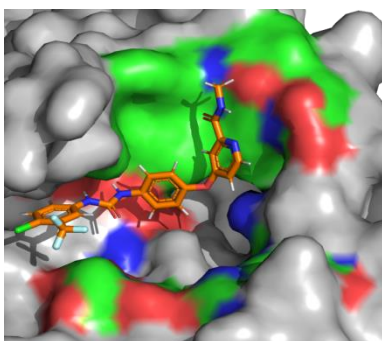


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graph TD; A[MAPs (TM Inspired approaches)] --> B[Down stream Processing & Chemo-profiling]; B --> C[Identification of lead molecules]; C --> D[High throughput Screening]; D --> E[Evaluation of Therapeutic potential]; E --> F((Natural Health Product)); F --- G[Quality Control]; F --- H[Clinical Trial]; F --- I[Regulatory Policy]; F --- J[Pharmacokinetics];
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5. DBT- NII Research team predicts potential molecules against COVID-19.

Ever since the first case of the respiratory disease COVID-19 was detected in the Wuhan province of China on 1st of December, 2019, the disease has rapidly spread all over the globe and has been declared a pandemic by the World Health

Organisation. While scientific research has successfully designed tools for rapid diagnosis of the disease, very little success has been achieved in the development of COVID therapeutics. The disease initiates following an infection with the virus SARS-CoV2 (Severe Acute Respiratory Syndrome- Coronavirus2), initially named as 2019-nCoV (2019 novel coronavirus). While over 80% of the infected people show mild flu-like symptoms, severe cases exhibit pneumonia, sepsis and organ failure. Interestingly, SARS-CoV2 is the seventh virus of its kind and the past few years have witnessed outbreaks from by its sister viruses causing both severe (SARS-CoV and MERS-CoV) and mild (HKU1, NL63, OC43 and 229E) diseases. Viruses are usually made of a layer of lipids, followed by a second layer of proteins forming a protective capsule around its genetic material. Once a virus infects a living organism, it hijacks the cellular machinery of the organism to make multiple copies of its genetic material, proteins and lipids, eventually leaving the infected body as many new viruses. The virus also carries key proteins that aid to the replication of its genetic materials and proteins. The SARS-CoV2 and its entire sister species use RNA as their genetic molecule. They harbour a protein known as “RNA-dependent RNA polymerase/RdRp”, which copies its RNA genome following infection into the host’s cells. Combining various computational and bioinformatics tools, our team at NII first determined the molecular structure of SARS-CoV2 RdRp, and further predicted a key molecular binding site within the RdRp. This site acts like a pocket for a key molecule called “guanosine triphosphate/GTP”. Earlier reports from other virus suggest that following the binding of GTP in this pocket initiates the process of viral genome replication by RdRp. In addition, we found many organic molecules that can effectively bind within this pocket and also designed a molecule that exhibits an exceptionally strong binding. The idea is to use these organic molecules to prevent the binding of GTP within the pocket, thus rendering the RdRp non-functional.



Computationally docked kinase inhibitor Sorafenib at the predicted active site pocket of the NiRAN domain from SARS-CoV2 RNA dependent RNA Polymerase. (Sorafenib presented in stick model; Red indicates positively charged regions, blue indicates negatively charged regions and green indicates neutral regions, grey indicates regions beyond GTP-binding pocket)

6. COVID-19 Outreach Efforts by DBT-inStem

inStem is one of the founding partners of the pan-institutional website [COVID-Gyan](#), launched on Apr 03, 2020. The website is updated regularly with interesting and scientifically-vetted content relevant to COVID pandemic, keeping the common man in view. The content are available in English and other vernacular languages.

COVID-19

HOW DOES IT AFFECT YOU?

Coronavirus Disease 2019 (COVID-19) is a pandemic caused by Severe Acute Respiratory Syndrome Coronavirus 2, also called SARS-CoV-2. Despite the widespread awareness regarding COVID-19, many are still unaware about how it affects the human body.

SARS-CoV-2 starts its journey in the nose, mouth, or eyes and travels down to the alveoli in the lungs. Alveoli are tiny sacs of air where gas exchange occurs.

