Going together to go far – DBT-THSTI's partners that aided its role in DBT India Research Consortium

To date, DBT India COVID-19 Research Consortium has enrolled more than 2000 COVID-19 positive patients and is following them into their recovery period and collecting valuable clinical information and blood samples at different periods. The samples are processed and stored in a state-of-the-art biorepository at DBT's Translational Health Science & Technology Institute (THSTI), Faridabad.

This biorepository currently houses nearly 4000 specimens at different time points which are being distributed to the academic institutions and industry to accelerate the innovations in COVID-19 diagnostics. In response to requests, the biorepository has distributed a total of about 2400 sera samples and 55 naso- and oro-pharyngeal swabs to date. Eight development sera panels (including samples from 100 participants), one naso-oro-pharyngeal panels (75 samples), four evaluation sera panels (samples from 100 participants), pooled positive standard and pooled negative standard have been shared. This national resource will help the industry to quickly deliver products that can help the nation in winning this battle against the COVID19 pandemic.

One of the essential tools in the fight against the new Coronavirus disease is diagnostic tests to identify infected individuals. Multiple private and public institutions in India have come forward in this fight and have contributed towards this. But these tests have to be stringently evaluated before they can be used in public health settings. Such a strict evaluation is possible if a collection of well-characterized blood samples is available.

A DBT India COVID-19 Research Consortium was set up between autonomous institutes under Department of Biotechnology (DBT) and multiple public and private hospitals in Delhi National Capital Region. The consortium is coordinated by THSTI. The hospitals that are part of this consortium, from where most of the participants have been enrolled, are Maulana Azad Medical College and affiliated Lok Nayak Hospital in Delhi and ESI Medical College Hospital, Faridabad.

The other clinical partners that have contributed to this national effort are, Civil Hospital, Gurugram, Haryana; Civil Hospital, Palwal, Haryana; Al-Falah School of Medical Science & Research Centre and Hospital, Dhauj, Haryana; Medanta Hospital, Gurugram; Shaheed Hasan Khan Mewati Government Medical College, Nalhar, Haryana; SGT Medical College, Gurugram, Haryana; and Lady Hardinge Medical College, New Delhi. The research institutions in this consortium are THSTI, Faridabad, National Institute of Immunology, New Delhi, and International Center for Genetic Engineering and Biotechnology, New Delhi.

Link: https://www.thsti.res.in/news.php
Link: https://thsti.res.in/index.php
Link: https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_01BB_17Aug2020.pdf

New insight into bacterial social communication in natural host: Evidence for interplay of heterogeneous and unison quorum response

Using novel QS-responsive *Xanthomonas campestris* pv. *campestris* (*Xcc*) bioreporters and cabbage as a model plant pathogen-host, Scientists at DBT's Centre for DNA Fingerprinting and Diagnostics (DBT- CDFD), Hyderabad have now demonstrated a detail lifestyle of the pathogen in which QS-regulated virulence associated functions are involved in adaptation at different stages of infection in its host plant. Here, team found a stage specific interplay of heterogeneous and homogeneous QS-response in the wild-type *Xcc* population *in planta*. During early stage of systemic infection, presumably under nutrient sufficient condition, QS-responsive cells contribute to spread and establishment of disease phenotype. The QS non-responsive cells act as free-loaders of QS-signal molecules, increasing the available signal strength for QS-responders within the population.

However, during the later stage of disease, presumably under condition of nutrient limitation due to the large increase in bacterial load, bet-hedging may be disadvantageous as the free-loaders share the limited resources. At this stage, QS-responsive cells have growth advantage probably by the production of 'private goods' required for survival under these condition. Our findings suggest that the interplay of heterogeneity and homogeneity in QS-response gives a stage specific adaptive advantage to the pathogenic bacteria within host environment during systemic infection.

Many microbes exhibit quorum sensing (QS) at a high cell density to cooperate, share and collectively perform multiple social tasks within the community, where QS regulates the coordinated production of exo-products as 'public goods' that are beneficial to the population as a whole. Such social tasks include the production of virulence associated functions such as components involved in biofilm formation, extracellular enzymes, extracellular polysaccharide and surfactants that promote motility and spread. Both animal and plant pathogenic bacteria significantly depend on QS-regulation to coordinate their colonization and infection of the host tissue for a successful disease establishment.

In general, QS-response and regulation has been studied under laboratory conditions *in vitro*, where the QS-responding bacterial population exhibits heterogeneous QS-response with the emergence of both QS responders and non-responders irrespective of their parental kind, as a possible bet hedging survival strategy. It is believed that heterogeneity in

performing social task may have adaptive functions, such as division of labour and sharing of environmental resources. However, very little was known about nature of phenotypic heterogeneity in bacterial QS-response inside the host. It was unclear whether the inherent stochastic heterogeneity in the QS-response exhibited under laboratory condition is influenced by change in environmental conditions, and whether there is selection pressure to cooperate under natural conditions particularly in host-pathogen interaction.

