

## PPE2 protein of *Mycobacterium tuberculosis* inhibits innate defense by decreasing ROS production in macrophages

Study conducted at Centre for DNA Fingerprinting and Diagnostics (CDFD), Hyderabad we have found that one of the PE/PPE family protein of *Mycobacterium tuberculosis* (*M. tb*), PPE2, can limit oxidative stress mediated by reactive oxygen species (ROS). PPE2 is shown to be a secretory protein. Bioinformatics analysis revealed the presence of eukaryotic like SH3 domain and a PxxP motif in PPE2. PPE2 protein interacted with p67<sup>phox</sup> subunit of NADPH oxidase in the cytosol and hindered the migration of cytosolic subunits p47<sup>phox</sup> and p67<sup>phox</sup> from cytosol to membrane.

Unavailability of subunits p47<sup>phox</sup> and p67<sup>phox</sup> at the membrane resulted in faulty assembly of NADPH oxidase complex and as a result inhibition in ROS production was observed. Further, to investigate the role of SH3-like domain and PxxP motif in PPE2 mediated ROS inhibition, we mutated conserved residues in SH3-like domain (Y209A, W236A, and P249A), deleted a PxxP motif ( $\Delta$ 540-543). Team observed that W236A mutation could not inhibit ROS generation, also, it failed to inhibit PPE2-p67<sup>phox</sup> interaction. This suggested that W236 residue in SH3 like domain of PPE2 is probably crucial for PPE2-p67<sup>phox</sup> interaction. PPE2 expression in *M.tb* improves the intracellular survival of *M.tb* as PPE2-deficient *M.tb* poorly survive inside macrophages. This suggests that PPE2 is important for intracellular survival of *M.tb* in macrophages.

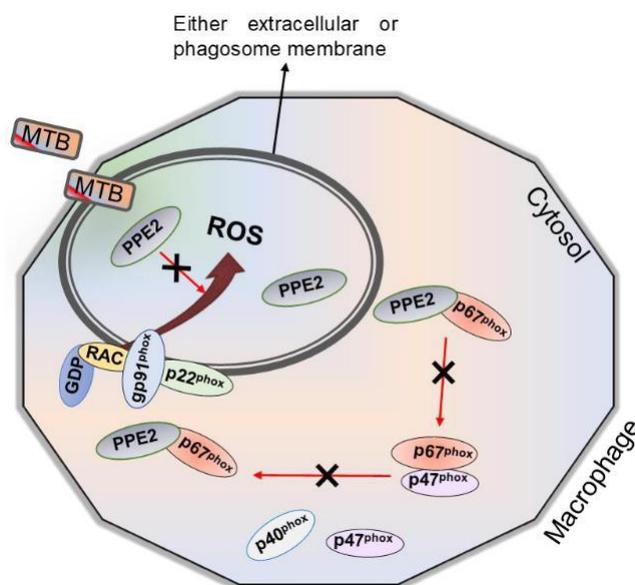


Figure showing the mechanism of ROS inhibition by PPE2 during *M. tuberculosis* (MTB) infection

In macrophages, assembly of NADPH oxidase complex is required for ROS generation. In *M. tuberculosis*-infected macrophages, PPE2 is secreted out and interacts with cytosolic subunit p67<sup>phox</sup> preventing the translocation of p47<sup>phox</sup> and p67<sup>phox</sup> at the membrane to form a complex with gp 91<sup>phox</sup>. Thus, NADPH oxidase activity is reduced causing poorer ROS generation.

The study suggested that PPE2 may be an important target for the development of novel drugs against *M. tb*. PPE2 inhibits the production of ROS in a very coordinated manner to diminish oxidative stress. Further studies on PPE2 will expand our understanding of host and mycobacterial interactions and the role of oxidative stress in TB pathogenesis which may help in the development of new drugs to control tuberculosis.