Designed by [Aravind Ravikan](#)
www.aravindravika.com
[@aravindravika](#)
[@aravindravika](#)

Healthy

Gas Exchange
 Each sac of air, or alveolus, is wrapped with capillaries where red blood cells release **carbon dioxide** (CO₂) and pick up **oxygen** (O₂). Two alveolar cells facilitate gas exchange: **Type I** cells are thin enough that the oxygen passes right through, and **Type II** cells secrete **surfactant** - a substance that lines the alveolus and prevents it from collapsing.

Normal gas exchange

WHAT CAN YOU DO?

1 Preventative Actions

There is currently no proven treatment for COVID-19, so adopting the best practices for preventing infection is crucial. These include:

- Physical distancing** - keep a distance of at least 2 meters between you and others outside of your home
- Proper hand-washing** - wash your hands for at least 20 seconds
- Cough or sneeze into your elbow or a tissue and immediately wash your hands after

Infected

SARS-CoV-2 Structure

- Membrane protein
- Nucleocapsid (enclosed RNA)
- Lipid membrane
- Envelope protein
- Spike protein

Viral Infection
 The spike proteins covering the coronavirus bind ACE2 receptors on type II alveolar cells, allowing the virus to enter the cell via endosome or membrane fusion and release its RNA. The RNA "hijacks" the cell, telling it to assemble many more copies of the virus and release them into the alveolus. The host cell is destroyed in this process and the new coronaviruses infect neighbouring cells.

Moderate

Immune Response

- After infection, type II cells release **inflammatory signals** that recruit **macrophages** (immune cells).
- Macrophages release **cytokines** that cause vasodilation, which allows more immune cells to come to the site of injury and exit the capillary.
- Fluid accumulates inside the alveolus.
- The fluid dilutes the surfactant which triggers the onset of alveolar collapse, decreasing gas exchange and increasing the work of breathing.
- Neutrophils** are recruited to the site of infection and release **Reactive Oxygen Species (ROS)** to destroy infected cells.
- Type I and II cells are destroyed, leading to the collapse of the alveolus and causing **Acute Respiratory Distress Syndrome (ARDS)**.
- If inflammation becomes severe, the protein-rich fluid can enter the bloodstream and travel elsewhere in the body, causing **Systemic Inflammatory Response Syndrome (SIRS)**.
- SIRS may lead to **septic shock** and **multi-organ failure**, which can have fatal consequences.

Stay Home
 Symptoms may start to show (e.g. dry cough, fever, etc.)

Prevention develops
 Breathlessness of breath

Hospitalization
 Dangerous for high-risk individuals; secondary infections may occur

Intensive Care (ICU)
 Patients may require ventilators and life support

Complications unrelated to COVID-19 may occur
 Will require care; patients may recover at any point during the process

Severe

Impaired Gas Exchange
 When the immune system attacks the area of infection it also kills healthy alveolar cells. This results in three things that hinder gas exchange:

- Alveolar collapse due to loss of surfactant from Type II cells
- Less oxygen enters the bloodstream due to lack of Type I cells
- More fluid enters the alveolus.

Greatly hindered gas exchange

2 Stay Healthy

Make a routine of eating a well-balanced diet, drinking plenty of water, getting enough sleep, exercising and monitoring your mental health. Reach out to family and friends for support.

3 Stay Informed

With a situation that changes daily, it is crucial to stay informed so you know if any changes have occurred both globally and in your community. Make sure to look for evidence-based sources to avoid misinformation.

Severely hindered gas exchange

4 Donate

Consider donating to local businesses or online funding campaigns if you have financial flexibility. If you have spare time, consider volunteering for community initiatives, such as helping deliver food to those in need.

