



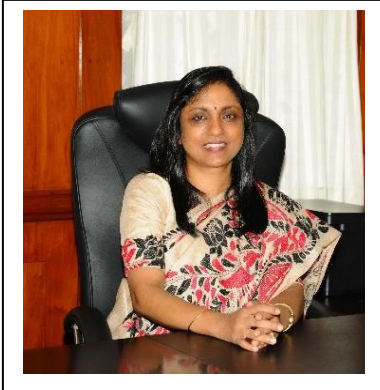
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INDIAN COUNCIL OF
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NIV
NATIONAL INSTITUTE
OF VIROLOGY

ICMR-NIV NEWSLETTER

January - June, 2021 Issue 1

Director's Message



Like the rest of the world, India is experiencing a devastating wave of COVID-19. It is a proud moment for me to state that the ICMR-NIV has gained the scientific and technical expertise to meet almost any eventuality in the field of emerging viral infections. Whether due to highly pathogenic viruses as observed during the Nipah virus outbreak in Kerala in the recent past or due to the ongoing COVID-19 crisis, ICMR-NIV has responded in its best capacity. The institute has been at the forefront of this pandemic and the exemplary services rendered by ICMR-NIV in the preparedness and fightback against COVID-19 have been recognized nationally. The India Today's award for the

best testing facility, 'Award of excellence' by the elets Healthcare leaders forum for SARS-CoV-2 diagnostics, and the Atal Bihari Vajpayee tribute to 'Titans of Technology 2021' for having catalyzed the creation of India's indigenous vaccine for COVID-19, to name a few.

The honorable Prime Minister Mr. Narendra Modi has launched the "Bharat Ka Amrut Mahotsava" (March 2021 – August 2022) covering activities from all states and Union Territories to showcase India's glorious history, culture, technological development and digital intervention strategies. A 75-week long festival has been flagged off on March 12 2021 as part of the celebrations to mark 75 years of our independence. We at ICMR-NIV have decided to initiate several activities as a part of this celebration. One of these is the initiation of a quarterly ICMR- NIV Newsletter.

This inaugural issue has received an overwhelming response as can be seen from the articles in this issue. The main article is devoted to the establishment of a Satellite Centre for One Health in Nagpur, Maharashtra. The article penned by our former Director Dr. DT Mourya gives a perspective and the importance of this centre.

Apart from this, 'NIV Contribution in fighting COVID-19' during the year highlights the path-breaking efforts of NIV in combating the COVID-19 pandemic. There are some interesting sections also, which include an interview of Dr. Paresh Shah about his research journey in NIV and the experiences of NIV alumni. We would be delighted to have your feedback and suggestions.

Finally, I wish you all a pleasant reading of this inaugural issue of the 'ICMR-NIV Newsletter'.

Wishing you and your families, safe days ahead.
Happy Reading! Jai Hind!

Priya Abraham

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Satellite Centre for One Health, Nagpur: ICMR-NIV's perspective



Dr. DT Mourya

ICMR-Chair for Virology & Zoonoses
Former Director, ICMR-NIV, Pune

One Health is a multisectoral, interdisciplinary, and collaborative approach to attain optimal health for animals, the environment, and humans. There is a pressing need for increased communication and collaboration between professionals such as doctors, veterinarians, and social scientists, and this is where building capacity in One Health would be beneficial across disciplines. The best available evidence from different fields needs to be collected and shared, which is a framework that One Health provides. Increased funding from governments and foundations must be prioritized to support such interdisciplinary professional development and research. The One Health approach also considers the cultural components of pandemics. For example, wildlife trade for traditional medicine and food is common in many cultures. It is important to incorporate anthropologists and social scientists when designing and implementing policies for wildlife trade and consumption for these policies to be effective and sustainable. There has been some movement operationalizing One Health globally by international organizations including the Food and Agriculture Organization, the World Organisation for Animal Health, and the World Health Organization. These organizations signed an agreement in 2008 to share the coordination of activities that investigate and address health risks at the human-animal-environment interface and developed a strategic framework that contributed to

the management of the 2008 H5N1 influenza virus pandemic. Responses to pandemics continue to be tackled as isolated events and not as a reflection of a larger problem. Exacerbated by the changing environment, the increase in novel pathogens suspected to have emerged from wildlife, such as SARS-CoV-2 is a symptom of a deteriorating world. A paradigm shift is needed in how we think about and act on health. One Health provides a framework for us, and it is time to widely promote and adopt its message of connectivity.