The *M. tb* is one of the most successful pathogens of humans and causes tuberculosis (TB) disease. *M. tb* has evolved several adaptive skills and evasion mechanisms to hijack the immunologically educated host to suit its intracellular lifestyle inside macrophages. Macrophages phagocytose mycobacteria and gets trapped inside the phagosome. Phagosome gets associated with lysosome. During this process, there are production of reactive oxygen species (ROS) creating an oxidative stress which mount an effective host-defense mechanism to kill mycobacteria. However, *M. tb* has evolved strategies to avoid oxidative stress caused by “ROS”.

## **Lt Gen Madhuri Kanitkar delivers the 32<sup>nd</sup> NCCS Foundation Day Oration**

The Department of Biotechnology's institute, the National Centre for Cell Science (NCCS) celebrated its 32<sup>nd</sup> Foundation Day on 26<sup>th</sup> August, 2020. NCCS is an autonomous institution of the Department of Biotechnology, Govt. of India, located in Pune. Registration as a Society under the name, „National Facility for Animal Tissue and Culture Collection“ (NFATCC) in 1988 formally marked the inception of what is now called NCCS. NCCS has flourished through its journey over more than three decades under the able leadership of the Founding Director, Dr. Ulhas Wagh, followed by two former Directors, Padma Shri Dr. Gyan Chandra Mishra and Dr. Shekhar Mande, who is presently The DG of CSIR, and the current Director, Dr. Manoj Kumar Bhat.

NCCS celebrated completion of 32 years with a Foundation Day Oration delivered online by the Chief Guest, Lt Gen Madhuri Kanitkar, Deputy Chief Integrated Defence Services (Medical). Lt Gen Kanitkar is the third woman officer and first paediatrician to reach the rank of Lt Gen, the second-highest rank in the armed forces. She is also a member of the Prime Minister's Science, Technology, and Innovation Advisory Council (PM-STIAC), and a member of the Board of Governors of the Medical Council of India. The topic of her oration was, "Aligning Research to Health Care - Challenges and Opportunities", a very pertinent topic in current times.



Virtual felicitation of Chief Guest, Lt Gen Madhuri Kanitkar, after she delivered the 32<sup>nd</sup> NCCS Foundation Day Oration

Lt Gen Kanitkar gave a very lucid bird's-eye-view from a clinician's perspective, of the current challenges, and the opportunities available to streamline research with health care. She started with stating the strong need to align education, research and public health, and have them operate in a circle, with each driving the other with a patient-centric focus. She stressed the need to use a top-down approach to prioritize and optimally use the funding available for research. She further said that being aware of the evolving trends of the disease burden in the country, and co-evolving research to address these needs, could make the research count more. She also talked about the paradigm shift in health care being brought about by modern tools like machine learning, AI, GIS and telehealth, and their value in current times. She expressed the need to collaborate to leverage the wisdom gained from big data analytics of the large population of India for the benefit the masses. She said that genome mapping of the Indian population will be one of the focus for research in the near future, given that precision medicine is one of the PM-STIAC missions. She put forth the strategic importance of „one health“, a wholistic approach towards achieving optimal health outcomes taking cognizance of the interconnection between people, animals, plants and their shared environment, especially given the current trend of increasing zoonotic and environment-associated diseases.

She introduced the audience to the science and technology cluster being developed by the office of the Principal Scientific Adviser (PSA) to the Government of India, with details of the first cluster planned in Pune. She then highlighted how India had risen to the COVID challenge and turned it into an opportunity for meaningful collaborations - between Government Departments and institutions, as well as between diverse disciplines like mathematics and public health - to tackle the current crisis. Using the example of developing a vaccine against COVID-19, she stressed the need for research to be conducted in an ethical manner, to make it meaningful. Highlighting the need to bring together integrative medicine and research, she briefly spoke about the ongoing Yoga Nidra research at the AFMC in Pune. She also gave a sneak peek into the proposed plans of the office of the PSA to address mental wellness through positive mental health initiatives.

