

BIOTECH EXPRESS

Editorial: Workshop on Scientific Communications: Nurturing the budding scientific minds

Press Release: FABA Academy Launched on 19th Feb, 2020 during BioAsia 2020

CURRENT NEWS

- ▶ 34th DBT Foundation Day Celebrated
- ▶ Thermo Fisher Expands with \$11.5 Billion Takeover of Qiagen
- ▶ World's Largest Stem Cell Bio-Bank Launched at Lund University
- ▶ UoH life sciences incubator ASPIRE BioNEST among top 10
- ▶ Union Budget 2020: How much allocated for science
- ▶ Abbott India launches vaccine against 4 strains of influenza virus
- ▶ Biogen and Sangamo Ink \$2.7 Billion+ Neurodegeneration Deal
- ▶ Gilead to Acquire Forty Seven for \$4.9 Billion
- ▶ Merck and AMCM / EOS Cooperate in 3D Printing of Tablets
- ▶ Second patient has been cured of HIV, study suggests
- ▶ First coronavirus vaccine trial



Editorial News: Prof T P Singh became the first Indian to receive all G.N. Ramachandran Awards of our country

Guest Article: Curcumin: From Extraction to bioavailability

Guest Article: Oral Enzymatic Supplement: An Effective Approach For Treating Gluten Intolerance



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Editorial

Workshop on Scientific Communications: Nurturing the budding scientific minds

By Pratyush Kumar Das (Editorial Board Member, Biotech Express)

A 2days workshop – Cum – TrainingProgramme titled “**Guided Publishing & Ethics**” was successfully conducted by **NronBioventure** (Bhubaneswar) in association with **Biotech Express**, **JABET** (Journal of Advanced Biotechnology and Experimental Therapeutics) and **Macon Enviro Technologies Pvt. Ltd.** The workshop was conducted in two different batches (19 – 20 February 2020 and 28 – 29 February 2020) under the supervision of Mr.Pratyush Kumar Das (Head, Publication and Programme Coordinator) at NronBioventure premises at Bhubaneswar. The workshop was attended by 40 graduate and postgraduate students belonging from different institutes and streams of life sciences including biotechnology, microbiology, botany, and pharmaceutical sciences.

Gone are the days when very limited people used to plunge into extensive research which may be attributed to the lack of infrastructure and funding opportunities at the time. However, recent advancements in the field of science and support from the government agencies in the form of several research grants and funding have led to a sharp rise in the interest in research.

Nowadays students from life science backgrounds are getting more inclined towards higher education and for a career in research. But, to be frank enough the budding researchers are unable to express their views and prove their mettle in the respective fields leading to being unemployed. “**In the current scenario of ‘Publish or Perish’, it becomes of utmost importance for the budding researchers to understand the basics of communicating their research ideas perfectly to stand out amongst the crowd**”, the Director of Nron, Mr.Sunakar Nayak quoted.

Keeping the problem in mind, the workshop (a very first of its kind) was designed and aimed at providing detailed information to the students about Article and Thesis preparation, Publications, Plagiarism, and other relevant topics. The students were also provided with an insight on scientific presentations, abstract preparation, keyword selection, data synthesis, and the entire publication process too. The students were motivated to generate new ideas from existing studies by identifying the research gap in different fields of life sciences and to think about possible future directions.

The workshop culminated with an evaluation test, based upon which top-performing students were awarded certificates and memento. Among the first batch of students, Miss. Susmita Pati (M.Sc. Biotechnology) of Trident Academy of Creative Technology (TACT), Bhubaneswar bagged the first position followed by Miss. Sweta Priyadarshini (M.Sc. Biotechnology) of Siksha 'O' Anusandhan (Deemed to be University), Bhubaneswar. The third position was jointly awarded to Miss. Alena Priyadarshini Mishra (M.Sc. Biotechnology) of Siksha 'O' Anusandhan and Miss. Priyanka Parida (M.Sc. Biotechnology) of TACT, Bhubaneswar.

In the second batch Mr. Gaurav D. Patel, a student of B.Tech. (Biotechnology) of Siksha 'O' Anusandhan, was awarded the first prize. Miss. Chirasmita Mohanty and Mr. Subhanjan Satapathy (M.Sc. Biotechnology) of Siksha 'O' Anusandhan were adjudged as the joint winners for the second spot, while Miss. Nirali Patel (M.Sc. Biotechnology) of the same university received the third prize.



