COVID-19 testing outreach effort - Upcoming graphic novel on COVID awareness at inStem, Bengaluru

To create necessary awareness with proper scientific backing about COVID-19, busting the myths and bringing in the ongoing research across the country, faculty at DBT's Institute of Stem Cell and Regenerative Medicine (inStem), Bangalore has created an informative graphic novel which will be launched very soon.

Graphical narration (colloquially referred to as 'comics') has a rich history in our culture, with series such as Amar Chitra Katha demonstrating the trans-generational power of this medium. As a faculty at inStem with deep interests in cartooning and graphical narration, Arvind's effort in developing this comic is to create awareness in non-specialist readers, especially children, about the current health crisis.

The comic is based around two curious young children Bharath and Fatima who learn about COVID-19, the immune system and vaccines from their fictional uncle. We hope that this effort with anticipated translations into local languages will serve as a widespread platform for science education and communication. The inStem, Bengaluru along with the Bangalore Life Science Cluster (BLiSc) plans to launch this as an awareness campaign on social media very soon.

Here's a snippet of the cover page of the upcoming graphic novel titled 'Bharath and Fatima learn about COVID-19'

InStem is one of the founding partners of **COVID-Gyan**, a pan-institutional website that has been proactive in COVID-19 outreach efforts. The constant effort of COVID-Gyan since its launch has been to create necessary awareness with proper scientific backing about COVID-19 across the country.

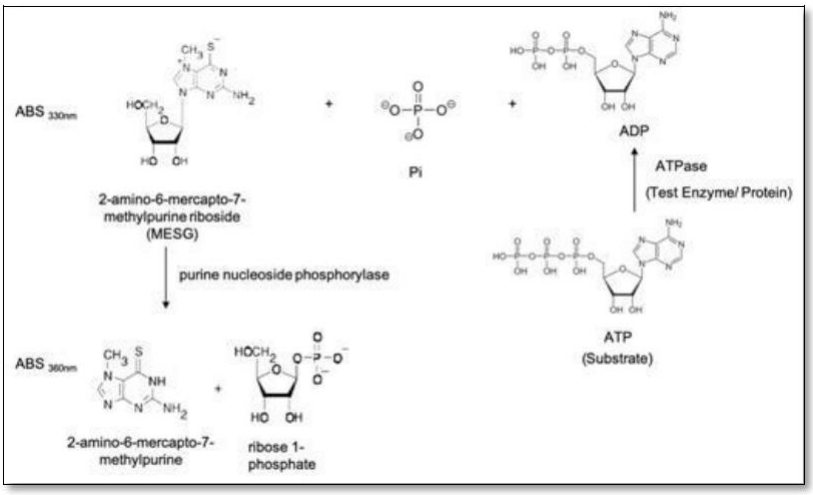
Link: https://instem.res.in/

Link: https://www.instem.res.in/content/COVID-19-testing-effort-bangalore-life-science-cluster

Link: https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_01BB_24Aug2020.pdf

ATPase activity
of *Escherichia coli* expressed AAA+-ATPase protein

Scientists at DBT's Regional Centre for Biotechnology (RCB), Faridabad, have provided a detailed protocol to determine the ATPase activity of a recombinant AAA+-ATPase protein (General Control Non-repressible-4 [(GCN4]) by spectrophotometric absorption at 360 nm to measure the accumulated inorganic phosphate. ATPases are the enzymes that breakdown ATP to ADP and release inorganic phosphate (Pi).



In general, the substrate 2-amino-6-mercapto-7-methylpurine riboside (methylthioguanosine, a guanosine analog: MESG) is enzymatically converted in the presence of Pi by purine nucleoside phosphorylase (PNP) to ribose 1-phosphate and 2-amino-6-mercapto-7-methylpurine. The spectrophotometric shift in maximum absorbance at 330nm for the MESG substrate and subsequent conversion product at 360nm due to enzymatic conversion was measured. The GCN4-His-tagged recombinant protein was expressed in *Escherichia coli* BL21 cells and purified using Ni-NTA column.