Towards the end of her oration, Lt Gen Kanitkar talked about the establishment of the Multidisciplinary Research Unit (MRU) and the Research Wing at the AFMC, and the collaborations between NCCS and the Armed Forces Medical College (AFMC), which are exemplary of efforts towards bringing research and health care together. The latter were initiated as partnerships between individual scientists and doctors at the two institutions, under the guidance of the then Maj Gen Velu Nair, who was the Dean of the AFMC at the time. Subsequently, during her tenure as the Dean and Dy Commandant of the AFMC, Lt Gen Kanitkar further facilitated collaborations between NCCS and the AFMC Research

Wing, recognizing the need for sustained interactions at the institutional level. Lt Gen Kanitkar then laid out the future directions envisioned for meaningful academic and research collaborations with NCCS as well as other organizations.

She then shared the wisdom gleaned from her multiple roles as a soldier, teacher and doctor, and stressed the need for a fit mind and a fit body, and for living a well-balanced life. Stating that she enjoyed the role of being a mentor the most, Lt Gen Kanitkar concluded the oration by quoting some lines from the “*Atharva Shirsha*” to highlight the mentor-mentee bond which is of paramount importance in all fields, including in research.

NCCS was established with a mandate of three main functions: Serving as a National Cell Repository, Research in cell biology, and Human Resource Development. Since inception, NCCS has been at the forefront of basic research in diverse areas of cell biology that address challenging questions about human health, especially those related to cancer, diabetes, infectious diseases, functioning of the immune system, regeneration of tissues like bone, role of gut microorganisms in health and disease, stem cell biology, etc. In recent years, it has expanded into newer research areas like structural biology and neurobiology.

The myriad of contributions made by scientists of NCCS have gained worldwide recognition through publications in renowned scientific journals and many prestigious awards, including the Padma Shri and S. S. Bhatnagar Prizes. A paper published by NCCS this year in Nature Structural and Molecular Biology has recently been cited among the top 5% of all research outputs scored by Altmetric.

Upholding its mandate, the national animal cell repository of NCCS has been providing valuable services since inception, which has been instrumental in supporting cell biology research at various institutions across the country. NCCS has created a state-of-the-art infrastructure for the characterization and authentication of cell lines, and routinely upgrades its services. The Centre of Excellence at NCCS, called the National Centre for Microbial Resource (NCCS-NCMR), which is the largest individual collection of microorganisms in the world, has played a major role in the preservation & characterization of the nation’s microbial biodiversity, and in supporting microbiology research in India.

NCCS also contributes immensely to capacity building of the nation through several teaching and training programs that have been instrumental in honing young scientific talent. With 135 PhD students currently on board, almost 300 research scholars have received a PhD degree since the inception of NCCS. NCCS also imparts training to students who carry out short-term research projects at NCCS as project trainees and summer trainees selected by the Indian Academy of Sciences. NCCS also conducts the annual coursework for Ph.D. students

registered with the Department of Biotechnology, S. P. Pune University. Since inception, NCCS has trained over 300 Project Trainees and over 200 Summer Trainees, and over 350 students have undergone the PhD coursework.

NCCS has been actively engaged in various activities to facilitate the ongoing efforts against the outbreak in the country. It is one of the Government laboratories identified to carry out testing for COVID-19, given its expertise in biotechnology research. NCCS has tested more than 17000 samples from Maharashtra. Further, NCCS has also provided guidance and assistance, and shared resources to help other research and academic organizations, such as IISER-Pune and ARI, to set up COVID testing facilities on their respective campuses. NCCS is also one of the national COVID-19 bio-repositories recognized by the ICMR.

NCCS has also contributed genome sequences of the virus as a participant of the pan-India 1000 genome consortium of the Department of Biotechnology, which has analyzed the genome sequences of the virus from clinical samples collected across the country. COVID-19 related research initiatives are also underway at NCCS to generate proof of concept towards developing diagnostics and vaccines. The national cell repository at NCCS has also been facilitating COVID-related research at other organizations by supplying cell cultures, which are necessary to carry out this work. It has supplied 23 cultures to 14 organizations across India so far, including national research organizations, a medical college, a University and a private company.