Images from the workshop: Topic Discussions, Student interactions, and Award Distribution.

Editorial News

Prof T P Singh became the first Indian to receive all G.N. Ramachandran Awards of our country

SASTRA - G. N. Ramachandran Award for Excellence in Science – 2020

On February 28, 2020, Prof T P Singh was conferred with the SASTRA - G. N. Ramachandran Award for Excellence - 2020. He has now got all G.N. Ramachandran Awards of our country including Dr. G.N. Ramachandran Award of the Kerala State Council of Science, Technology and Environment in the year 2017, Professor G.N. Ramachandran-Born day Lecture Award of the Central University of Haryana in the year, 2016, Professor G.N. Ramachandran Lecture Award of the Society of Biological Chemists of India in the year 2015, Professor G.N. Ramachandran CSIR Gold Medal for the Excellence in Biological Sciences and Technology in the year 2006 and Professor G.N. Ramachandran 60th Birthday Commemoration INSA Medal in the year 2006.



Profile

Prof. T. P. Singh is a scientific leader who has made noteworthy contributions in the field of Rational Structure based drug design, Protein Structure biology and X-ray crystallography. He has established the research programmes on protein structure determination and structure-based rational drug design at All India Institute of Medical Sciences, where he leads a vibrant scientific group. He has consistently demonstrated exceptional leadership qualities from the beginning of his career, when the country was still in its infancy in the areas of molecular biology, protein crystallography and drug design. He has made exceptional contributions and led



the nation to the point where India can boast of standing among the first in the world, where the number of protein structures determined are concerned. Despite several challenges in terms of infrastructure and facilities over the years, he has created a scientific hub in the form of an active research group which as a nucleus, has produced not only significant scientific results and discoveries but has also created new group leaders who have branched out and created many more scientific core groups in the nation. He has published more than 400 research papers in leading international journals.

He has also mentored more than 100 MSc, PhD, MD and Post-Doc students who are currently independent group leaders in leading scientific institutions in various parts of the country. He has made significant collaborations with other academic institutions as well as industry partners all over the country. He has been nominated as a fellow of six national and international academies, namely, The World Academy of Sciences, Indian National Science Academy, National Academy of Sciences, Indian Academy of Sciences, Alexander von Humboldt Foundation and Biotech Research Society of India.

In addition to the Ramachandran medals, he has been awarded various national and international awards over the years, for instance, the Jawaharlal Nehru Birth Centenary Lecture Award of INSA (2011), Annual Award of the Instrumentation Society of India (2011), CSIR Foundation Day Lecture award (2010), Goyal Prize in Life Sciences (2007), Sir J. C. Bose Memorial Award of the Indian Sciences (2006), K.K. Foundation award for Science and Technology (2001), Canadian Development agency Award (1991), Humboldt - Foundation Fellowship Award (1978). Additionally, he has served as a Vice President (Foreign Affairs) in the Indian National Science Academy.

Work

The three-dimensional structures of at least 30 classes of proteins including enzymes from the multi drug resistant bacteria *Acinetobacter baumannii*, lactoferrins from several species, lactoperoxidases from different mammalian species, peptidoglycan recognition proteins, hyaluronidase lyases, peptidyl-tRNA hydrolases, ribosome inactivating proteins and its complex with a natural ligands from parasitic plant mistletoe and other plants, bifunctional inhibitor proteins from various plant sources and several serine proteases and their inhibitors have been determined in his laboratory. The elaborate structural studies of proteins from several important systems which are important potential drug targets such as phospholipases A2 (PLA2), cyclooxygenases (COX-2), lipoxygenases (LOX), endothelin receptor, endothelin converting enzyme, mammary gland/breast cancer regression proteins and matrix melanosomal proteins as well as their complexes with natural and designed synthetic ligands, recent proteins such as lactoperoxidase, hyaluronidase enzyme, peptidyl-tRNA hydrolases and TIM barrel based inhibitor proteins are being carried out.



Education and Early Years

Prof. Tej P. Singh obtained his M.Sc. degree with first rank from University of Allahabad. He started his research career in 1971 as a Ph.D. student at the Indian Institute of Science, Bangalore under the supervision of Professor M. Vijayan. He obtained his Ph. D degree in the mid 70's working on X-ray crystallographic structure determinations. Soon after obtaining his Ph.D. degree, he worked for a year as a lecturer at the University of Indore. He then spent more than two years (1978–1980) as an Alexander von Humboldt / Max-Planck, post doctoral fellow in the German laboratory of Professor Robert Huber, who later received the Nobel Prize in 1988. After his return to India he worked as a reader at Sardar Patel University (1980–83) and an additional professor (1984–85) in the Department of Biophysics at the All India Institute of Medical Sciences, New Delhi. He was appointed professor and head of the department in 1986.