This purified protein was then used for the quantitation of Pi in solution or the continuous determination of Pi released due to the ATPase activity of GN4, an AAA+-ATPase protein conserved in many eukaryotes, which in plants regulates stomatal aperture during biotic and abiotic stress in plants.

Link:https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_01BB_25Aug2020.pdf

Dextrasol: Indigenously produced dextranase using solid state fermentation

Dextranases are the most efficient method of hydrolyzing the dextrans at sugar mills. Dextrasol from Varuna Biocel Pvt Ltd supported by DBT**'s** Biotechnology Industry Research Assistance Council (BIRAC), a PSU under Department of Biotechnology (DBT) is an indigenously produced dextranase which hydrolyses the dextran. Dextrans are undesirable compounds of sugar cane. They are high molecular weight polysaccharides formed by the action of the dextransucrase enzyme from contaminant microorganisms that are home to the plant sap. Some bacterial strains like, *Leuconostoc* sp. bacteria have shown ability to synthesize alphaglucan polysaccharides (dextran) from the sucrose released from sugarcane. An increase in the level of dextran (greater than 1000 mg/kg on Brix basis) increases the viscosity of the sucrose solutions in the milling and refining processes and also interferes with overall process control. There is an economical and technical need to control dextran. Many countries have fixed the standard of dextran in sugar.

It is need of sugar industry, which is a major industrial sector supporting agricultural economy. The production technique of dextrasol involves locally available raw materials and resources with no environmental load; hence the technology is highly economically viable. With this patented technology, Varuna Biocel has sold over 97 tons of dextrasol which is priced at rupees 1000 a kg plus taxes. The product also occupies a huge market share in states of Uttar Pradesh and Maharashtra.

Link: https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_01BB_26Aug2020.pdf

Cervical cancer: Risk factors, symptoms and overview of the disease

In general, cell cycle is tightly regulated, whereas, in cancer the cell division is faster without any regulation and checkpoint. Current research at DBT's National Institute of Biomedical Genomics (NIBMG), Kalyani, focuses on understanding many aspects of the cervical cancer especially the genes/pathways abnormally regulated in it, and how viral protein interact host protein to deregulate normal cellular pathway to initiate the infection and cervical cancer development. The area of focus is to understand what makes the cells undergo continuous cell growth and division followed by HPV16 virus infection.

Cervical cancer occurs due to changes in the cells of a women's cervix, which connects womb (uterus) with vagina of a female. This cancer affects deeper part of the vagina and it has the capability to spread (Metastasize) other parts of the body usually vagina, rectum, liver, lungs and bladder. Most of the cases of cervical cancer are caused by a viral infection called Human papillomavirus. It is a slow growing cancer type and it is diagnosed by colposcopy/ Pap test.

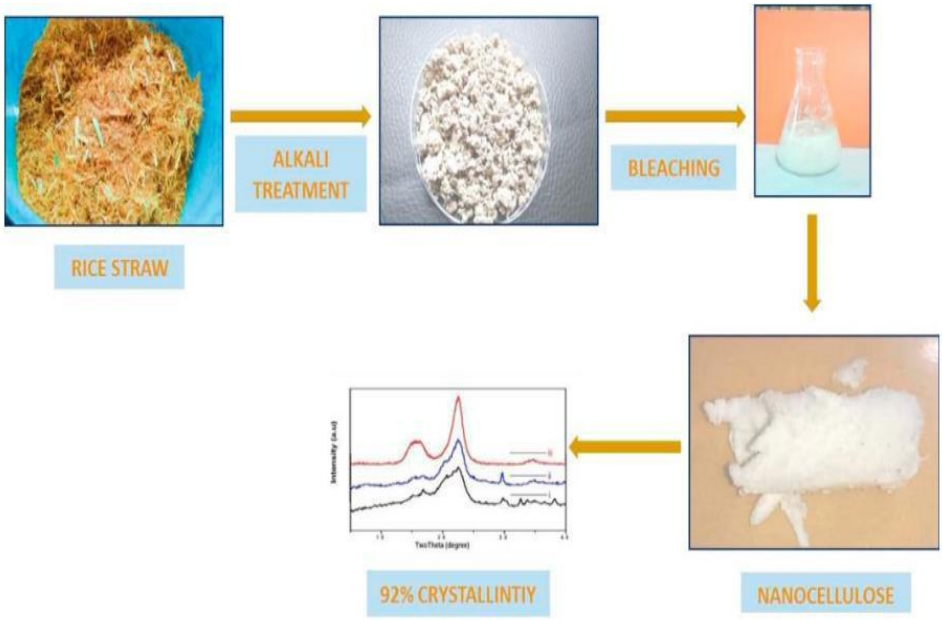
Risk factors for cervical cancer include starting to have sex before the age of 16, having multiple sexual partners, taking birth control pills especially for more than 5 years, having more number of children, smoking, having a weakened immune system and having Sexually transmitted disease (STD) e. g., AIDS. Symptoms of cervical cancer include experiencing pain during sex, unusual vaginal bleeding such as after sex, between periods or after menopause, unusual vaginal discharge, pelvic pain, weight loss and lack of appetite.