**Link:** [https://twitter.com/DBT\\_NCCS\\_Pune/status/1298677064631902209](https://twitter.com/DBT_NCCS_Pune/status/1298677064631902209)

**Link:** [https://vigyanprasar.gov.in/wp-content/uploads/vigyan\\_samachar\\_dbt\\_01BB\\_8Sep2020.pdf](https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_01BB_8Sep2020.pdf)

## DBT-IBSD'S Covid19 testing laboratory completes its first 1,000 tests

The Covid19 testing laboratory set up by the Department of Biotechnology's Institute of Bioresources and Sustainable Development (DBT-IBSD) at Imphal, Manipur in collaboration with Jawaharlal Nehru Institute of Medical Sciences (JNIMS) has crossed the first milestone, with the testing of 1,000 samples.

The Indian Council of Medical research (ICMR) New Delhi had given its approval to the DBT-IBSD-JNIMS laboratory on 11th July 2020 for testing COVID samples.



**DBT-IBSD-JNIMS COVID19 Testing Laboratory at Imphal, Manipur  
Completes its First 1000 tests**

❖ DBT-IBSD-JNIMS Covid-19 testing laboratory at Imphal, Manipur has crossed the first milestone of having tested the first 1000 samples earlier this week.

**Congratulations to  
these frontline  
Warriors of  
DBT-IBSD!!**

JNIMS  
IBSD  
Manipur



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

**Link:** [https://vigyanprasar.gov.in/wp-content/uploads/vigyan\\_samachar\\_dbt\\_01S\\_7Sep2020.pdf](https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_01S_7Sep2020.pdf)

## **DBT- NCCS scientist selected for Miltenyi Biotec MACS Project Grant**

Dr. Sharmila Bapat, scientist at the Department Of Biotechnology's National Centre for Cell Science (DBT-NCCS) in Pune, has been selected to receive the Miltenyi Biotec MACS Project Grants 2020. Dr. Bapat had submitted an abstract for this competitive grant, which was selected as one of the winning abstracts. She is one of three awardees selected from the Asia Pacific region this year.



Dr. Sharmila Bapat

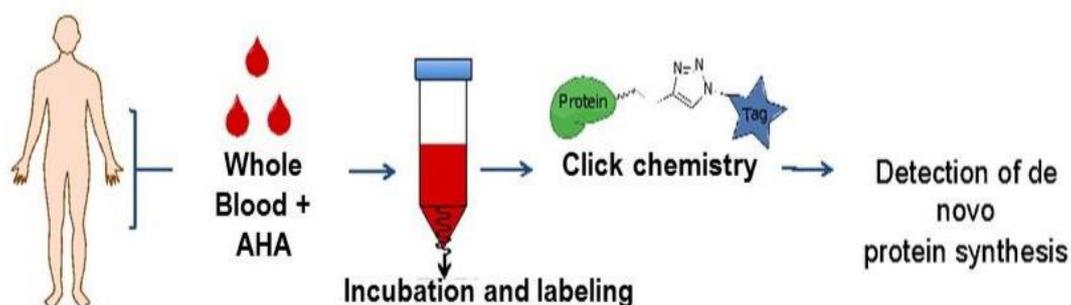
Miltenyi Biotec is a global biotechnology company headquartered near Cologne in Bergisch Gladbach, Germany. The company is a provider of products and services that support scientists, clinical researchers, and physicians across basic research, translational research, and clinical applications.

The Miltenyi Biotec MACS Project grant is open to all established scientists and clinicians, postdoctoral scientists, trainee clinicians, postgraduate students, junior and senior investigators, which are employed in Singapore, India, or Thailand.

