DBT-inStem scientists decipher role of immune cells in growth of animals

Studies over the years have described the systemic control of signals emanating from tissues like the brain, thyroid and liver on the growth of animals. A large body of research implicates the brain and body fat (liver equivalent) as central players in coordinating growth and nutritional balance in multicellular animals. An underlying connection between immune cells and growth is also evident, although a detailed understanding of this cross-talk is scarce.

A recent study by Tina Mukherjee and her group at the Metabolism and Development (MAD) lab at the Department of Biotechnology's Institute for Stem Cell Science & Regenerative Medicine (DBT-inStem) has deciphered the role of innate immune cells in animal growth both during normal times and in conditions of nutrient stress.

The study, which was conducted on fruit fly (*Drosophila melanogaster)* found that the larvae of the insect that was lacking in blood cells produced smaller adults with signs of insulininsensitivity. Moreover, when they were exposed to a high-sucrose diet (HSD), the adults were further growth retarded than normally seen in regular animals raised on HSD.

In contrast, larvae that carried an increased number of activated macrophage-like plasmatocytes showed no defects in adult growth when raised on HSD and grew to sizes almost comparable with that seen with regular diet.

These observations implied that there was a central role for immune cell activity in growth control. Mechanistically, the findings reveal that immune cells had an influence on the balancing of fat body inflammation and insulin signaling both normally and under conditions of nutrient overload as a means to coordinate systemic metabolism and adult growth.

The immune system of *Drosophila* is akin to the mammalian innate immune system, which refers to the non-specific defense mechanism in the body and is the primary response initiated immediately upon invasion with a foreign pathogen. This work reveals how interactions between cells of the immune system (cellular arm) and material released by cells (secretory or humoral component) can influence animal growth.

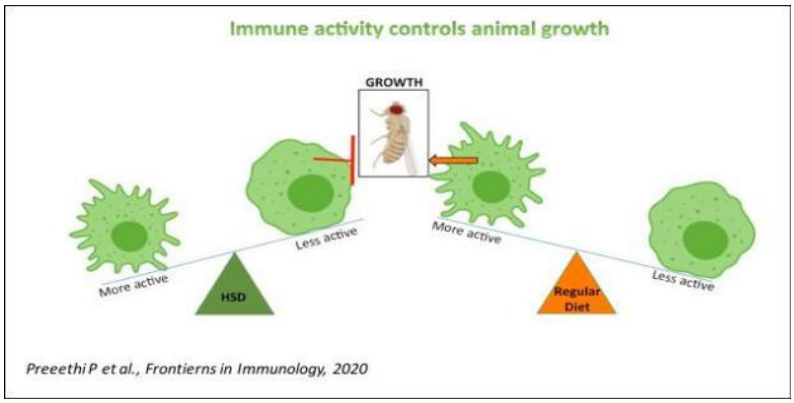
The study assumes importance as animal development and growth is reliant on proper nutrition and metabolism. Organs coordinating metabolism therefore play a central role in

growth control. Growth failure is a commonly observed problem when there are any alterations in metabolic condition as seen early in childhood cases with diabetes.

Thus, much of the focus in the field of growth and metabolism has always been centered around organs like thyroid, liver, and brain to name a few. The new investigation shows immune cells as an important component of nutritional control, systemic metabolism, and animal growth eventually. It further highlights immune cell state and functions as a central component of organismal growth.

The findings from this work and on-going research by the scientists is expected to provide a deeper understanding on the nature of this cross talk initiated by immune cells and reveal novel mechanistic insights of underlying developmental paradigms operating in animal growth that may be broadly conserved across mammalian systems as well.

A research paper on the work has been published recently in *Frontiers in Immunology* Journal (July 2020) titled '*Immune Control of Animal Growth in Homeostasis and Nutritional Stress in Drosophila'.* An article on this has also been posted on DBT-inStem's website.