There is more than one type of cervical cancer based on cells such as squamous cell carcinoma which arises in the cell lining of the cervix and is observed in 90% of the cases, Adenocarcinoma, arises in the cells that produce mucus and mixed carcinoma which has the futures of both the types of cancer. The treatment options may vary depending on the stage and severity of the disease. In general, chemotherapy (anti-cancer drugs) and radiotherapy or combination of both is the most popular treatment options.

Link: https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_01BB_27Aug2020.pdf

Development of cellulose nanofibers from rice straw with improved delignification and better crystallinity

In this work the effect of alkaline pretreatment and delignification on rice straw (RS) for the production of cellulose nanofibers (CNF) was studied. RS was initially treated with NaOH at moderately high temperature, which resulted inalkaline cellulose fibers (ACF) with 31% yield. Furthermore, delignification of ACF with sodium chlorite at moderate temperature generated in α-cellulose was carried out. Subsequent mechanical treatment with high pressure homogenization effectively converted α-cellulose into nanocellulose with minimum residual lignin content and good crystallinity index (92%) as found by X-ray diffraction analysis. Complete removal of lignin was confirmed by FTIR and TGA studies. Importantly, the dimensions of the nanocellulose particles derived from rice straw was in the range of 10-50 nm as observed by Transmission Electron Microscopy (TEM). The work has been carried out at DBT's Center of Innovative and Applied Bioprocessing (CIAB), Mohali.



The biorefinery of the extraction of cellulose from rice straw biomass via chemo-mechanical process for the development of cellulose nanofibers has been presented in this work. The process was optimized for pretreatment and delignification followed by mechanical treatment for conversion to nano-dimensions. The process described in this study will be useful for scale up. Rice is a widely grown crop that leaves substantial quantity of post-harvest straw in the field. Rice straw (dry stalks of rice) can be defined as an

underutilized by-product. In recent decades nanocellulose has become an attractive choice for several end users due to their exceptional mechanical, thermal, and biological properties. Nanocellulose is non–toxic, completely biodegradable and biocompatible and it doesn't create any adverse effect on health and environment.

Link: https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_01BB_28Aug2020.pdf

DBT-RCB signs MoA for antiviral activity testing against SARS-CoV-2

The department of biotechnology's Regional Centre for Biotechnology (DBT-RCB) has signed a memorandum of agreement with Satej Global Science, Ahmedabad to identify scope of services for antiviral activity testing against SARS-CoV-2.

(representative picture of lab testing)

Under the MoA, DBT-RCB is providing antiviral activity testing against SARS CoV-2 in cell culture models at a non-cytotoxic concentration of the test substance to meet the growing need for in vitro antiviral assays for the new drug candidate/test substances. Satej Global Science shall reimburse the cost of services.

Link: https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_03S_31Aug2020.pdf

The Case of the Missing Limbs!

Embryonic development and organogenesis and the genetic and non-genetic factors that regulate them, have always been areas of extensive research and have aroused a great deal of interest amongst basic scientists as well as clinicians across the world.