**Link:** [https://vigyanprasar.gov.in/wp-content/uploads/vigyan\\_samachar\\_dbt\\_01S\\_9Sep2020.pdf](https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_01S_9Sep2020.pdf)

## CNS-inStem – NYU researchers develop method to identify newly synthesized proteins in blood

In an international collaborative project with scientists from New York University, Aditi Bhattacharya of the Centre for Neurodevelopmental Synaptopathies (CNS) at Institute for Stem Cell Science & Regenerative Medicine (inStem), Bengaluru along with Chhaya Patole of Mass Spectrometry Facility at the Bangalore Life Science Cluster (BLSc), Bengaluru, have developed a method to incubate, label and then detect newly synthesized proteins in freshly collected blood via mass spectrometry. Testing the proof of concept in mice and rat blood, the group was able to identify proteins from erythrocytes, lymphocytes, and platelets in samples. Read about the proteomic work done in this project that has adopted cutting edge peptide identification algorithms to enhance peptide detection [here](#).



The ability to test proteomic changes in the blood dynamically has critical implications to the discovery and tracking of biomarkers for a variety of metabolic, myeloid and infectious diseases. The biomarkers can range from detection of viral/bacterial peptides to validating whether a specific biochemical pathway has been engaged by a given drug as a part of treatment efficacy monitoring. However, to date it has been cumbersome to identify newly synthesized proteins from whole blood derived from usual blood collection methods.

A website report titled ‘CNS,inStem – NYU Researchers Develop Method to Identify Newly Synthesized Proteins in Blood’ based on Dr. Aditi Bhattacharya’s latest work published in *Journal of Proteome Research*, Aug 2020.

**Link:** [https://vigyanprasar.gov.in/wp-content/uploads/vigyan\\_samachar\\_dbt\\_02BB\\_7Sep2020.pdf](https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_02BB_7Sep2020.pdf)

## **DBT–IBSD distributes surface disinfectant in Meghalaya and Sikkim**

The Department of Biotechnology's Institute of Bioresources and Sustainable Development (DBT-IBSD) has distributed the Institute made surface disinfectant to the State Bank of India and its ATM booth at 3rd Mile, Upper Shillong, Meghalaya and to the students of Human Development Foundation of Sikkim (HDFS) Boys Hostel at Chongay Tar in East Sikkim.

The distribution at the SBI branch in Upper Shillong was made in the presence of Ms. A. P. Sooting, Branch Manager, and her team. The HDFS boys hostel in East Sikkim provides education to underprivileged children. The initiative of distribution was taken up under the guidance of the Director, IBSD, Prof. Pulok K. Mukherjee with an aim to protect COVID-19 frontline workers and others. The Department of Biotechnology's Institute of Bioresources and Sustainable Development (DBT-IBSD) has its head office in Imphal, Manipur and has centres in Shillong, Gangtok, Aizawl. It has been taking steps to help boost the capacity of the various States in the northeastern region of the country to meet the challenges posed by the COVID-19 pandemic that is sweeping across the world.

### **Links to news clips of the above outreach activities**

1. <https://meghalaya.gov.in/press/content/37780>
2. <https://spnewsagency.com/the-ibsd-shillong-distributed-disinfectant-and-hand-sanitizer-to-sbi-bank-upper-shillong/>
3. <https://www.indigenoussherald.com/TripuraNews/dbt-ibsd-distributes-disinfectant-and-hand-sanitizer-14013.html>
4. <https://theshillongtimes.com/2020/08/28/disinfectants-sanitisers-distributed/>
5. <http://www.meghalayamediaprovider.com/2020/08/27/6520/>
6. <https://www.sentinelassam.com/north-east-india-news/meghalaya-news/dbt-ibsd-distributed-sanitizers-in-meghalaya-498369>

**Link:** [https://vigyanprasar.gov.in/wp-content/uploads/vigyan\\_samachar\\_dbt\\_02S\\_7Sep2020.pdf](https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_02S_7Sep2020.pdf)