Reference: Preethi P, Tomar A., Madhwal S., Mukherjee T. (2020) Immune control of animal growth in homeostasis and nutritional stress in Drosophila. Frontiers in Immunology. (Published on July 31, 2020)

Link: https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_01S_14Aug2020.pdf

DBT-CDFD study on genetic affinities of Gujjar and Ladakhi populations

The Union Territories of Jammu and Kashmir (J&K) and Ladakh in North India with its wide variety of landscape, is a congruence of several languages and cultural practices. The region is believed to have served as a corridor for ancient human migrations between the Indian subcontinent and North-East Asia, Eurasia and Africa.

The populations in the region offer a unique opportunity to investigate the past anthropological and demographic events which might have shaped the extant human population diversity. In a new study, scientists at the Department of Biotechnology's Centre for DNA Fingerprinting and Diagnostics (DBT-CDFD) have sought to decipher the genetic diversity encompassed by Gujjars from the Jammu region of J&K and the Ladakhi populations.

A previous study had found that the two communities - Gujjars and Ladakhis exhibited lower genetic affinity towards other populations in their geographical proximity. To better understand the genetic diversity in these populations, a battery of DNA markers located on autosomes, Y-chromosome and the mitochondrial genome were employed.

The principal coordinate and cluster analysis based on autosomal DNA markers indicated Gujjars and Ladakhis were genetically distant to each other as well as to other reference populations of India, which was in concordance with Y-chromosomal analysis.

The genetic affinity of Gujjars in Jammu region to Pashtuns in Baghlans and Kunduz provinces of Afghanistan and Pashtuns and Sindhis in Pakistan indicated their past genetic relatedness and a common ancestry. On the other hand, Ladakhis were found to be genetically close to Chinese (Uighurs and Han) and Nepalese (Magar) populations, which might be due to their close geographic proximity.

Y-haplogroup (which represent a group of individuals who have inherited a common set of markers)-based studies suggested that the Gujjars are less diverse as compared to Ladakhis. The presence of many rare haplogroups in Ladakhis portrays rich accumulation of male-mediated contribution in the past.

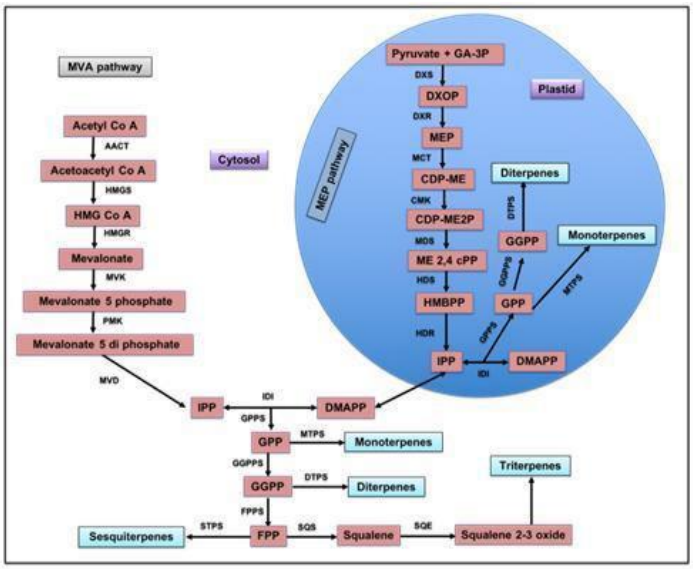
The mitochondrial DNA analysis supported the findings that the Gujjars are less genetically diverse as compared to Ladhakis, which perhaps may be due to the endogamous cultural practices in this group (where they marry within a specific community or caste or group). The Y-chromosomal and mitochondrial analysis showed higher genetic differentiation among males than females indicating patrilocality among these populations.

The present study is the first comprehensive attempt to determine the genetic relatedness of the Gujjars and Ladakhis to populations within India and elsewhere in the world and would help in gaining deeper insights into genetic diversity and demographic settlement in this part of the world.