Quotes from his students

Imitiyaaz Hassa and Pradeep Sharma said, Prof. Tej P. Singh has been a dream mentor and guiding light to his students. He is a person who leads by example and inspires everyone to work hard with dedication and devotion. He always has words of encouragement to lift the moral of students whenever they are struggling with difficult projects. He has inculcated in his students a great deal of scientific temperament by his analytical approach to scientific problems, sharp intelligence, and investigative approach. Prof Singh's intellectual contri-

butions, along with his magnanimous personality and humble nature, makes him a rare scientist and a leader whose influence and impact will be felt for generations to come.

Comments from the Biotech Research Society, India BRSI

BRSI is overwhelmed to announce that Prof TP Singh, President of BRSI has been conferred G. N. Ramachandran Award for excellence in Physics instituted by SASTRA which carries a cash prize of Rs 5.00 lakh and a citation and was presented on February 28, 2020 at SASTRA Campus in Thanjavur.

Prof. Tej P. Singh is currently SERB Distinguished Fellow at the Department of Biophysics, All India Institute of Medical Sciences, New Delhi. His main research fields include Structural Biology, Biological Crystallography, Protein Structure Determination and Peptide Design; Rational Structure Based Drug Design. He is known for his work in the fields of Rational Structure-based drug design, Protein Structure biology and X-ray crystallography. He has played an active role in the development of drug design in the fields of Antibacterial therapeutics, Tuberculosis, Inflammation, Cancer and Gastropathy. The three-dimensional structures of various proteins including lactoperoxidase, peptidoglycan recognition protein, lactoferrin from several species, ribosome inactivating proteins, bifunctional inhibitor proteins from plant seeds and various serine proteases and their inhibitors have been determined by his group. The elaborate structural studies of proteins from several important systems as potential drug targets such as phospholipase A2, cyclooxygenase, lipoxygenase, endothelin receptor, endothelin converting enzyme, breast cancer regression proteins and matrix metanosomal proteins as well as their complexes with natural and designed synthetic ligands have been carried out. He had developed the rules of peptide design with alpha, beta – dehydro - amino acids through extensive studies using syntheses, and X-ray and NMR structure determinations. These design rules are being exploited for making specific peptides to act as tight inhibitors of target enzymes and potent antagonists of target receptors for eventually leading to useful therapeutic agents.

He initiated a new programme on Clinical Proteomics at the All India Institute of Medical Sciences in which it is intended to characterize all the proteins that are expressed during various patho/physiological conditions. The newly identified proteins will either be useful as biomarkers or they may be associated with the progression of diseases making them important targets for drug design.

Prof Singh is one of most outstanding scientist in India and contributed significantly for the growth of science and society through his dedicated efforts. He is Fellow of the Biotech Research Society, India, Third World Academy of Sciences, Indian National Science Academy, National Academy of Sciences, Indian Academy of Sciences, Alexander von Humboldt Foundation. Prof Singh has been decorated with a large number of awards and honors which include Distinguished Professorship of the University of Mysore, Distinguished Lecture Award of the A.P. Science Congress, Professor D.M. Bose Memorial Award of the Bose Institute, Kolkata, Thathachari Memorial Science Award for Science and Technology, Jawaharlal Nehru Birth Centenary Lecture Award of INSA, Annual Award of the Instrumentation Society of India, Doctor of Science, D.Sc. (h.c.) conferred by Karnataka State Open University, Mysore, CSIR Foundation Day Lecture award, Goyal Prize in Life Sciences, Professor G.N. Ramachandran CSIR Gold Medal for Excellence in Biological Sciences and Technology, Professor G.N. Ramachandran 60th Birthday Commemoration INSA Medal, Sir J. C. Bose Memorial Award of the Indian Sciences - Congress, K.K. Foundation award for Science and Technology, Canadian Development agency Award, etc.

We congratulate Prof TP Singh, the President of the Biotech Research Society, India for this prestigious award.