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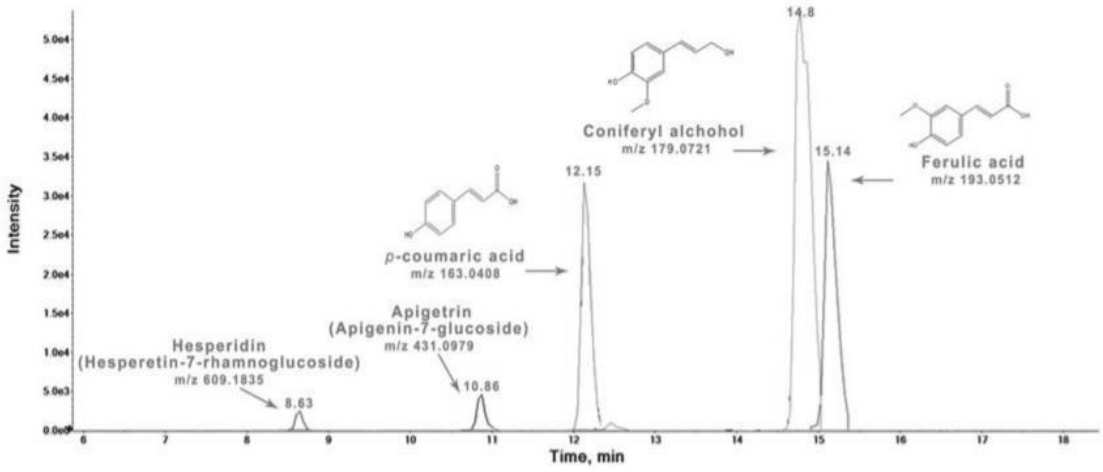
Phenolic compounds from *Lagenaria siceraria* (Calabash) could help in management of oedema, hypertension, obesity and related metabolic disorders

Scientists from DBT's Institute of Bioresources and Sustainable Development (DBT-IBSD), Imphal and Jadavpur Univeristy have studied *Lagenaria siceraria* (bottle gourd), which is a popular food plant among Indians, and contains a large number of phenolic compounds with several medicinal benefits, mentioned in Indian System of Medicine (ISM). The main objective of the study was to investigate the carbonic anhydrase inhibitory potential and inhibitory mechanism of the most potent fraction of *L. siceraria* fruits.



The extract and fraction of dried fruit of *L. siceraria* screened for their *in vitro* carbonic anhydrase II (bCA II) inhibitory activity. The active fraction was purified by using flash chromatography. The bioactive compounds were identified and quantified through liquid chromatography quadrupole time-of-flight tandem mass spectrometry (LC-QTOF-MS/MS) and reverse-phase high-performance liquid chromatography (RP-HPLC). Finally, the underlying carbonic anhydrase inhibitory mechanism of the compounds was explained by enzyme kinetics and molecular docking study.

The LC-QTOF-MS based identification of the most active fraction revealed the presence of phenolic compounds. The results of the enzyme inhibition assay revealed that coniferyl alcohol, ferulic acid and p-Coumaric acid inhibited bCA II activity [half maximal inhibitory concentration (IC50) value range of 80 to 250μM] in a dose dependent manner. The kinetics

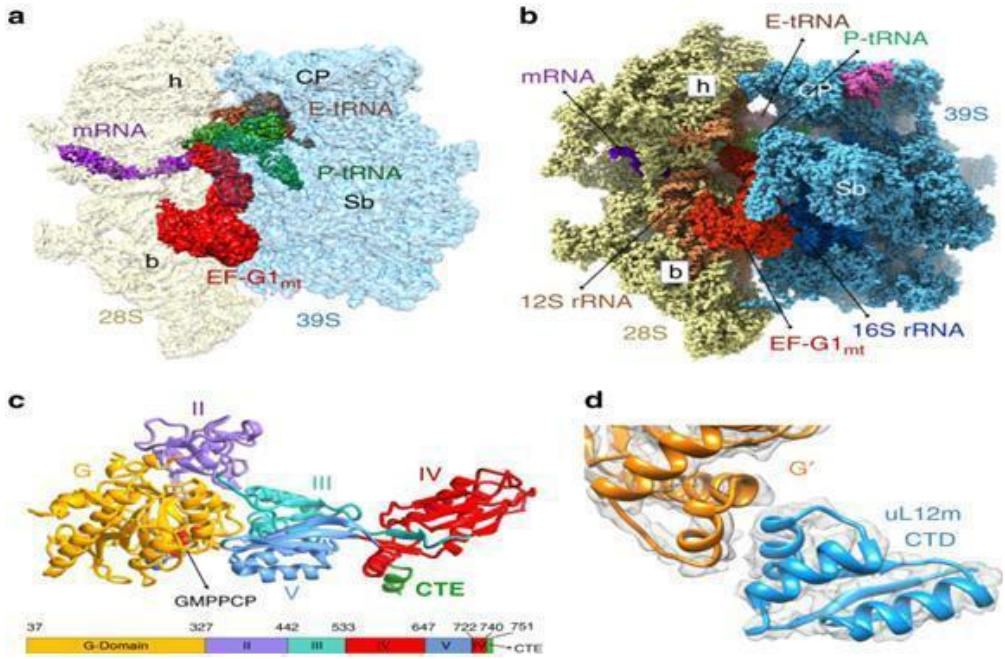
study of enzyme inhibition revealed that p-Coumaric acid binds to the enzyme competitively whereas the non-competitive type of inhibition was observed for ferulic acid and coniferyl alcohol. The molecular docking study explored the interaction mechanism of phenolic compounds at the active site of bCA II.

The present research led them to conclude that, the phenolic compounds from *L. siceraria* serve as major contributors for carbonic anhydrase inhibition, which could play a useful role in the management of oedema, hypertension, obesity and related metabolic disorders.