Link: https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_01S_13Aug2020.pdf

Metabolic engineering opening new avenues for therapeutics

Team of researchers including Dr. Richa Mehra, Ashish Kumar Pandey and Manoj Kumar Soni at Regional Centre for Biotechnology (RCB), Faridabad has published a book chapter on 'Metabolic engineering opening new avenues for therapeutics'. The chapter focuses on increasing global burden of diseases and high cost of therapeutics, which derives the rewiring of metabolites for better yield and production.



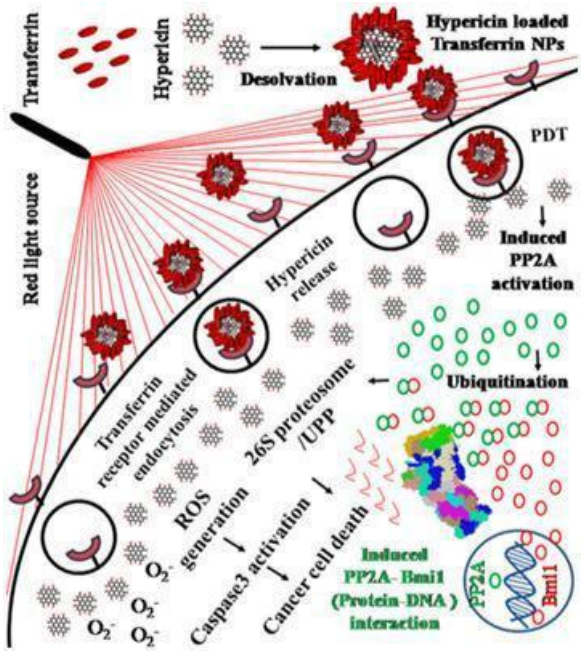
Metabolic engineering is a useful tool to facilitate a well-planned hypothesis of metabolic flux and metabolic control on a suitable host to develop value-added products especially therapeutic compounds. The driving force behind these strategies is the sustainable development, cost factor, and increasing demands. Several strategies like gene overexpression, heterologous pathways, by-product elimination and transporter/co-factor engineering are commonly employed to optimize the engineered products.

The chapter provides a broad overview of metabolic engineering, describing common strategies used for metabolic engineering, plant metabolic engineering, microbial metabolic engineering with evident examples and challenges of metabolic engineering. The chapter has been published in '*Engineering of Microbial Biosynthetic Pathways*'.

Link: https://doi.org/10.1007/978-981-15-2604-6_14
Link: https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_01BB_13Aug2020.pdf

Hypericin-loaded transferrin nanoparticles induce PP2A-regulated BMI1 degradation in colorectal cancer-specific chemo-photodynamic therapy

The present study carried out at Regional Centre for Biotechnology (RCB), Faridabad enlightens the targeted photodynamic therapy (PDT) with potential photosensitizer hypericin nanocomposite in the development of epigenetic-based CRC therapy. For this study, hypericin-loaded transferrin nanoformulations (HTfNPs) were synthesized, thus, overcoming the compromised hydrophobicity and poor bioavailability of the placebo drug. Targeted PDT with hypericin nanocomposite-induced BMI1 degradation assisted colorectal cancer (CRC) retardation.



In the present study, transferrin nanoparticles were reported to control the premature release of hypericin and improve its availability with better targeting at the disease site. Targeted intracellular internalization to colon cancer cells having a differential expression of transferrin receptors, *in vivo* biodistribution, stability and pharmacokinetics provide promising applications in the nanodelivery system. The *in vitro* anticancer efficiency, cell cycle arrest at the G0/G1 phase, and elevated reactive oxygen species (ROS) generation confirm the anticancer effect of nanoformulation.