A number of genes that play a vital role in embryonic development have been identified primarily through studies based on animal models. For some of these developmental genes, phenotypic predictions based on studies of knock-out models of mice and other organisms are available. However, human syndromes with the expected phenotype (manifestations) related to variants in these genes are yet to be reported.

The T-box4 (TBX4) gene is one such gene known to be a crucial regulator of embryonic hindlimb development. Animal models in which theTBX4gene is knocked out have been reported to have complete absence of hindlimbs. In humans, a syndrome called Small patella syndrome, associated with skeletal defects of the pelvis and lower limbs, has been known to be caused by heterozygous mutation (single mutation in only one copy of the gene) in the TBX4 gene. However, the defects are relatively less severe: there are no reports in humans of complete absence of lower limbs associated with mutations in this gene.

Recently, scientists at the Department of Biotechnology's Centre for DNA Fingerprinting and Diagnostics (DBT-CDFD), Hyderabad, identified a fetus with a hitherto undescribed multiple malformation syndrome associated with complete absence of both lower limbs along with sacrococcygeal agenesis, left heart hypoplasia, bilateral lung hypoplasia, hydrouretero nephrosis and hydrops.

The findings were noted in the antenatal scan and then confirmed through fetal autopsy evaluation following termination of the pregnancy. It was the third pregnancy of a consanguineous couple who had two previous similarly affected pregnancies. With the help of the powerful tool of next generation sequencing-based Whole Exome Sequencing, the researchers identified a homozygous mutation (same mutation on both copies of the gene) in the TBX4 gene in the fetus and subsequently through Sanger sequencing technique, both parents were confirmed to be heterozygous carriers for the mutation.

Interestingly, both the carrier parents had features of Small patella syndrome, the milder TBX4-associated disorder. The syndrome reported in this fetus is a novel monogenic syndrome with an autosomal recessive inheritance pattern with a 25% risk of recurrence in each offspring of the carrier couple.

Identification of the mutations in the family led to accurate recurrence risk assessment for the couple and based on this, it is possible to provide definitive prenatal or preimplantation genetic diagnostic testing for their subsequent pregnancies. The study has also provided valuable confirmation about the role of the Tbx4 factor in development of lower limbs in human embryos also, similar to that identified in animal models in previous research studies.

The findings have been published in the international journal European Journal of Human Genetics in January 2020.

Link: https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_01S_26Aug2020.pdf

DBT-InSTEM scientists pave way for developing new biomarkers for diseases

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.

In a collaborative project with scientists from New York University, faculty from the Centre for Neuro developmental Synaptopathies, along with faculty from Mass Spectrometry Facility at the Bangalore Life Science Cluster, 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. The proteomic work done in this project has adopted cutting edge peptide identification algorithms to enhance peptide detection.

This research work provides proof of principle evidence for a what may be rapidly deployable method to label newly synthesized proteins in the freshly collected blood samples to detect dynamic protein shifts and develop novel biomarkers for a variety of disease conditions. The work has been published recently in American Chemical Society's Journal of Proteome Research (Aug 2020) titled 'Optimization of protocols for detection of de novo protein synthesis in whole blood samples via azide-alkyne cycloaddition.'

Reference:

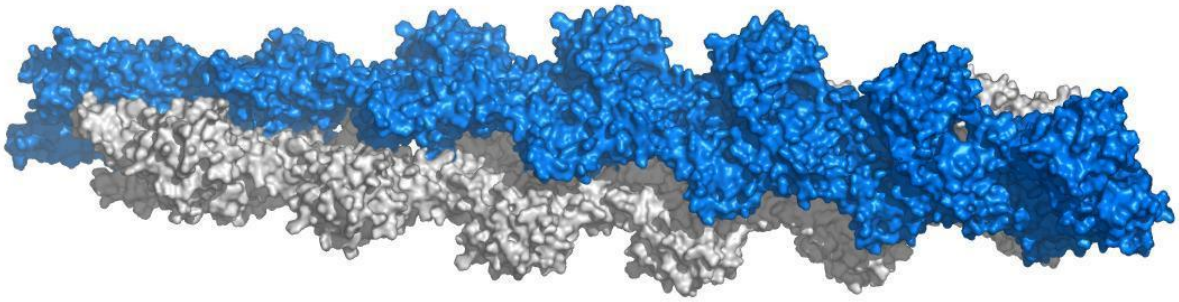
Bowling H.L., Kasper A., Patole C., Venkatasubramani J.P., Leventer S. P., Carmody E., Sharp K., Berry-Kravis E., Kirshenbaum K., Klann E., and Bhattacharya A. (2020) Optimization of protocols for detection of de novo protein synthesis in whole blood samples via azide-alkyne cycloaddition. *Journal of Proteome Research* (Published on Aug 04, 2020)