Guest Article

Oral Enzymatic Supplement: An Effective Approach For Treating Gluten Intolerance

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Abstract

Celiac disease (CD) is an autoimmune enteropathy that is triggered by partially hydrolysed gluten proteins. A life-long adherence to gluten-free diet is the only effective treatment currently available for CD. Gluten proteins present in wheat, rye and barley cereals are the main stimulating factor for this disease. There are three main causes of celiac disease: the environmental trigger (gluten), genetic susceptibility, and unusual gut permeability. Gluten intolerance affects genetically predisposed individuals carrying the prerequisite genetic markers HLA-DQ2 or -DQ8. Gluten is a heterogeneous mixture of insoluble proteins i.e. gliadins and glutenins. It is rich in proline and glutamine residue content which renders the gluten proteins largely inaccessible to human proteases of the gastrointestinal tract driving the abnormal immune intestinal response. A 33-mer from α -gliadin is currently considered the most immunogenic peptide and are resistant to gastrointestinal digestion. Unfortunately, a majority of patients have difficulty complying with this diet, adversely affects the quality of patient life, and the response to therapy is poor. Therefore, efforts are going on to explore alternative approaches and develop novel therapies. Based on mechanisms of action, these therapies may be classified into five broad categories: Engineering gluten-free grains, decreasing intestinal permeability by blockage of the epithelial zonulin receptor, inducing oral tolerance to gluten with a therapeutic vaccine, microwave thermal treatment of hydrated wheat kernels and degrading immunodominant gliadin peptides using probiotics with endopeptidases or transglutaminase inhibitors. Oral therapy involving exogenous prolylendopeptidases able to detoxify ingested gluten was therefore propounded as an alternative effective treatment to the diet. Developments of new enzymes or enzymatic cocktails offer potentially more potent therapeutic tools and provide new hope for enhanced, lifelong celiac disease management with improved patient compliance and better quality of life.

Keywords: gluten, gliadin, endopeptidases, transglutaminases, immunodominant, autoimmune

Introduction

Celiac disease (CD) is a chronic inflammatory immune mediated small intestinal disorder. It is also known as gluten sensitivity, gluten intolerance, celiac sprue, gluten sensitive enteropathy and non-tropical sprue. The name 'celiac' is derived from the Greek for 'suffering in the bowels'. It is mainly triggered by the partially digested gluten proteins in the genetically susceptible individuals, which results in villous atrophy, crypt hyperplasia and mucosal inflammation (Rey et al., 2016). Celiac patients may show a wide range of symptoms ranging from diarrhea, constipation, vomiting, malnutrition, or failure to thrive, to chronic fatigue, joint pain, anemia, osteoporosis, or migraines (Lammers et al., 2014). CD can occur at any age and can affect a variety of organ systems. Early recognition and treatment of CD are important to prevent complications such as malnutrition, osteoporosis, infertility, and gastrointestinal malignancies (Bakshi et al., 2012).

The sequences convey poor overall digestion kinetics, generating peptides of 30–40 amino acid residues in length that resist further digestion by both intestinal exo- and endoproteases (Fasano et al., 2003). A fraction of these products, primarily from α and γ -gliadin, have affinity for human leukocyte antigen (HLA) DQ2 and DQ8, which are MHC class II molecules associated with over 90% of CD patients (Kaukinen et al., 2014). The peptides are large enough to span multiple antigenic regions, and present glutamine residues for enzymatic deamidation in the celiac mucosa. The inflammatory response is significantly amplified by this deamidation, as HLA affinity is increased by the conversion of glutamine to glutamate (Sapone et al., 2003).

Epidemiology

Earlier it was thought that CD was most prevalent in those areas where gluten containing grains were staple food. Over time, there is an increasing incidence of CD has been observed in areas that were previously considered as CD-free. This may be occurred due

to global changes in the diet, mostly related to higher consumption of wheat-based products (eg, pasta, pizza). Recent studies showed that the overall prevalence of CD in general population is more in the Western countries, as in Europe and the United States, the mean frequency of CD in the general population is approximately 1%. The prevalence of CD is as high as 2% to 3% in Finland and Sweden, whereas it is only 0.2% in Germany, although these areas share a similar distribution of causal factors (level of gluten intake and frequency of HLA-DQ2 and -DQ8). In the Northern part of India, the frequency of CD seems to be higher, so called "celiac belt," a finding that is at least partially explained by the wheat-rice shift from the north to the south (Catassi et al., 2014).