In the exploration of mechanism, nanotherapeutic intervention by activation of PP2A, Caspase3 and inhibition of BMI1, EZH2, 3Pk, NFκB was evident. An exciting outcome of this study uncovered the camouflaged role of PP2A in the regulation of BMI1. PP2A

mediates the ubiquitination/degradation of BMI1, which is revealed by changes in the physical interaction of PP2A and BMI1. This study confirms the anticancer effect of HTfNP-assisted PDT by inducing PP2A-mediated BMI1 ubiquitination/degradation demonstrating an epigenetic-driven nanotherapeutic approach in CRC treatment.

Epigenetically regulated therapeutic intervention of cancer is an emerging era of research in the development of a promising therapy. Epigenetic changes are intrinsically reversible and providing the driving force to drug resistance in CRC. The regulation of polycomb group (PcG) proteins, BMI1 and EZH2, and the associated CRC progression hold promises for a novel treatment regime. Dr. Prasenjit Guchchait (Professor, RCB), co-authored a research article with other collaborators.

Link: https://doi.org/10.1021/acsbiomaterials.9b01844

Link: https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_01BB_11Aug2020.pdf

DBT-InStem fellows bag Biotech Ignition Grants

Dr. Abrar Rizvi & Dr. Anupam Dutta, both post-doctoral fellows in Prof. Colin Jamora's laboratory in the Inflammation and Tissue Homeostasis theme at the Department of Biotechnology's Institute for Stem Cell Science & Regenerative Medicine (DBT-inStem) have been awarded the 16th Biotech Ignition Grant (BIG) recently. This grant is the flagship scheme of the Biotechnology Industry Research Assistance Council (DBT-BIRAC) open to innovators in life sciences whose research projects have great commercialisation potential.

The BIG Scheme enables technology innovators and entrepreneurs to pursue a promising technology idea, establishing and validating proof of concept (POC) for it. It mainly supports high level innovation in the biotech sector and is not meant for basic research projects. As part of this scheme, successful BIG Innovators receive up to Rs 50 lakh (USD 70,000 approx) for a duration of up to 18 months.

Dr. Abrar has been is granted the funding to develop treatments for fibrosis, which contributes to 33% of deaths worldwide but for which there is no effective therapy, and Anupam's project will test new approaches for accelerating wound healing.

Link: https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_02S_13Aug2020.pdf

Genomics to develop plant-based therapies for SARS-CoV-2

COVID-19 caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is devastative to the humankind for which neither vaccines nor precise therapeutic molecules for treatment are yet to be identified. The search for new drugs and repurposing of existing drugs is on. Alongside, research on plants to identify novel therapeutic compounds or testing the existing ones is also progressing. Genomics and biotechnology offer various tools and strategies to manipulate plants for producing those complex biopharmaceutical products.

A review article prepared by a group of scientists at the Department of Biotechnology's National Institute of Plant Genome Research (DBT-NIPGR) and Department of Plant Sciences at the School of Life Sciences in University of Hyderabad and published in ScienceDirect enumerates the scope for research on plant-based molecules for their potential application in treating SARS-CoV-2 infection.

Strategies to edit gene and genome, overexpression and silencing approaches, and molecular breeding for producing target biomolecules in the plant system are discussed in detail. Altogether, the review provides a roadmap for expediting research on using plants as a novel source of active biomolecules having therapeutic applications.

Minireview article link:
https://www.sciencedirect.com/science/article/pii/S0888754320308958?dgcid=author

Link: https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_01S_10Aug2020.pdf

International Centre for Genetic Engineering and Biotechnology (ICGEB) featured as South-South Galaxy partner of the Month

Department of Biotechnology's International Centre for Genetic Engineering and Biotechnology (ICGEB), New Delhi has been featured as the partner of the Month (July 2020) by the South-South Galaxy team as recognition of its remarkable work in the field of South-South cooperation. South-South Galaxy is a global knowledge sharing and partnership brokering platform, supported by United Nations Office for South-South Cooperation (UNOSSC).

Currently, ICGEB counts 65 member states with majority of member states are countries of the Global South. Efforts of ICGEB for implementing South-South cooperation in all of its actions, promoting scientific cooperation, capacity building and technology transfer were greatly appreciated. The ICGEB acknowledged the offer a modern model for cooperative action, including knowledge exchange and peer learning for human capital development in support of the local Governments.