Link: https://onlinelibrary.wiley.com/doi/abs/10.1002/pca.2975?af=R
Link: https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_01BB_20Aug2020.pdf

Structures of the human mitochondrial ribosome bound to EF-G1 reveal distinct features of mitochondrial translation elongation

In this work, Scientists from DBT - Regional Centre for Biotechnology (DBT-RCB), Faridabad presented the 2.68–3.96 Å cryo-EM structures of the human 55S mitoribosome in complex with the human mitochondrial elongation factor G1 (EF-$G1_{mt}$) in three distinct conformational states, including an intermediate state and a post-translocational state. These structures reveal the role of several mitochondria-specific (mito-specific) mitoribosomal proteins (MRPs) and a mito-specific segment of EF-$G1_{mt}$ in mitochondrial tRNA ($tRNA_{mt}$) translocation.



In particular, the mito-specific C-terminal extension in EF-$G1_{mt}$ is directly involved in translocation of the acceptor arm of the A-site $tRNA_{mt}$. In addition to the ratchet-like and independent head-swiveling motions exhibited by the small mitoribosomal subunit, team also discovered significant conformational changes in MRP mL45 at the nascent polypeptide-exit site within the large mitoribosomal subunit that could be critical for tethering of the elongating mitoribosome onto the inner-mitochondrial membrane.

The mammalian mitochondrial ribosome (mitoribosome) and its associated translational factors have evolved to accommodate greater participation of proteins in

mitochondrial translation. Dr. Prem Singh Kaushal (Assistant Professor, RCB), co-authored a research article with other collaborators on ‘Structures of the human mitochondrial ribosome bound to EF-G1 reveal distinct features of mitochondrial translation elongation’.

Link: https://doi.org/10.1038/s41467-020-17715-2

Link: https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_01BB_21Aug2020.pdf

Coronavirus targets multiple organs: way forward for science

COVID-19 caused by SARS-CoV-2 has infected a large number of people worldwide and has caused a global medical emergency. Healthcare professionals have been working to devise appropriate therapeutic strategies against the virus and it has been a big struggle mainly due to the diverse range of symptoms and multiple-organ failure in infected patients. Several broad-spectrum antiviral drugs are being used for treatment. However, there is yet no specific drug or vaccine against the virus. Multiple-organ failure due to hyperactivity of the immune system resulting in cytokine storms is a major reason for death among the 5% critically ill patients. In a mini review article published in Frontiers in Medicine, researchers from the Department of Biotechnology's National Institute of Plant Genome Research (DBT-NIPGR), New Delhi, have discussed the damage caused by COVID-19 on different organs of the human body.

Article link: https://www.frontiersin.org/articles/10.3389/fmed.2020.00370/full
Link: https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_01S_17Aug2020.pdf

DBT-BIRAC supports a new solar dehydrator for fruits & vegetables

Millions of tons of fresh fruits and vegetables are wasted every year. Preservation of fruits and vegetables is a common problem that farmers face and they lose a lot of their produce due to lack of post-harvest handling and storage facilities. A Maharashtra based start-up S4S Technologies has devised a simple yet innovative technology that uses solar energy to dry food, reducing spoilage and alleviating rural poverty. The food dehydrator can help farmers preserve their produce from 6 months to 1 year. This enables them to protect themselves from price fluctuation and ensure adequate availability of agri-animal products. It also ensures a stable nutrition supply for the entire family as the dryer retains the nutrients in the produce. Thus, it gives scope to overcome under-nutrition and creates a low-cost solution to improve dietary diversity.

Unique Features:

Electricity- free solution 2-3 times
cheaper than other solar dryers.
Zero operating cost.
Retains more nutrition.
Better colour, flavour and hygiene than open sun drying

Sun-drying has been used by women since ages. The company has decided to empower and make women farmers their target audience. These women farmers cum entrepreneurs produce dehydrated vegetables with the use of the solar conduction dryer technology. S4S provides solar dryers to farmers to process vegetables and buys back processed foods from them.

It helps to:

• Reduce post-harvest loss

• Produce preservative-free nutrition-rich products for improved nutrition for rural families

• Provides assured income via-buy back to farmers

• Promotes gender equality and livelihoods

S4S aggregates the produce, does quality check and secondary processing and further sells them to a range of B2B and B2C consumers. This start-up assumes importance as it steps up to solve several problems at once as it reduces food spoilage, extends food shelf life and allows nutritional value retention, helping the largely agriculture-dependent population to earn more.

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DBT-BIRAC strengthening tech transfer capabilities in India

The Department of Biotechnology (DBT) is committed for development of affordable and effective biopharmaceutical products and services. DBT's Biotechnology Industry Research Assistance Council (DBT-BIRAC) is implementing the Department's Industry-Academia Collaborative Mission to accelerate discovery research to early development for biopharmaceuticals. The mission was approved by the Union Cabinet, with a total cost US$ 250 million, with 50% co-funding by the World Bank.

Also known as the National Biopharma Mission (NBM), this program supports establishment of Technology Transfer Offices (TTOs) that are critical for value realization of biotech innovation for inclusive growth. The TTOs facilitate translation of publicly funded research results into products and their delivery to markets by licensing innovation to enterprises. They also facilitate inter-institutional collaborations by collectively engaging them in creating market presence for their innovations.

Indian research results have significant potential to transform markets and this under-realized prospect is addressed by providing strong impetus to the technology transfer process with TTOs created and managed by professionals having skills in technology management.

Technology transfer strengthening is a long-time commitment and for the first time the NBM has committed significant resources for creation of technology transfer office framework and strengthening technology transfer professionals for the advancement of publicly funded research.

The TTOs identify inventions, protect them with due assessment of patentability, shape commercialization strategy and identify enterprises for licensing innovations for accelerated delivery to markets. With a vibrant start-up ecosystem emerging in the country, they have potential to create and nurture spinouts too that can support the inventors to create their own enterprises for commercialization.