The establishment of the Satellite Centre for One Health (SCOH) is supported by ICMR as a sub-center of the National Institute of Virology, Pune in collaboration with Maharashtra Animal & Fisheries Sciences University, Nagpur. The infrastructure of the center would have Animal Research laboratories and a high-risk pathogen handling wing that would include state-of-the-art Biosafety level-3 & -4 laboratory facilities and other laboratories proposed for: virology, small animal experimentation facility, bacteriology, anti-microbial resistance unit, mycology, pathology, parasitology, immunology, toxicology, serology, bioinformatics, protozoology and helminthology laboratories, in addition, state-of-the-art molecular biology, tissue culture and hybridoma technology laboratories.

The Center's network would focus on disease surveillance in animals (domestic and wild) which would include rodents, bats, wildlife, poultry [ardeid & aquatic birds], livestock and pet animals, fisheries as well as facilities to study ectoparasites, vector biology and toxicology. The passive surveillance strategy will be to follow event-based Investigations to pick up a zoonotic infection of high consequences for humans. Besides this, the center would help in generations of human resource for "One Health". The main research areas proposed are: the pathogens, source of the pathogen, mode of transmission to the host, susceptibility of the host, and exit of the pathogen from the host. The expected outcome of the establishment of "Satellite Centre for One Health

includes: improved joint coordination and collaboration between major stakeholders in control of zoonoses and effective international engagement, improved preparedness and response capacity, better surveillance and laboratory testing and human resource development in the areas of one health.

The SCOH would focus on the various aspects of emergency preparedness with special emphasis on public health surveillance and laboratory capacity-building approaches. The proposed activities would provide support to the National One Health Program with regards to emergency preparedness which is key to control the emerging public health challenges at both national and global levels. This will also be an asset to the national program on capacity building with a well-built national network and international collaborations of relevant stakeholders.

ICMR-NIV contributions in fighting COVID-19

ICMR-National Institute of Virology (NIV) has played a pivotal role in the nation's fight against COVID-19 and the institute's contribution has been on several varied fronts. ICMR-NIV, Pune, is a WHO-designated National Influenza Centre (NIC) and has established the diagnostic test protocols for the nation. NIV detected the first three cases of SARS-CoV-2 in India on January 30th, 2020.

Preparedness of network laboratories for testing:

Until mid-February 2020, the ICMR-NIV was the only diagnostic laboratory that could detect COVID-19. It first began training personnel of 13 laboratories that were part of the Virus Research Diagnostic Laboratory (VRDL) network of laboratories set up to detect emerging viral infections across the country. The network has since expanded to its 106 laboratories, extended to 1206 government-owned ones, most of which have been trained by NIV to conduct the reverse transcription real-time polymerase chain

reaction (RT-PCR) tests for COVID-19. The testing reagents supplied by ICMR-NIV have been the backbone of testing for SARS-CoV-2 in different laboratories across the country.

Quality Assurance:

ICMR-NIV participated in the WHO Global External Quality Assurance System (EQAS) Programme for detecting SARS-CoV-2 and achieved a 100% score in the global PT panel for SARS-CoV2 by WHO vide letter dated June 15, 2020. NIV as an apex laboratory also conducts quality assurance/quality control for 105 government laboratories, on a quarterly basis.

Quality control and Assurance @ ICMR -NIV

EQAP Panel for detecting SARS-CoV-2 (May 15, 2020)
EQAP Panel 18 (2019) for detection of Influenza (June 2020)
QCMD EQAS (UK) for Other respiratory viruses including human CoVs

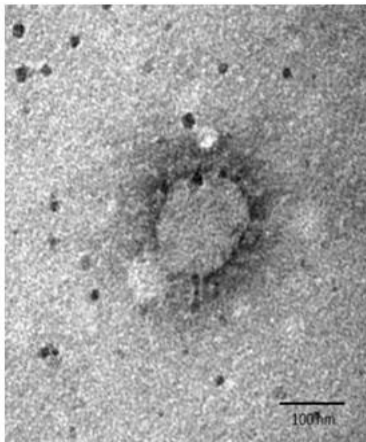
Diagnostic support:

ICMR-NIV & its field units at Mumbai, Bangalore and Kerala contributed in a major way for the sample testing (diagnostic support) for the respective states by shouldering the huge case load. As of today, ICMR-NIV and its field units have completed 318,442 RT-PCR (01.06.21) tests. NIV has shipped out its reagents amounting to 57 lakh reactions across the length and breadth of the country to ~1200 government laboratories.