To read the articles posted on the website, click: <https://covid-gyan.in/articles>. For FAQs related to COVID-19, click: <https://covid-gyan.in/faqs>. To access for infographics and posters click: <https://covid-gyan.in/infographics>. For videos from experts, click: <https://covid-gyan.in/videos>. For audio/podcasts, click: <https://covid-gyan.in/audio>

7. COVID-19 Research Efforts by DBT-inStem

[Dr. Dasaradhi Palakodeti](#) and his team in inStem have contributed experimental support to an algorithm developed by scientists at IIT, Bombay and NCBS-TIFR Bangalore. The algorithm called “Tapestry” is an attempt to explore economical and scalable ways to test more people during epidemics such as the ongoing COVID-19 pandemic, which has strained testing capabilities worldwide. Tapestry is a novel quantitative nonadaptive pooling scheme to test many samples using only a few tests. The underlying molecular diagnostic test is any real-time RT-PCR diagnostic panel approved for the detection of the SARS-CoV-2 virus. In cases where most samples are negative for the virus, Tapestry accurately identifies the status of each individual sample with a single round of testing in fewer tests than simple two-round pooling. A companion Android application BYOM Smart Testing which guides users through the pipetting steps required to perform the combinatorial pooling was also developed by the investigators. The results of the pooled tests can be fed into the application to recover the status and estimated viral load for each individual sample.

Link: <https://www.medrxiv.org/content/10.1101/2020.04.23.20077727v2>

8. Structural and Functional Implications of Non-synonymous Mutations in the Spike protein of 2,954 SARS-CoV-2 Genomes

A team of Scientists at Corona Research & Intervention Group, DBT - Rajiv Gandhi Centre for Biotechnology, Thiruvananthapuram have studied structural and functional implications of non-synonymous mutations in the spike protein of 2,954 SARS-CoV-2 genomes. Information on mutations within the circulating strains of the virus is pivotal to understand disease spread and dynamics. Dr. Shijulal and team at

DBT-RGCB have analysed the mutations associated with 2,954 globally reported high quality genomes of SARS-CoV-2 with special emphasis on genomes of viral strains from India. Molecular phylogenetic analysis suggests that SARS-CoV-2 strains circulating in India form five distinct phyletic clades designated R1-R5. These clades categorize into the previously reported S, G as well as a new unclassified subtype. A detailed analysis of gene encoding the Spike (S) protein in the strains across the globe showed non-synonymous mutations on 54 amino acid residues. Among these, the research team pinpointed 4 novel mutations in the region that interacts with human ACE2 receptor (RBD). Further in silico molecular docking analyses suggested that these RBD mutations could alter the binding affinity of S-protein with ACE2 that may lead to changes in SARS-CoV-2 infectivity. Strikingly, one of these RBD mutations (S438F) was found unique to a subset within the R4 clade suggesting intrinsic S-protein variations in strains currently circulating in India. The research team's findings revealed a unique pattern of SARS-CoV-2 evolution that may alert vaccine and therapeutic development.

<https://www.biorxiv.org/content/10.1101/2020.05.02.071811v1.full.pdf>

9. Catching up with the progress made in COVID-19 research – Key takeaways from last week's COVID-19 Ask the Experts webinar

DBT-THSTI, DBT/Wellcome Trust India Alliance, IAVI and Nature India conducted the sixth webinar in the series COVID-19 Ask the Experts. Promising to address many pressing points in COVID-19 research and the future course of the pandemic, the panel had Dr. Gagandeep Kang, Executive Director of THSTI; Dr. Shahid Jameel, CEO, India Alliance and Dr. Jacob John, Professor, CMC, Vellore. More than 350 registrations were received for this webinar which was by far the highest.

Here are the key takeaways from the webinar:

On how the pandemic is progressing: There is recognition of the ailment, science informing the intervention of the disease and understanding of clinical picture is changing. Virus may be very inclusive but the pandemic certainly isn't. Technology advances are aiding due to which vaccine is in clinical trial in just two months. But at the same time, there is [an] infodemic and fake news to deal with.

On how the disease will progress in the coming months: The panellists felt that Mathematical models are just models. They need data to be followed, which is difficult at the initial stage of pandemic.

On lessons learned for vaccine development from animal models of immune response: The ChAdox1 vaccine has been successful in a study done on monkeys (primates). However, data in humans subjects is awaited.

On SARS-CoV-2 mutations: There is no evidence that there are multiple strains. Lots of sequences show that the virus is evolving but no evidence that it has become a different virus. So, we need not worry about the impact of mutations on vaccine development.