Five TTOs have already been established across the country with a view to strengthen the technology transfer capacity, evenly in India. These are located at:

- IKP Knowledge Park, Hyderabad
- Centre for Cellular and Molecular Platforms (C-CAMP), Bengaluru
- KIIT Technology Business incubator, Bhubaneswar
- Biotechnology Business Incubation Facility (BBIF), Foundation for Innovation and Technology Transfer (FITT), New Delhi and
- Entrepreneurship Development Center (EDC), Pune

Two other TTOs are in the process of being created within the aegis of the Mission. The TTOs have necessary digital tools for patent analysis and management, licensing transactions management and post-license monitoring. The new ones will bring under their fold more institutions that need professional support for advancing their research results to markets.

The TTOs established with NBM support have made significant progress in the recent past. TECHEX.IN is a Technology Transfer Hub operated by EDC at Venture Center, Pune, that aims to help technology developers and technology commercialization entities find each other, forge partnerships and advance the technology closer to the market in a win-win partnership.

It has recently conducted many important trainings: an online session on ‘Negotiation Techniques for Technology Entrepreneurs and Innovation Managers’ was conducted on 30th May 2020, another on ‘COVID-19 drug candidates: Understanding patent landscapes and navigating patent barriers’ on 8th June 2020 and a third online training programme on ‘Understanding and Negotiating Non-disclosure Agreements (NDAs) and Material Transfer Agreements (MTAs)’on 13th June 2020. Further training sessions on ‘Ideating and evaluating commercializable R&D: Thinking frameworks and examples’ and ‘basics of IP and filing of patents’ were conducted on 17th July and 8th Aug 2020 respectively.

IKP-PRIME, at IKP, Hyderabad also conducted online training sessions on ‘an insight into IP management’ and ‘scope of patenting AI inventions’ on 24th and 31st July 2020 respectively.

‘Need for IP protection’ and ‘Creating value from your invention’ were dealt with in training sessions conducted on the 5th and 19th of Aug 2020.

Another NBM supported TTO-Innovation -Technology transfer office (i-TTO) at Foundation for Innovation and Technology Transfer, Indian Institute of Technology- Delhi, recently transferred a technology entitled "Unique C1-C2 spacers with occipital-cervical fixation" developed by Prof. Sarat Chandra, AIIMS supported under BIRAC’s BIG grant to Med Solutions, New Delhi

Link: https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_01S_20Aug2020.pdf

Molecule designed to tackle drug resistance in hospital acquired infection

Drug resistance is a public health concern that threatens to undermine decades of medical progress. ESKAPE (Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter spp.) pathogens cause most nosocomial infections, and are frequently resistant to carbapenem antibiotics, usually leaving tigecycline and colistin as the last treatment options. However, increasing tigecycline resistance and colistin's nephrotoxicity severely restrict use of these antibiotics.

In a Project supported by DBT at IISc Bengaluru, the researchers have designed antimicrobial peptides using a maximum common subgraph approach. Their best peptide (Ω76) displayed high efficacy against carbapenem and tigecycline-resistant Acinetobacter baumannii in mice (Figure 1). Mice treated with repeated sublethal doses of Ω76 displayed no signs of chronic toxicity. Sublethal Ω76 doses co-administered alongside sublethal colistin doses displayed no additive toxicity. These results indicate that Ω76 can potentially supplement or replace colistin, especially where nephrotoxicity is a concern. To the knowledge, no other existing antibiotics occupy this clinical niche. Mechanistically, Ω76 adopts an α-helical structure in membranes, causing rapid membrane disruption, leakage, and bacterial death.

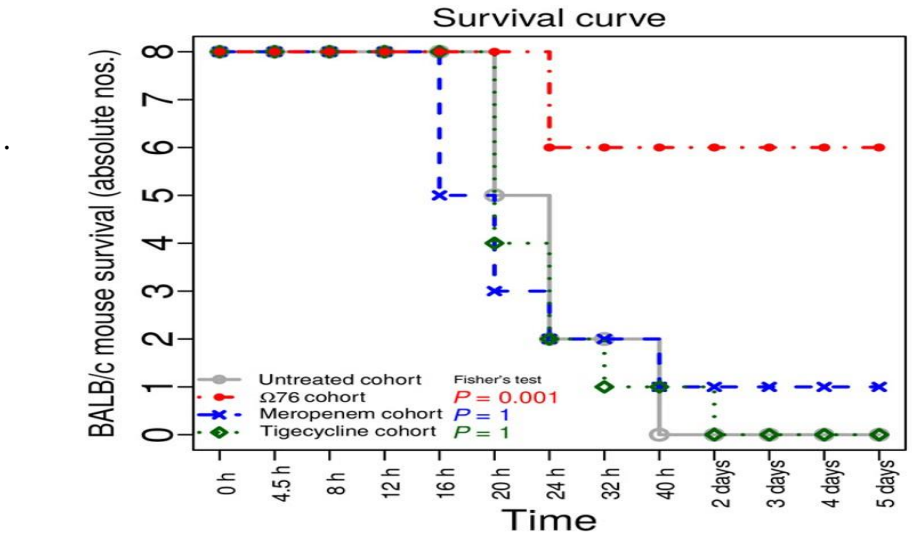

Figure: *In vivo* efficacy of Ω76 using a BALB/c mouse peritoneal model of infection

Link to research paper: https://advances.sciencemag.org/content/5/7/eaax1946.full
Link: https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_01S_21Aug2020.pdf

A page from India's story to make a desi COVID-19 vaccine: DBT-THSTI steps up to become DBT's nodal centre for COVID-19 vaccine development support

Team from CEPI at THSTI in August, 2019. L-R: Gunnstein Norheim, Dawn O Connell, Gagandeep Kang, Richard

Wilder, Melanie Saville, Amrita Sekhar, Arun Kumar, Debra Yeskey. Source: THSTI Image Repository

The DBT's Translational Health Science and Technology Institute (DBT-THSTI), Faridabad was enabled as a key component of the Ind-CEPI programme of Department of Biotechnology in 2019 to establish a translational assay laboratory and develop Biosafety Level-3 facilities to support the development of vaccines against emerging infectious diseases.