ICMR-NIV also provided international support through screening of samples from the Maldives, screening of evacuees quarantined at the ITBP camp who were Indian nationals stranded in Wuhan, China, Iran and Italy and the Indian evacuees from the Diamond Princess cruise ship.

Isolation of SARS-CoV-2 and variants:

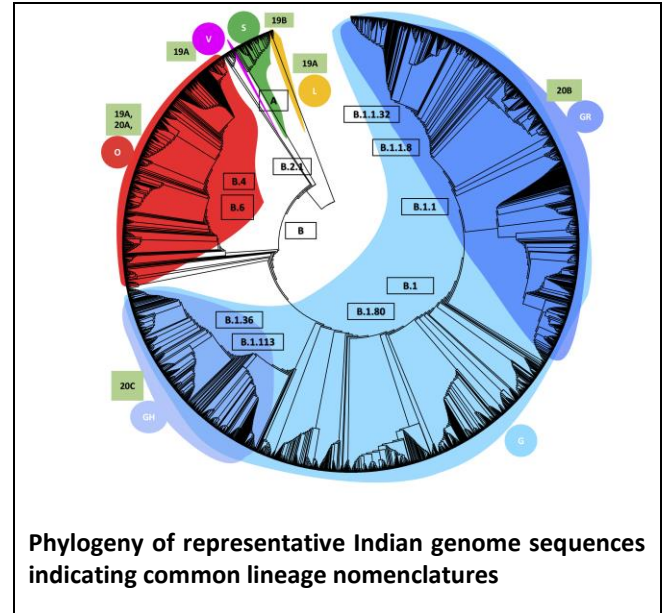
ICMR-NIV was the first to isolate the virus in India. This was possible because a dedicated team worked round the clock in the Maximum Containment facility of the institute. This provided an opportunity to develop indigenous ELISA, neutralization assay, development of inactivated vaccine and screening of anti-viral drugs. With continuous efforts, ICMR-NIV isolated many SARS-CoV-2 variants like B.1.1.7 (United Kingdom), B.1.351 (South Africa), P2 (Brazil), B.1.617 (India), etc.



Electron microscopy image of the SARS-CoV-2 virus isolated at ICMR-NIV

Genome Sequencing:

Whole-genome sequencing and virus isolation of the early positives further helped to confirm the identity of the virus with origin from Wuhan, China. ICMR-NIV is one of the members of the Indian SARS-CoV-2 Genomic Consortia (INSACOG). Further continuous molecular and genetic surveillance is being undertaken by next-generation sequencing of the SARS-CoV-2 genomes. Thus far, about 5500 whole genomes representing the country have been sequenced.



Phylogeny of representative Indian genome sequences indicating common lineage nomenclatures

Development of indigenous kits and assays for testing SARS-CoV-2:

ICMR-NIV could successfully isolate SARS-CoV-2 in March 2020 and could make sufficient amounts of virus antigen for developing the first indigenous human IgG ELISA kit (COVID KAVACH ELISA) to detect antibodies against the virus. This ELISA technology has been handed over to seven different companies.




ICMR-NIV also developed the most specific antibody assay associated with protection, known as the neutralization assay. This is very useful to screen recovered individuals who volunteer to provide plasma (convalescent plasma) for treatment for

severe cases of COVID-19. Also, this test is invaluable for assessing vaccine and therapeutic antibodies efficiency. RT-PCR kits (both TaqMan chemistry and SYBR green dye-based assays) were developed at ICMR-NIV.

Phase I: Multiple tube assays: 2/3/4 tube assays

Phase II: Two tube assays (mostly duplex assays)

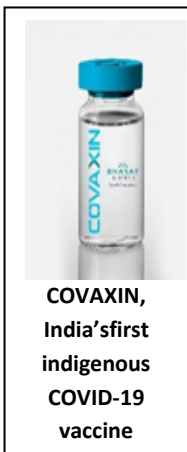
Phase III: Single tube assays (multiplex assays)



LAMP Assays: SYBR green-based read out Visual read out assay (Color change)

Development of indigenous vaccine for COVID-19:

A dedicated team in the Maximum Containment Facility attempted virus isolation from the samples received from VRDL laboratories during March 2020 round the clock to successfully isolate SARS-CoV-2 virus from India. The isolate was characterized for its growth characteristics, morphology and genome. The characterized virus stock was transferred to a commercial partner, Bharat Biotech International Limited, Hyderabad for developing inactivated whole virion vaccine candidate. Further both the partners worked hand in hand to assess the quality of purified inactivated virus stock. ICMR-NIV used three selected



vaccine formulations (BBV152) for preclinical animal challenge study in SARS-CoV-2 animal models, i.e., Syrian hamsters and rhesus macaques. A three-dose immunization study in hamsters spanning 7 weeks followed by virus challenge demonstrated protective efficacy of the candidate formulations by a potent humoral immune response, early viral clearance from the lower respiratory tract and absence of pneumonia. The candidates were further taken up to a challenge study in rhesus macaques, a model more similar to humans following a two-dose vaccine regimen. The candidates induced potent immune response by 3 weeks and caused early viral clearance from the respiratory tract protected the macaques from pneumonia by a challenge as early as on 28 days. These preclinical studies substantiated the immunogenicity and protective efficacy of the vaccine candidate and paved the way for the Phase II/III clinical trial approval for COVAXIN. These efforts led to providing India its own indigenous vaccine to fight against the pandemic. Clinical trial data (Phase 1, 2 and 3) shown good efficacy and further its effectiveness were studied against the emerging variants. The vaccine is approved for EUA and is being used in the country. NIV has partnered with two major vaccine companies for performing pre-clinical studies in the maximum containment(BSL-4) laboratory of the institute.



Virus handover to Bharat Biotech team on 30th April 2020 for the preparation of indigenous vaccine

Training of Laboratories within India:



ICMR-NIV has also undertaken training of the National Disaster Relief Force, laboratory personnel from the State Health laboratories of Maharashtra, Karnataka and Goa. NIV has also trained other government institutes in Pune in testing for the virus. Since teaching and training is another core activity of NIV, it has also prepared a video on COVID-19 testing and bio-safety practices for use by ICMR in its support of smaller laboratories.

Dissemination of knowledge:

NIV has thus far published around 41 research articles, review articles, editorials, perspectives, etc. in reputed journals. NIV contributed an article entitled “COVID-19 Virology”, in YOJANA (June 2020 issue), a development monthly magazine devoted to socio-economic issues that helps UPSC students to improve their current affairs. A chapter entitled “SARS-CoV-2: The new kid in the block” was contributed to the Manorama Year Book 2021.

The Director and scientists participated in several panel discussions, webinars for various audiences, media queries from Times of India, Indian Express, Hindustan Times, Lokmat, Ei Samay (West Bengal), Dainik Bhaskar, Economic Times, The Week, etc. including local newspapers- Deshdoot, Lokmat. The CNA channel and the Discovery Channel featured the institute’s contribution in a documentary titled “COVID-19: India’s war against the virus”.

ICMR-NIV Alumni



Minal Dakhve Bhosale

General Manager- R&D

Mylab Discovery Solutions Pvt. Ltd.

Makers of Asia's First ID-NAT | India's First Covid-19 Test

I am fortunate to have been a student of ICMR – National Institute of Virology (NIV), Pune, during 2007-2009. The ICMR-NIV is the apex laboratory in India with state-of-the-art infrastructure and expertise for research in virology.

Two years of Master’s degree at NIV was an exceptionally outstanding educational experience to enrich my knowledge and personality. The knowledge I gained at NIV paved the way for my future growth. It allowed me an easy, smooth, and rewarding transition from a novice to a professional in the diagnostic and research industry. Learning by doing is the unique feature of NIV culture. The Master’s project was the true start-up for our career where we learn to work independently, troubleshoot the issues, and develop solution-based approaches. While working in the corporate sector, being an NIVian gives a special standing, and I can proudly say that I belong to NIV. NIV works cohesively as a family when there are public health challenges. NIV has excellent academic facilities including state of the art scientific library, one-to-one mentoring sessions with eminent scientists and in-course dissertation opportunities. You face real-life research challenges with innovative solutions as part of the master’s dissertation. During my dissertation, I carried out research at the WHO-recognized National Influenza Centre, with access to