In this moment of global crisis when the need for South-South and triangular scientific cooperation is greatly desired, efforts of ICGEB are well recognized. ICGEB has responded with efforts to directly provide rapid assistance to its constituency with diagnostics, surveillance and capacity enhancement for handling the COVID-19 crisis, bringing critical information and technologies to where they are most needed.

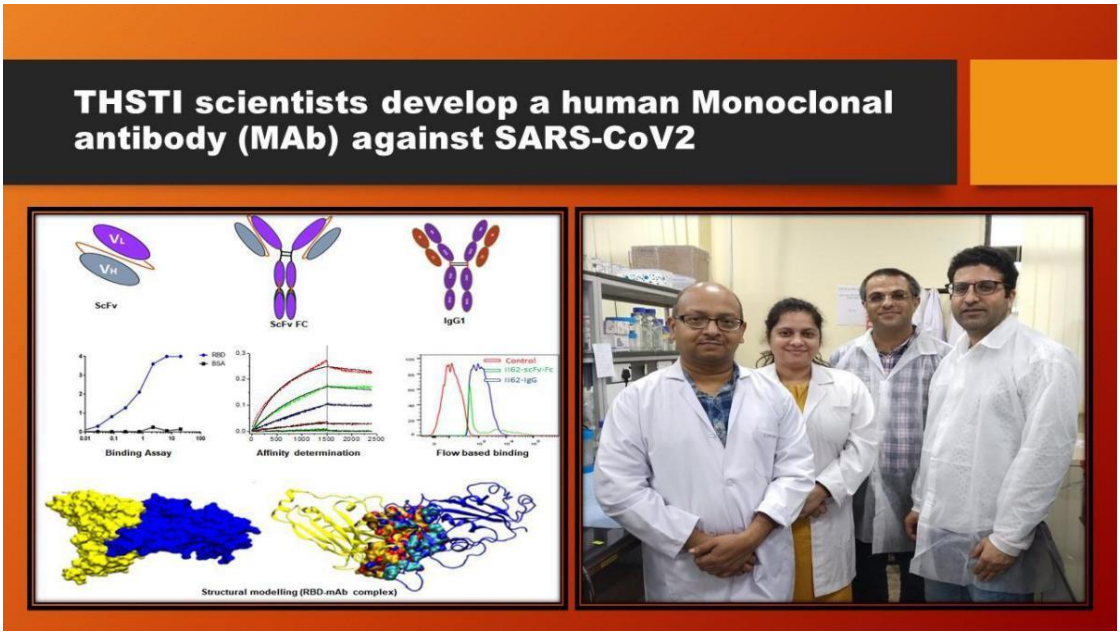
The detailed information on ICGEB's resources, tools and know-how, ICGEB offers to fight the SARS-CoV-2 virus is also made easily available on the link https://www.icgeb.org/covid19-resources/ to its member states.

Link: https://www.icgeb.org/icgeb-south-south-cooperation-partner-of-the-month/

Link: https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_01BB_10Aug2020.pdf

DBT-THSTI scientists take a step towards a therapy for SARS-CoV2

A team of scientists from the Infection and Immunity Programme of the Department of Biotechnology's Translational Health Science and Technology Institute (DBT-THSTI), led by Dr. Rajesh Kumar, has developed a human monoclonal antibody (mAb) against the receptor-binding domain (RBD) of SARS-CoV2. The monoclonal antibody has been shown to bind to the receptor-binding domain (RBD) protein of SARS-CoV2 with high affinity and specificity. The RBD of the spike protein of SARS-CoV2 is the primary target for neutralizing antibodies to block infection.



The team hopes the new development will facilitate COVID-19 research activities across the country.It has developed different formats of this mAb - scFv, scFv-Fc, and IgG1 against COVID-19. This well-established platform will allow isolating neutralizing antibodies against COVID-19, which might be helpful as an alternate therapeutic.