The early preparatory work led to THSTI being able to rapidly ramp up the establishment of assays and model systems to support vaccine developers in India to advance their programmes. THSTI is now working in collaboration with companies involved in vaccine development such as Mynvax and Zydus Cadila for evaluation of samples from their pre-clinical studies to for neutralising antibodies titres against live virus are being determined by micro- and plaque reducing neutralisation assays. The vaccine candidates which induce appropriate immune response and neutralising antibodies titres would be further evaluated in hamster and transgenic Ace2 mice model of infection and challenge.

At the time of writing this report, THSTI was also in discussion with several other vaccine companies to support them for pre-clinical and clinical studies.

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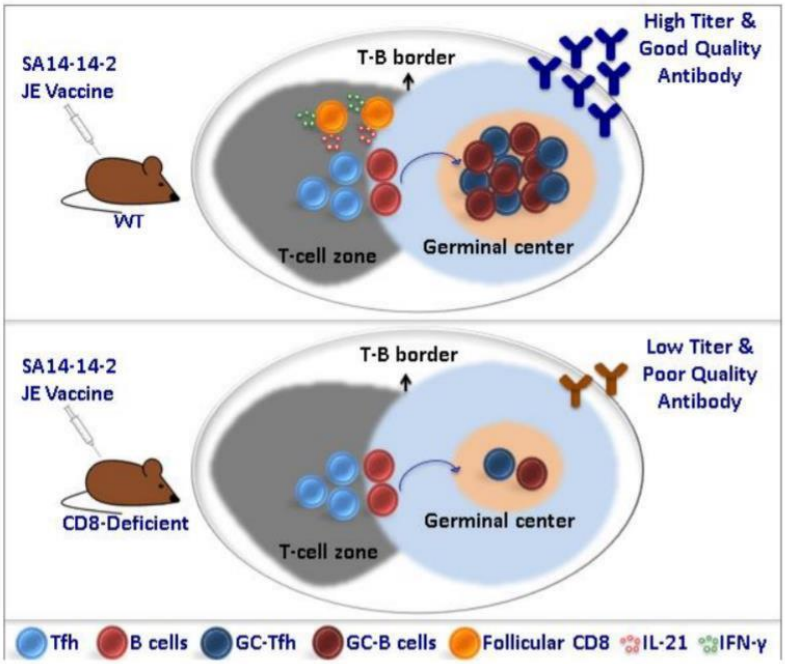
NII Scientists uncover an exceptional role of CD8$^+$ T cells in shaping the protective antibody response to a human flavivirus vaccine

In a new study, coming up in European Journal of Immunology, the team of scientists at BDT's National Institute of Immunology (NII), New Delhi has shown that SA14-14-2 Japanese Encephalitis (JE) vaccine induced protective humoral immunity is largely dependent on CD4+ T cells and is augmented by CD8+ T cells. Although, SA14-14-2 vaccine-primed CD8+ T cells are not protective, they influence the overall process of the development of protective antibodies. The work performed in mice, is the first to implicate the CD8+ T cells in shaping the antibody response to a human vaccine.



This probably means that an ideal vaccine should synchronize both the CD8+ T cells and Tfh cells to achieve higher magnitude and good quality of protective antibodies' says Nimesh Gupta, Ph.D., who led the study.

The Intergovernmental Panel on Climate Change (IPCC) emphasize the research on vector borne diseases as main objectives of future research on human health. The mosquito-borne flaviviruses have been the major concern. Now with the expansion of mosquito vectors due to urbanisation and global warming, people in many countries are at higher risk to get infection by these deadly viruses.

It would be better if we develop a vaccine that can confer protection against multiple flaviviruses like JE virus, West Nile virus and Zika virus'says Nimesh Gupta. Flaviviruses show a high degree of sequence homology, which could be targeted while developing a multi-virus vaccine. This could happen if we know what cellular determinants need to be exactly pulled to get the ideal antibody responses.

For this study, the team utilized animal models to understand the mechanism of protective immunity conferred by the SA14-14-2 vaccine. In a series of virus challenge studies, study show that CD4+ T-cells alone, but not CD8+ T-cells, are sufficient to confer vaccine-mediated protection. However, the CD4-mediated protection was potentiated in the presence of vaccine-primed CD8+ T cells. The microanatomical structures 'germinal centers' in the secondary lymphoid organs, where the antibody response and memory is conceived, were thoroughly investigated by the team after the single dose immunization. By using CD8-deficient mice or by removing the CD8+ T cells during the immune response to this vaccine, researchers show that both the protective traits of CD4+ T cells and the quality of antibody response to the vaccine are impaired in absence of CD8+ T cells. The team further demonstrates that this is mainly due to the impaired differentiation of GC-Tfh cells, a specialized CD4+ T-cell subset crucial for GC development, leading to the poor germinal center response to the vaccine.