Gluten protein

Gluten is a heterogeneous mixture of insoluble storage proteins of wheat, barley and rye, which are deposited in the endosperm of the developing cereal grain. It is comprised mostly of glutenin and prolamines, and when mixed with water it generates molecular networks that impart useful viscoelastic properties to flour dough (Green, 2005). Of these, prolamines are the gluten components that are implicated in CD; they are found variously in different grains as gliadins in wheat, secalins in rye, a mix of both in triticale, hordeins in barley, and avenins in oats. In wheat, gliadins are in turn composed of sub-fractions α/β , γ , $\omega 1$, $\omega 2$ and $\omega 5$. The α -gliadin sub-fraction has the maximum immunogenicity in CD, contributing the most to toxic epitopes upon digestion (Yoosuf and Makharia, 2019). It is rich in proline (15%) and glutamine (35%) residue content which renders the gluten proteins largely resistant/sterically inaccessible to human proteolytic enzymes of the gastrointestinal tract driving the abnormal immune intestinal response (Ludvigsson et al., 2013).

Immune response to gluten

Digestion of gluten protein by luminal proteases results in

larger oligopeptides which are immunogenic in CD and some of them include, the most immunotoxic, 33-mer peptide 57–89 (with the amino acid sequence LQLQPFQPQLPYPQPLPYPQQLPYPQPQPF (Yoosuf and Makharia, 2019). The partially digested gliadin peptides enter the lamina propria of the small intestine by a transporter protein called zonulin. Gliadin uptake by zonulin is known as paracellular pathway. It is structurally similar to the zona occludens toxin associated with *Vibrio cholera* and has been observed to be a controller of epithelial permeability. Through this pathway, gliadin products bind

to the chemokine receptor CXCR3 on the luminal side of the intestinal epithelium. This interaction in turn enhances the formation of zonulin, which ultimately relaxes the interepithelial tight junctions via PAR2/EGFR (Protease activated receptor 2/Epithelial Growth Factor Receptor) pathway. This increased permeability leads to influx of gliadin. An alternative pathway implicated in gliadin uptake is the transcellular pathway. This involves secretory Immunoglobulin A (IgA) that co-localizes with another molecule, the CD71 to promote transcellular uptake of gliadin products into the lamina propria (Fasano et al., 2011). CD71