Further, the availability of an extensive array of SARS-CoV2 specific monoclonal antibodies can help design vaccines through structural vaccinology.This part of the research work has been submitted to a peer-reviewed journal for consideration. The research is funded by DBT.

The other co-investigators in the project are Drs. Shubbir Ahmad, Sweety Samal, Tripti Shrivastava, Hilal Ahmad, Shailendra Asthana, Chandresh Sharma, Shailendra Mani, and Adrash Chiranjivi.

Link: https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_02S_10Aug2020.pdf

Study shows distinct mutation pattern in SARS-CoV-2 virus from west India

The National Centre for Cell Science (DBT-NCCS) in Pune, an autonomous institute of the Department of Biotechnology (DBT), has recently submitted 90 whole genome sequences of the COVID-causing SARS-CoV-2 virus to the global database, GISAID.

The sequences were obtained from samples of patients from Pune, Satara and Nashik districts of Maharashtra who tested positive for COVID. These sequences were compared with those reported from other Indian and global sources, to identify any variations. Four variations were found to be predominant.They were present in most of the sequences.

Three mutations appeared to be more frequent in samples from symptomatic patients, and more prominent in samples from women. Some correlations were also observed between sequence variations and patient age, with six mutations found to be frequent in the samples from younger patients, but absent in senior patients. New and distinct patterns of mutations were observed in the viral genomes from each of the districts included in this study. These analyses thus revealed a newly emerging pattern of unique linked mutations in the genome sequences from western India, indicating that region-specific evolution of the virus genome might have occurred during the lockdown period.

This work was carried out by NCCS in collaboration with B. J. Medical College and the Armed Forces Medical College in Pune, and with support from Dr. T. P. Lahane, Director, DMER, Maharashtra. The findings of this study were recently uploaded on the preprint server, bioRxiv (https://www.biorxiv.org/content/10.1101/2020.07.30.228460v1), where they are available to anyone interested in learning the details of this study.

Genome sequencing of SARS-CoV-2 was undertaken by NCCS as a participant of DBT's pan-India 1000 genome consortium, which was set up to sequence the genomes of the virus from clinical samples collected at different locations in the country. This initiative, aimed at understanding the genetic variations in the virus across the country, is being coordinated by the National Institute of Biomedical Genomics (NIBMG), and involves several national research institutions. The consortium recently crossed the first milestone of sequencing 1000 SARS-CoV-2 genomes.

Since the start of the COVID-19 pandemic and identification of the virus that causes the disease, a global rush to sequence its genome has resulted in 75,000 viral genomic sequences from across the globe being uploaded on the global GISAID database so far. This is not surprising, since genome sequences provide valuable insights that are necessary to track and trace the outbreak, to design and evaluate diagnostic tests, and to identify potential

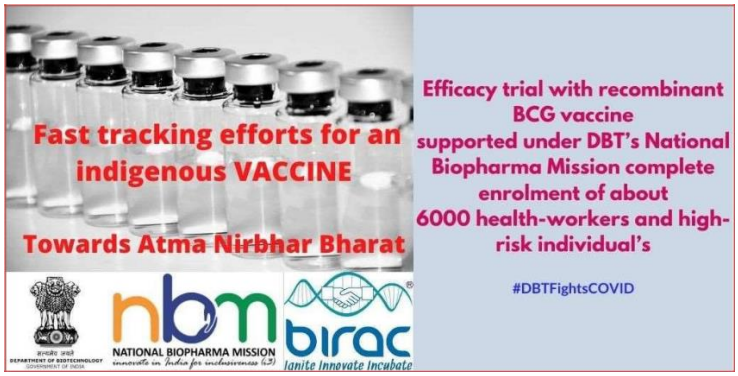
intervention strategies. NCCS has been contributing to the national efforts towards these goals, through genome sequencing as well as other ongoing diagnostics and research initiatives.