This is an exciting cellular interplay underlying the potent protective antibody responses. To understand if this cellular interplay could be generalized, we are studying the individual simmunized with SA14142 vaccine and also extending our observation to other live attenuated vaccines' says Nimesh Gupta, who is heading the Vaccine Immunology Laboratory. The world is awaiting an ideal vaccine to fight against the ongoing Coronavirus pandemic. It may be useful to explore if synchronizing the Tfh-cell and CD8 T-cell response could help in inducing the potent protective antibodiesbyaSARS-CoV-2 vaccine.

The study titled 'CD8+ T cells are crucial for humoral immunity establishment by SA14-14-2 live attenuated Japanese encephalitis vaccine' also authored by Anurag Kalia and Mona Agrawal of Vaccine Immunology Lab was supported by the grants from the Department of Biotechnology and the institutional funds from the National Institute of Immunology, India.

Future vaccines may be rationalized for precisely balancing the CD8+ T cells and Tfh cells interplay to exert potent protective antibody response.

Japanese encephalitis is the leading cause of acute encephalitis in Asia and the western pacific region with more than 68,000 clinical cases reported annually. With the case fatality rate of 30% and the permanent neurologic or psychiatric sequelae in 30–50% of patients, JE has been most dreaded flavivirus encephalitis.

There is no anti-viral treatment available for JE but it's a vaccine preventable disease. Several inactivated preparations are in use as the traveler's vaccines. TheSA14-14-2 live attenuated JE vaccine has been included in national immunization programs of JE affected countries. However, the protective immunity conferred by this historical vaccine wanes with time. Lack of understandingon how this historical vaccine works has been a limitation in development of superior vaccines and in revising the immunization policies in endemic regions.

The risk is rising with continuously expanding JEV geographical range and recently circulating new virus genotypes that can affect all age groups. This calls for a timely development of an effective vaccine that can prevent from JEV and related flaviviruse side-ally in a 'One Life One Dose' regimen.

Link: https://onlinelibrary.wiley.com/doi/abs/10.1002/eji.202048745

Link: https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_02BB_18Aug2020.pdf

DBT-BIRAC helps set up mRNA-based vaccine manufacturing platform

The Department of Biotechnology's Biotechnology Industry Research Assistance Council (DBT-BIRAC) has facilitated the establishment of a 'first-of-its-kind' mRNA-based vaccine manufacturing platform in India. DBT has provided seed funding for the development of a novel self amplifying mRNA-based vaccine candidate for COVID19 by Gennova under its Ind-CEPI program.

Gennova has developed the vaccine candidate (HGCO19), in collaboration with HDT Biotech Corporation, Seattle, US, that has demonstrated safety, immunogenicity, neutralization antibody activity in rodent and non-human primate models. The company is working aggressively to ensure first human injection by the end of the year, subject to Indian regulatory approvals.

HGCO19 has all the necessary information to guide the host cells to make the antigen - spike protein of the virus. It is supported by 'lipid inorganic nanoparticle (LION)' as a delivery vehicle. The neutralizing antibody response of the vaccine in mice and non-human primates was comparable with the sera from the convalescent patients of COVID-19, above the recommended titre of 1:160 for neutralizing antibodies by US-FDA.

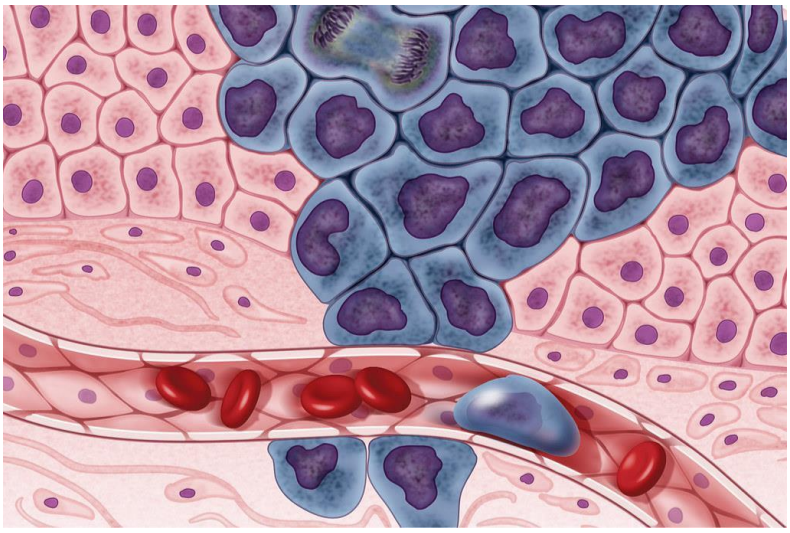
Further advantages of HGCO19 are its mRNA platform design and delivery vehicle. HGCO19 uses a 'self-replicating mRNA platform' that ensures low injectable dose (dose-sparing effect) and sustained antigen release for a longer duration. 'LION delivery system'

used for HGCO19 has adjuvanting property, enhanced storage stability, reduced adverse effect, improved permeability and better bioavailability.

Link: https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_02S_17Aug2020.pdf

DBT-NIBMG scientists working to find cell types behind cancer recurrence

One of the major challenges in cancer treatment is tumour recurrence. Most patients initially respond well to therapy, but often for some, the tumours recur and cancer comes back after some time. The tumors that recur do not always respond well to the treatment as they did the first time, thus resulting in less chances of survival rate of cancer patients.



Tumour is a complex ecosystem consisting of several cell types and each shows a distinct transcriptomic profile i.e. have a different pattern of expression of the genes. The diversity within the tumour is called intra-tumour heterogeneity. Intra-tumour heterogeneity is increasingly appreciated as a determinant of treatment failure/recurrence and thus one of the main reasons for poor overall survival in cancer patients.