Link: https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_01S_27Aug2020.pdf

Structural insights into actin filament recognition

The July bulletin of the DBT-WT India Alliance has featured the recent publication of Dr. Minhaj Sirajuddin of the Cytoskeleton Lab of the Department of Biotechnology's Institute of Stem Cell and Regenerative Medicine (DBT-InSTEM).

Minhaj is the first EMBO YIP Investigator from India and a recipient of a Wellcome Trust - DBT India Alliance Intermediate Fellowship. Research findings titled 'Structural insights into actin filament recognition by commonly used cellular actin markers' was published in EMBO Journal (June 2020).

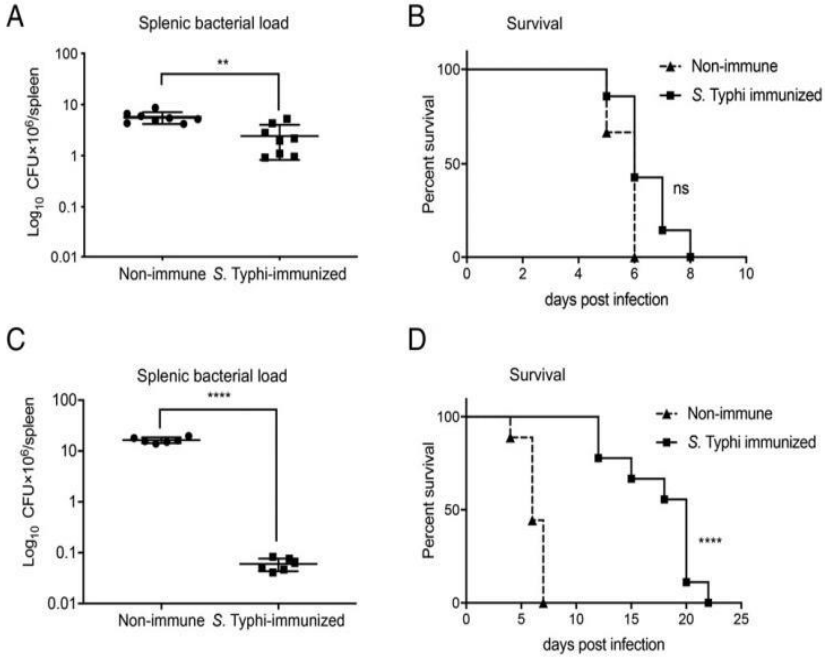


Actin filaments are an important cytoskeleton component of cells that are involved in motility and transport of materials inside cells. These are also crucial for the maintenance of shape and therefore, integrity of cells. Minhaj Sirajuddin and his research team have determined the structures of actin filament bound to commonly used actin markers by exploiting the power of Cryo-EM facility available on campus. These structures allow for a comparative analysis of three markers bound to actin filament, thus offering valuable insights into their interaction. Read about the structural insights into actin filament recognition by commonly used cellular actin markers and the detailed findings of this research work here.