real-time PCR machines and sequencers which was hugely valuable. After my Masters, I worked at the National Influenza Centre for five years. While working in the Influenza department, a reference laboratory for South-East Asia, I had the opportunity to interact with SEA scientists through projects and training which also enhanced my technical and presentation skills. I was able to serve the nation during the 2009 swine flu [influenza A(H1N1)pdm09] pandemic. This was a turning point in my career which transformed me to a researcher. Working at NIV gave me a bigger platform to pursue my dreams. I would like to express my gratitude towards Dr. MS Chadha for trusting me always and Dr. Varsha Potdar for mentoring me well. Dr. Potdar who was strict and kind, taught me huge dedication and made me realize the importance of public health. Studying and working at NIV was a journey of innovation, engagement and impact which will be the base of career development for the rest of my life. Now I am a proud General Manager-R&D at Mylab Discovery Solutions Pvt. Ltd., Pune, where I was instrumental in developing the first made-in-India commercial test kit for SARS-CoV-2 detection. I dedicate my success to my NIV family and I will keep working passionately for the society.

Choices and Challenges



We interacted with Dr. Paresh S. Shah (Scientist 'E' & Group Leader, Dengue/Chikungunya Group and Diagnostic Reagent Facility), who would be superannuating soon. Excerpts from the interview:

1. What are your reflections on the beginnings in

ICMR-NIV, mentors and colleagues?

I had joined the Biochemistry Group of ICMR- NIV in 1980 and started with the standardization of biochemical assays. Later, I received training in sequencing using radiolabelled nucleotides at Bhabha Atomic Research Centre, and with Dr. DA Gadkar's guidance, established a sequencing facility in the institute. I had the great privilege to work with and learn from eminent scientists including Dr. Kalyan Banerjee, Dr. DA Gadkari and Dr. AC Mishra and Dr. Cecilia Dayaraj and Dr. DT Mourya. I also fondly remember my brief but memorable interactions with Prof. Dr. Priya Abraham, who taught us openness and frankness in research and administration. I am thankful to all my mentors and colleagues who helped and supported me during my tenure in NIV.

2. What have been your major career achievements?

During my stint in the Biochemistry department, our team developed and characterized a cell line persistently infected with Japanese encephalitis virus, which helped in demonstrating overwintering of the virus (how the virus stays latent during winter and re-surfaces during the post-monsoon period). We also isolated temperature-sensitive mutants and characterized many of them. We initiated the IgM ELISA for diagnosis of JE, and also developed diagnostic PCR assays and sequencing protocols. In 1985-86, we organized the first International Workshop on Molecular Diagnostic Assays for JE at NIV. After re-designation as Dengue/Chikungunya Group, we contributed to the investigations of several outbreaks of these infections in Maharashtra, NCR New Delhi, Kerala, Tamil Nadu and Orissa. We also successfully developed a recombinant NS1 protein of the dengue virus, and monoclonal antibodies against the same. I initiated a pilot project on sero-prevalence of dengue IgG in Vadu, Maharashtra, which eventually led us to a country-wide serotyping/genotyping survey of dengue involving 24 Virus Research and Diagnostic Laboratories. In recent years, we initiated

studies on siRNAs in dengue and chikungunya infections and demonstrated the utility of siRNAs to inhibit these viruses *in vitro* and *in vivo*.

We successfully established the CGMP-certified Diagnostic Reagent Facility for the production of IgM Capture ELISA kits for dengue, JE and Chikungunya diagnosis. We have been supplying these kits to Sentinel Surveillance Hospitals under the National Vector Borne Diseases Control Program, Apex Referral Laboratories and Virus Research and Diagnostic Laboratories across the country, for more than 5 years, generating revenue for the institute. Dr. PS Sathe, Dr. Thakare and Dr. AC Mishra were key contributors to this initiative, and we faced several challenges in its establishment. I also contributed to the curriculum design of the MSc Virology course when it was started at ICMR-NIV.

3. What are the current barriers to progress in translational research and in addressing them?

Lack of exposure to novel technologies, probably, is a contributing factor. Also, there is often an over-reliance on molecular biology techniques. Engaging students and research associates for periods of 2-3 years would be helpful in developing new projects and novel technology.

4. What was the impact of COVID-19 on your work and life?

During the pandemic, we experienced major difficulties with logistics due to alternative resources and consumables.

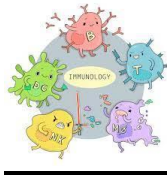
5. What is your message to the young researchers?

I would like to mention a couple of quotes: "Everything is theoretically impossible until it is done." (Robert A. Heinlein) "Research is to see what everybody else has seen, and to think what nobody else has thought." (Albert Szent-Györgyi)

Scientific Bench

Yadav, P.D., Ella, R., Kumar, S. et al. Immunogenicity and protective efficacy of inactivated SARS-CoV-2 vaccine candidate, BBV152 in rhesus macaques. *Nat Commun* 12, 1386 (2021).