Oral squamous cell carcinoma gingivo-buccal (OSCC-GB), which is the most common cancer in men in India, is mostly diagnosed at advanced stages. Despite progress in treatment strategies, survival rate has not significantly improved over time. Tumour recurrence is common and is one of the major reasons for poor prognosis of OSCC-GB patients. There is an urgent need to understand the underlying mechanism of recurrence.

Recent advances in single-cell genomics provide opportunities to explore intra-tumour heterogeneity at single cell resolution. Single-cell RNA-sequencing (scRNA-seq) studies in many

human cancers have revealed new insights into tumour heterogeneity and distinct subpopulations, which are essential for dissecting tumour related mechanisms in detail.

Using single-cell RNA-sequencing, a team of researchers at the Department of Biotechnology's National Institute of Biomedical Genomics (DBT-NIBMG), Kalyani, have generated single cell RNA sequence profiles for primary tumour by profiling thousands of cells from the primary tumour of OSCC-GB patients to identify the major cellular components and their features that could help in better understanding the behavior of a tumour and determine which of these features are associated with tumour recurrence.

The researchers observed cellular diversity within a tumour and between tumours in OSCC-GB that are characterized by different cell types with distinct gene expression profiles. Such diversity could influence response to therapy, recurrence and influence in inter-patient variability in survival period.