On repurposing drugs for curing COVID-19 : Repurposing of drugs is crucial and the fastest way to find a treatment. It will involve screening with licensed and known compounds to see if they have anti-viral effects. Also, looking for what worked for a related virus. Further, structural-aided drug design is the way to go; it is fast and crucial at the moment.

On challenges for good experimental/clinical research in India: In India, the lack of data systems is a challenge in public health research when amidst a pandemic. The ability to access the information is important to know the scale of the problem. Further, an assumption needs to be substantiated with data, which is lacking in current scenario and is a challenge to deal with.

https://twitter.com/India_Alliance/status/1256568147290832897?s=20

10. Augmenting domestic manufacturing to meet the national demands in the current COVID- crisis: DBT-AMTZ COMManD Strategy

DBT-AMTZ COMManD [COVID Medtech Manufacturing Development] strategy is to address the shortage of critical medical equipment in India and move progressively towards a stage of self-sufficiency. This an excellent example of how supportive governance and progressive science could be brought together to address immediate and futuristic priorities.

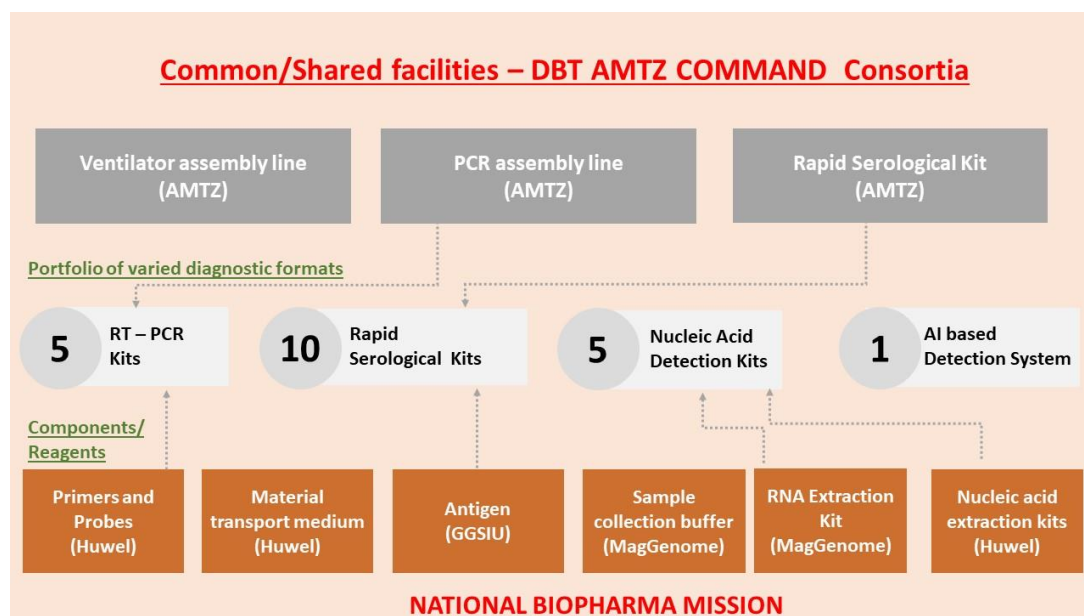
Andhra Pradesh MedTech Zone (AMTZ) is an established medical equipment manufacturing ecosystem and Department of Biotechnology(DBT) is a pioneer department within the Government of India for support of medical technologies sectoral growth. Under this strategy, DBT is supporting AMTZ which is Asia's first medical equipment manufacturing ecosystem, uniquely dedicated for Medtech and this initiative would be supported under DBT's National Biopharma Mission.

The COMManD strategy has 3 focal points.