The article describes preclinical study of India's first indigenous vaccine COVAXIN developed by Bharat Biotech International Limited (BBIL) in collaboration with ICMR- National Institute of Virology, Pune. The evaluation of the efficacy of the vaccine in animal models was done by the ICMR-NIV on a war footing basis when the country was in urgent demand of vaccines to fight against the pandemic. The fully characterized virus strain transferred by ICMR-NIV was inactivated using Beta-propiolactone and vaccine candidates (BBV152) were made by BBIL. Three candidates i.e., 3 µg with alum, 3 and 6 µg with alum-imidazoquinoline adjuvant were selected for the study based on preliminary immunogenicity and safety study in small animals. The immunogenicity of the candidates was evaluated in 15 rhesus macaques divided into 3 groups by two dose injections, 5 macaques were given placebo and used as control for the study. Protective antibody response was observed by third week post immunization. Further, a live virus challenge study was performed in the same animals four weeks post immunization at the containment facility and the protective efficacy of the candidate was evaluated in comparison with the virus control group. Clinical signs, chest radiography, haematological and serum biochemical parameters, cellular and humoral immune response and viral load reduction in organs were monitored. The amount of virus shed through nasal and oral cavity, viral load in various organs, bronchoalveolar lavage and the histopathological changes in lungs were compared with the placebo group. The vaccine candidates produced excellent immune response, induced virus clearance from the respiratory tract and also protected the macaques from pneumonia. The study substantiated the immunogenicity and protective efficacy of the BBV152 vaccine candidates.



IMMUNO-WAR

She had attacked the immune system so ferociously,
The innate immune system failed as a fighter,
No phagocytosis, no inflammation,
The macrophages just sailed in the titre.
She kept on increasing her stability,
Who did give her that increased permeability?
Skin and the mucous membrane begun to argue,
Thanks to cell mediated immune response who came to the rescue.
MHC Class I and II came up for a discussion,
Loading various opsonins, fired in her direction,
She covered her epitopes and exposed her capsule,
NK cells, dendritic cells, neutrophils all got fooled.
She became the strongest antigen and made the immune system tight,
Who will kill her now? Someone had to fight.
But, wait, someone almost crushed her out of sight,
Guess what? The monoclonal antibody became the hero of the night!!

Shubham Yadav

M.Sc. Virology (2019-2021)

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(This is an imaginary poem describing the basic phenomenon happening in the body in a poetic way. It doesn't intend to violate immunology rules.)

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Institutional Awards



Awards & Recognition of our Scientists



Prof. (Dr). Priya Abraham
(17th October 2020)

IHW Janani Awards for Medical Research Leadership Prof. Priya Abraham, Director NIV receives award from MoS Health Ashwini Choubey Honour Women Leadership with Janani Awards. (28th May 2021)

Corona warrior award 2020 from Governor of Maharashtra for the ongoing services in current COVID-19 pandemic (15th October 2020)



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Dr. Gajanan Sapkal

Dr. Varsha Potdar

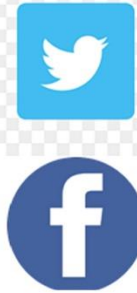
Media Outreach



National science magazine 'Vigyan Bharati' – AIR, New Delhi



Film for Discovery channel entitled "COVID-19: India's war against the virus"

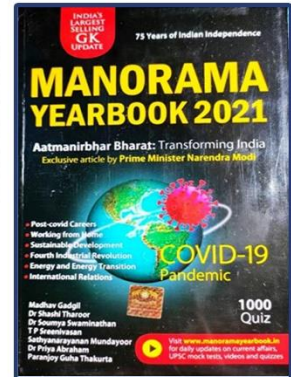


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Dignitary visits to the campus



Visit by Dr. Rajesh Tope, Honorable Health Minister, Maharashtra on March 19, 2020



Visit by Mr. Deepak Maisiker, Div. Municipal Commissioner, Pune district on June 10, 2020



Visit by Mrs. Supriya Sule, Honorable Member of Parliament, on January 12, 2021



Prof. Priya Abraham, Director-ICMR-NIV, Pune, welcoming Shri Narendra Modi, Honorable Prime Minister of India, during his visit to Pune on November 28, 2020