Link: https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_01S_28Aug2020.pdf

Accessibility of O-antigens shared between Salmonella serovars determines antibody-mediated cross-protection

Scientists at Department of Biotechnology's institute, the National Institute of Immunology (NII), New Delhi used a mouse model of infection to address whether infection or immunization with one *Salmonella* serovar can provide protection against other *Salmonella* serovars or not. Mice were immunized with live *Salmonella typhi* (this serovar does not cause disease in mice) and challenged with either *Salmonella enteritidis* or *S. typhimurium* (both these serovars produce disease in mice). Unimmunized mice infected with *S. enteritidis* or *S. typhimurium* had, as expected, bacteria present in high numbers in their spleens, and these mice died in a week. Mice immunized with *S. typhi* and challenged with *S. typhimurium* also died in a week even though there was reduction in splenic bacterial load in these mice. On the other hand, mice immunized with *S. typhi* and challenged with *S. enteritidis* survived till day 20 and these mice had greater reduction in splenic bacterial load. These results suggested that immunization with *S. typhi* provided greater resistance to mice against challenge with *S. enteritidis*.



To understand the reasons for this differential protection, team analysed if the immune responses generated in mice upon immunization with *S. typhi* were reactive with antigens of *S. enteritidis* and *S. typhimurium.* T cells from mice immunized with *S. typhi* readily responded to antigens of *S. enteritidis* and *S. typhimurium*, and secreted two important cytokines, IL-2 and IFN-γ. On the other hand, antibodies present in the sera of mice immunized with *S. typhi* bound live intact *S. enteritidis* but did not show detectable binding with live intact *S. typhimurium*. Further analysis revealed that the antibodies which bound *S. typhi* and *S. enteritidis* recognized carbohydrate antigens shared by these *Salmonella* serovars and these antigens were accessible on the surface of bacteria. On the other hand, even though there were antibodies present in the sera of *S. typhi* – immunized mice against carbohydrate antigens shared by *S. typhi* and *S. typhimurium,* these did not bind bacteria because the antigens were not accessible on the surface of bacteria.

These results suggested that antibodies against surface accessible carbohydrate determinants can provide significant immunity against *Salmonella* infection, and infection or immunization with one *Salmonella* serovar can impart antibody-mediated protection against another serovar provided the two share these surface accessible determinants. These findings have implications for understanding immunity against *Salmonellae,* and for designing effective vaccines against these pathogens. *Salmonella typhi*, which causes systemic infection, typhoid, in humans, shares a high degree of homology with non-typhoidal *Salmonella* serovars such as *Salmonella enteritidis* and *S. typhimurium* that produce only localized gastroenteritis in humans.

Link: https://www.jimmunol.org/content/early/2020/06/14/jimmunol.1900624
Link: https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_02BB_24Aug2020.pdf

Withania somnifera L. Dunal –A modern perspective of an ancient Rasayana from Ayurveda

Pharmacological data review conducted by scientists DBT's Institute of Bioresources and Sustainable Development (IBSD), imphal, revealed that *Withania somnifera* is a potential source for the treatment of a wide range of diseases especially anxiety and other CNS disorders. From its ancient use to its modern application, it has been proven to be non-toxic and effective clinically for human health and wellness. *W. somnifera* based herbal formulation has been marketed in the form of supplement, extract, capsule, powder etc.

Phytochemical studies on *W. somnifera* revealed the presence of important chemical constituents such as flavonoids, phenolic acids, alkaloids, saponins, tannins, and withanolides. The phytochemicals showed various pharmacological activities like anti-cancer, immunomodulatory, cardioprotective, neuroprotective, anti-aging, anti-stress/adaptogenic and anti-diabetic. Various clinical trials show that the plant extract and its bioactive compounds are used in the prevention and treatment of many diseases, such as arthritis, impotence, amnesia, anxiety, cancer, neurodegenerative and cardiovascular diseases, and others.

W. somnifera L. Dunal, commonly known as Ashwagandha, is an important medicinal plant that has been used in Ayurvedic and indigenous medicine for more than 3,000 years. According to Charaka Samhita, Susruta Samhita and other ancient texts, Ashwagandha is

known as Balya (increases strength), Brusya (sexual performance enhancer), vajikari (spermatogenic), Kamarupini (libido-enhancing), and Pustida (nourishing).