The institute has been contributing to the ongoing COVID surveillance in Maharashtra, having tested over 16,000 samples in 100 days. This was made possible by the determined and tireless efforts of several scientists, and members of the technical and other staff of NCCS.

Link: https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_03S_10Aug2020.pdf

Efficacy trial with recombinant BCG vaccine completed the enrolment of about 6000 health-workers and high-risk individuals

The Biotechnology Industry Research Assistance Council (BIRAC), a New Delhi based Govt of India Enterprise, funded the Serum Institute of India Pvt Ltd (SIIPL) under Department of Biotechnology's National Biopharma Mission for conduct of a multisite randomized double-blinded placebo-controlled phase III clinical trial of a recombinant Bacille Calmette-Guerian (rBCG) vaccine candidate (VPM1002).



The objective of this trial is to evaluate the ability of VPM1002 in reducing infection incidence and severe disease outcomes of COVID- 19 among high risk persons of advanced age or co-morbidities and high-exposure healthcare workers.

The BCG vaccine is given routinely to all new born babies as a part of the National childhood immunization programme to prevent tuberculosis, an infection caused by bacteria that mainly affects the lungs. It has beneficial heterologous effects and proven antiviral and immune modulatory properties that protect against infectious diseases through induction of trained innate immunity and heterologous adaptive immunity.

About 6,000 health workers and high-risk individuals including those in close contact of COVID patients have been enrolled in a clinical trial to determine if the rBCG can boost immunity to fight against the virus. The trial began in May and has completed enrolment of subjects in almost 40 hospitals across the country.

There is an urgent need to ensure the safety and health of HCWs who are on the forefront fighting the epidemic, household contacts of COVID positive patients and all other people

residing or working in COVID-19 hotspots/outbreak areas where there is a high risk of transmission of COVID-19 infection. Similar trials with rBCG are also approved by Paul Ehrlich Institute (PEI), and Health Canada.

Link: https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_02BB_10Aug2020.pdf

Mylab scales up production of test kits with support from DBT's National Biopharma Mission

The Pune-based Mylab Discovery Solutions was supported under National Biopharma Mission of Department of Biotechnology at Biotechnology Industry Research Assistance Council (BIRAC), New Delhi. With this strategic funding received under the COVID consortium, Mylab scaled up its production and development of COVID-19 Pathodetect testing kit. This production line at Mylab manufactures rapid and high throughput detection platform. Pathodetect utilizes a robust diagnostic methodology for use in public health laboratory settings for the screening and detection of CoVID-19. Its work flow reliably detects CoVID-19, and further discriminates CoVID-19 simultaneously within 2.5 hours compared to 7 hours or more hours required by other protocols.

Currently, Mylab has a manufacturing capacity of 2,00,000 RT-PCR and 50,000 RNA tests. Mylab has obtained CDSCO/India-FDA and ICMR approval to manufacture for NAT, HIV, HBV, HCV, and for detection of novel coronavirus 2019-n COV/SARS-COV-2. The company has recently launched Molecular laboratory machine Compact XL that can manufacture various reagents as well as perform various molecular tests in a single machine unit. The machine will help India in setting up the molecular diagnostic labs in rural India as it eliminates huge infrastructure costs, Capex and Opex costs since minimal number of employees - can do a large number of tests.

The coronavirus pandemic has lately posed new global challenges, and amid the outbreak the best measure is to test symptomatic patients to prevent or slow the spread of the virus, until a

suitable treatment is found. Currently, most pandemic-prone diseases, including COVID, are diagnosed accurately by polymerase chain reaction (PCR), a molecular technique that is the gold standard in diagnostics, and is also recommended by CDC. Therefore, having indigenous supplies of qualitative RT- PCR test kits was identified as a critical need in enhancing the testing ability across the country.

Link: http://ddnews.gov.in/sci-tech/department-biotechnology-supports-production-scale-test-kits-mylab

Link: https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_02BB_11Aug2020.pdf