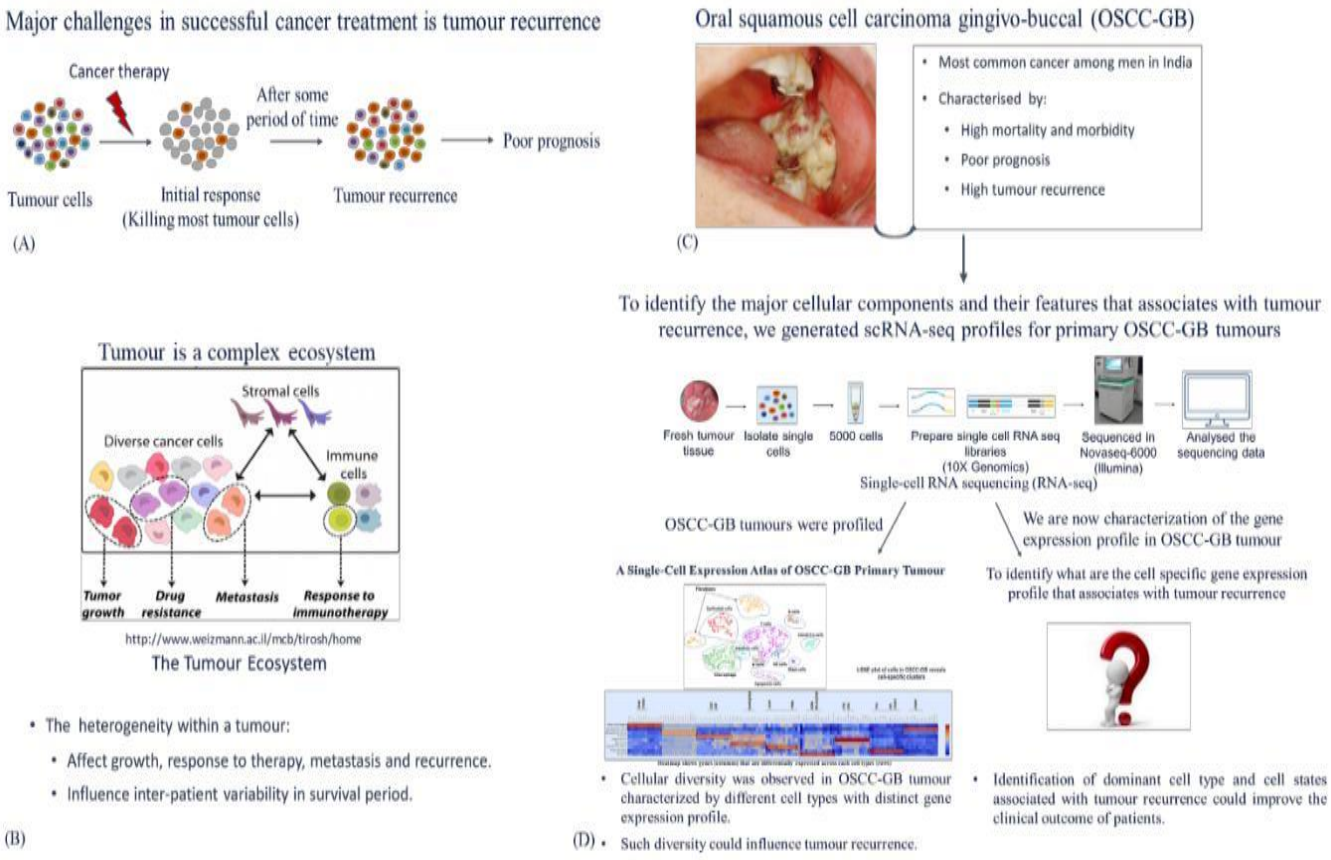


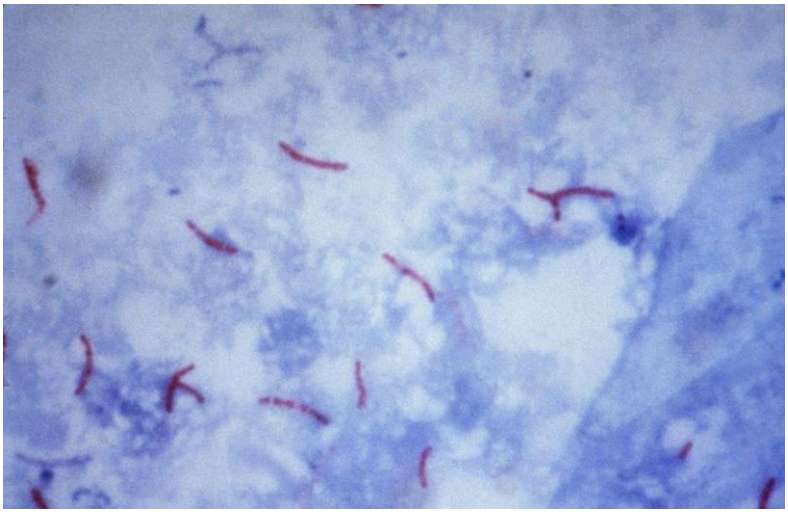
Figure: Infographic of the work

They are now characterizing these cells and their gene expression state to better understand the cell type and cell type specific gene expression profile that associates with tumour recurrence. Identification of dominant cell types and cell states in a subpopulation of OSCC-GB may help in stratifying patients that are most likely to recur for better treatment management that would improve the clinical outcome of the patient.

Link: https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_02S_19Aug2020.pdf

DBT funded study identifies biomarkers for TB

In order to reduce the burden of Tuberculosis, which is an infectious disease, there is a dire need to contain it's spread. One patient with active disease and symptoms such as cough can spread the infection to people who are in close contact with him/her, the most vulnerable being house-hold contacts (HHCs) who share the air-space with a TB patient. However, only some HHCs will develop the disease. Identifying those HHCs who are susceptible may help in preventing tuberculosis in them. Studying how they respond to the bacteria that causes TB (Mycobacterium tuberculosis) is one way of understanding their lack of immunity. This research study was supported by DBT and conducted at Bhagwan Mahavir Medical Research Centre, Hyderabad in collaboration with Univ of Texas Health Center, USA.



About 1,000 HHCs were enrolled in the study and followed-up for three years. The researchers studied their immune responses, such as the types of immune cells involved and their functions at baseline and repeated periodically for three years. Their cells were cultured and stimulated with antigens (proteins) in-vitro, to study their responses specific to Mycobacteria tuberculosis.

The study showed that development of TB in HHCs was not sex, but age dependent: young adults were at a high risk. Some of the immune cells, natural killer cells and T regulatory cells

were present in higher numbers in them and their circulating thyroid hormone T4 concentration was low. Further, the levels of cytokines IFN-γ, IL-13 and IL-10 were high but that of IL-1α was low.

In addition to these important findings, the other major highlight of the study was the development of an in-house technique. IFN-γ assay was standardized and developed to determine latent TB infection in HHCs. Being cost-effective, the assay is useful to detect tuberculosis in its latent stage. The group is also working on gene signatures to further understand the mechanism and other pathways involved in TB.

These findings, which are very crucial in identifying high risk young adults have been communicated to a peer-reviewed journal for publication. The biomarkers identified by us help in identifying at-risk HHCs. Immuno-prophylaxis or chemo-prophylaxis in these individuals may contain the disease thus leading to decline in the incidence of TB.

Link: https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_02S_21Aug2020.pdf

Defeating the devil in the waste: Remediation of infectious Covid-19 waste

Pictures of Covid-19 waste floating in sea and rivers or scattered outside garbage bins, with stray animals carrying masks in their mouths are in circulation on social media.

Low-income countries with weak health systems, crowded megacities and large populations of impoverished people are facing a huge challenge to dispose of Covid-19 biomedical waste generated every day. Failure to pay attention to the Covid-19 waste management may result in risk of poor outcomes during the pandemic which is far higher among those with comorbidities.

Wastes containing deadly microorganisms, toxins and particularly CoronaVirus are posing a risk of infection relapse and occurrence of future infection waves. Infectious waste originating from health care facilities and research activities produce mass scale single use waste including metal, plastic and glass lab consumables.

Becoming waste wise and controlling the biological risk at the segregation facilities to prevent cross-contamination can help combat Covid-19. Many options for the treatment of biomedical waste are available and should be adopted in such a health crisis.

The methods to be considered include use of chemicals disinfectants such as Sodium hypochlorite, dissolved chlorine dioxide, per-acetic acid, hydrogen peroxide etc. But, most chemical processes are water-intensive and require neutralizing agents. Mechanical processes involving compaction to reduce the volume of waste and shredding to destroy plastic and paper waste to prevent their reuse; irradiation processes exposing waste to ultraviolet or ionizing radiation in an enclosed chamber; and biological processes using enzymes for treating medical waste can also be employed. One needs to understand and segregate the waste first and choose an appropriate method for the waste treatment.

Bio-medical waste management needs committed government backing, good practices followed by both health-care workers and health care facilities, continuous monitoring and strong administration. It is our fundamental right of every citizen to live in a clean and safe environment. Segregation of waste at source and waste reduction should be of prime importance for management. Lack of education, awareness and trained personnel to manage the waste and paucity of the funds available to proper waste management systems are currently causing biggest challenges that the hospital and research centers are facing.

Dr. Pinky Kain of the Department of Biotechnology's Regional Centre for Biotechnology (DBT-RCB), Faridabad, (Principal Investigator, WT DBT IA Intermediate Fellow), published a short communication titled 'Defeating the devil in the waste: Remediation of infectious Covid-19 waste' in Acta Scientific Neurology.

Link:https://www.actascientific.com/pdf

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