Traditional uses of Ashwagandha in Ayurveda are very prominent in several texts where formulations with various dosage forms have been mentioned in Charaka Samhita, Susruta Samhita, Astanga Hridaya, different nighantus etc. The drugs were identified based on their composition containing Ashwagandha as one of the major ingredients and their medicinal uses.

Link: https://www.sciencedirect.com/science/article/pii/S0378874120330397#:~:text=Introduction-,Withania%20somnifera%20(L.),belongs%20to%20the%20family%20Solanaceae.&text=Among%20th%20e%20Ayurvedic%20%E2%80%9CRasayana%E2%80%9D%20herbs,adaptogen%2Fanti%2Dstress%20a%20gent.

Link: https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_02BB_26Aug2020.pdf

DBT-THSTI's researchers win grant for discovering drugs for COVID-19

Dr. Amit Awasthi and Dr. Sweety Samal of the Department of Biotechnology's Translational Health Science and Technology Institute (DBT-THSTI) have been awarded the Intensification of Research in High Priority Area (IRHPA)-SERB grants funded by Department of Science and Technology to support COVID-19 antiviral research.

The project will be implemented in partnership with The International Centre for Genetic Engineering and Biotechnology (ICGEB) and Madurai Kamaraj University, Madurai. THSTI will support in conducting animal studies in mice and hamsters for screening and identification of promising COVID-19 antiviral drugs. The project has been awarded for three years till 2023. This project is a part of DBT-THSTI's COVID-19 efforts in the field of animal studies for screening COVID-19 drugs.

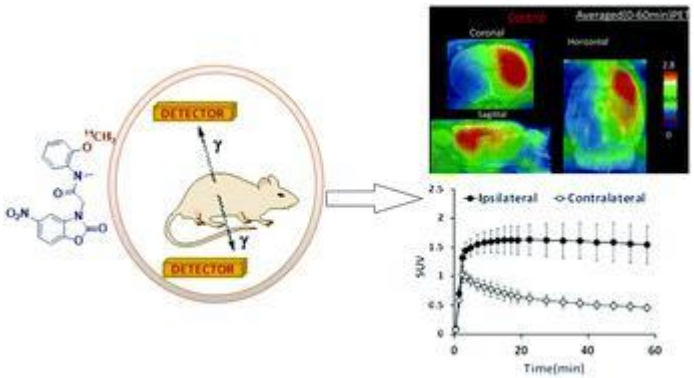
Link: https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_02S_24Aug2020.pdf

Synthesis & evaluation of radio-ligand for visualization of TSPO protein in Brain

Development of Imaging techniques for inflammation in the brain is an emerging field in current biomedical research. Scientists from around the globe are in search of newer methods and targets for brain inflammation imaging for clinical management of the brain related diseases and disorders.

A team of researchers at Babasaheb Bhimrao Ambedkar University (BBAU), Lucknow, have, in a project supported under Nanobiotechnology Program by Department of Biotechnology, evaluated a new radio-ligand for visualization of TSPO protein, namely [11C]N-(2-methoxyoxyphenyl)-N-methyl-2-(5-nitro-2-oxobenzo[d]oxazol-3(2H)-l)acetamide [11C]N′-MPB).

This PET ligand exhibited high binding affinity towards TSPO (Ki = 4.9 nM) and a suitable lipophilicity (log D) of 2.08 for brain imaging. A study on mice with respect to biodistribution showed significant accumulation of radioactivity in TSPO-rich organs such as heart, lungs, kidneys, and adrenal glands which is further supported by the contrast of radioactivity in PET images.



The findings have been published in the New Journal of Chemistry of Royal Society of Chemistry.

Ref. Publication:- Tiwari,AK, Zhang,Y, Yamasaki, T,Kumari N, Fujinaga M. Wakana Mori, Mishra, AK Radiosynthesis and evaluation of acetamidobenzoxazolone based radioligand [11C]N′-MPB for visualization of 18 kDa TSPO in brain; New Journal of Chemistry, 19, 2020

Link: https://vigyanprasar.gov.in/wp-content/uploads/vigyan_samachar_dbt_02S_28Aug2020.pdf