1. Supporting the startups and innovators that have till now taken support from DBT/BIRAC for medical technology projects. All these innovators and entrepreneurs are being supported by AMTZ, technologically facilitated towards the next level of product realisation. This includes steps such as inclusion of their innovative technologies in the formulation of appropriate standards, providing subsidised infrastructure for testing and validation, facilities for prototyping, partnership with manufacturing units and provision of startup space and furthering their chances of development and market access.
2. Many medical device manufacturers have the potential to make critical equipment like ventilators and diagnostic kits, thermal scanners or medical textiles, which is much needed in COVID context as well post-COVID period. However, to rapidly scale up the manufacturing, it would require a huge investment in plant and machinery, without which such scale-up will not be possible. DBT, therefore, is supporting AMTZ to invest in the plant and machinery in these companies which are situated within AMTZ campus in Vishakapatnam so that their rapid scale-up of infrastructure and production capabilities could be achieved.
3. Drafting of appropriate standards and safety norms, validation protocols for these medical technologies such as Ventilators, N95 masks and so on. This would be an important area of support to ensure that their quality and safety are upheld, at the same time ensuring their registration on government e market place and through the orders received by AMTZ from the government of India is met. This provides industrial partners with an avenue for market access.

DBT-AMTZ COMManD strategy is therefore a three pronged approach which has been put in place by the support of DBT, GOI and the ecosystem support of AMTZ, to ensure that rapid infrastructure capabilities are used for progressively improving the manufacturing capabilities of domestic manufacturing in the medical technology sector in a rapid and quality assured manner.

- The outcome of COMManD Strategy would be:**
- i) 10,000 kits (RT-PCR) per day increasing upto 40,000 kits per day by May 30th
 - ii) 10,000 units (antibody) per day increasing to upto 60,000 units per day by May 30th
 - iii) 3000 ventilators per month from the month of May
 - iv) 1000 infra red non touch thermal scanner per day



<https://www.birac.nic.in/>

11. Title of story: Convalescent Plasma: Potential Therapy for COVID-19

Department of Biotechnology & Biotechnology Research Industry Research Council recently announced a COVID-19 Research consortium call to support Diagnostics,

Vaccines, Novel Therapeutics, Repurposing of Drugs or any other intervention for control of COVID-19. The first phase of the call closed on 30th March 2020, the review is ongoing and 16 proposals have been recommended so far. Virchow Biotech Pvt Ltd has been awarded funding support under DBT's National Biopharma Mission to work on plasma therapy for COVID-19. Virchow Biotech has been commercially manufacturing intravenous immunoglobulin from human plasma since 2013 in a WHO-approved and dedicated plasma fractionation cGMP facility. Currently, they have the capacity to process over 300,000 litres of plasma annually. They are one of the largest manufacturers of human IVIG and human serum albumin in India.

They are the first company in India to identify Immunoglobulin Therapy, which can prove to be more promising as compared to direct plasma administration. Direct plasma therapy has several safety, efficacy and specificity concerns. Single transfusion might not be sufficient and transfer of other blood components may pose inadvertent risks. The sterility and specificity of Intravenous Immunoglobulins will help to prevent these risks and keep track of administered dosage.

The proposed immunotherapy procedure already has necessary approvals in place from Drug Controller General of India; Central Drugs Standards Control Organization and funding from Biotechnology Industry Research Assistance Council (BIRAC). The company plans to start its clinical trials for the same very soon.

The company has proposed to collect plasma from several human convalescent donors, in order to prepare a standardized immunoglobulin enriched for anti-COVID antibodies with a specific titer. Immunoglobulin treatment is increasingly recognized to treat a variety of diseases not just because of its ability to fight the infection but also due to its Immunomodulatory and Immunosuppressive activities. In the absence of other proven therapies, it is widely expected that these immunoglobulins will prove crucial in reducing the morbidity from the COVID-19 infection potentially saving valuable human lives.

To accelerate the efforts, it is desirable that more COVID-19 recovered patients should come forward to donate their plasma and serve the national cause.

12. COVID-19 diagnostic testing by DBT-ILS Bhubaneswar

COVID testing by DBT-ILS is going in full swing. As on date analysis more than 5000 samples obtained from 12 districts of Odisha were analysed following all safety precautions & with dedicated efforts of ILS scientists and students.



https://twitter.com/DBT_ILS?s=08

Health & Family Welfare Department and Hon'ble Chief Ministers Office, Govt of Odisha complemented @DBTIndia's AI @DBT_ILS for testing 901 COVID-19 samples on 3rd May 2020, contributing to nearly 40% of tests done in Odisha. A remarkable achievement indeed though sincere efforts of ILS staff & scholars.

https://twitter.com/DBT_ILS