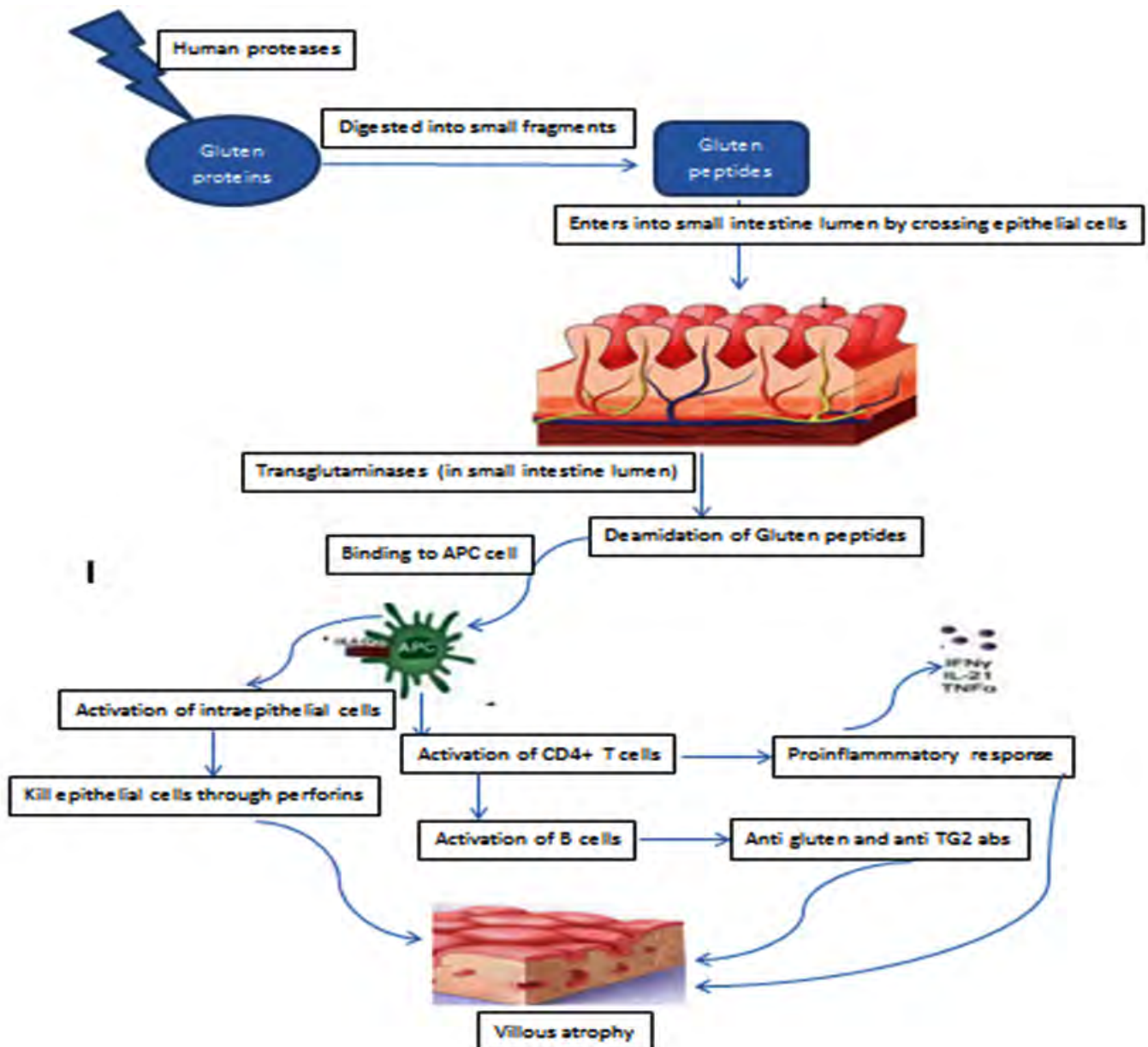


Fig.1. Mechanism of action involved in Immune response in CD (Tye-Din et al., 2018).

is the transferrin receptor, but is found to be expressed in higher amounts on the luminal aspect of intestinal epithelial cells in CD. The tissue transglutaminase-2 (tTG-2) enzyme modifies the digested gluten immunogenic peptides that have entered the mucosa, by deamidating their glutamine residues to glutamate. These negatively charged glutamate side chains have a higher potential to be recognized as immunogenic. Also, by virtue of the relatively large size of these partially digested proline containing fragments, and the negative charge of glutamate, they tend to settle and form bonds with the neighboring extracellular matrix, resulting in immobilized neoepitopes. The formation of these bonds may be directly catalyzed by the tTG

Ultimately, all the gluten-derived antigens are recognized and processed by the HLA-DQ2 and -DQ8 bearing antigen presenting cells (APCs), which activate CD4+ helper T cells, setting off an inflammatory cascade. Activated CD4+ cells release cytokines like Interferon- γ (IFN- γ) and Tumor Necrosis Factor- α (TNF- α), thereby further enhancing the permeability and facilitating a self-propagating mechanism of gliadin uptake. T-cells also activate B-cells which mature to produce antibodies against gluten and tissue transglutaminase-2 (celiac antibodies). These antibodies further contribute to the ensuing immune-mediated enteropathy. As well, the immunotoxicity is mediated through the increased production of interleukin-15 (IL-15) by the intestinal epithelial cells and the intraepithelial lymphocytes (IEL). This interaction ligand-receptor pairs activates the IELs and triggers them to kill epithelial cells through perforins, and other mechanisms (Yoosuf and Makharia, 2019).

Oral enzymatic therapy for celiac disease

A gluten-free diet (GFD) is the primary and obvious treatment option for CD patients, as it improves gastrointestinal symptoms within a few weeks. If patients strictly follow this diet the risk of concomitant autoimmune disease symptoms is reduced. However, many patients fail to comply with this lifelong adherence to this restrictive diet, as gluten is a common ingredient in diets throughout the world,

and gluten-free foods are not widely available. Therefore, maintaining a truly gluten-free status is both difficult and costly (See et al., 2015). Gluten-free foods are also more expensive than their gluten-containing counterparts. Compliance issues and hidden gluten contamination produce a constant low-level stimulation that remains the norm for a very large fraction of CD patients. Supplemental or even alternative treatment options are desirable but the bar is necessarily high (Mahadev et al., 2015). Alternative therapies must be safe, and at least as effective as a GFD in reducing both inflammation and pain. A variety of strategies are being considered based on our improved understanding of disease mechanism (McCarville et al., 2015), but successful alternatives to a GFD have yet to emerge (Janssen et al., 2015). Therefore, efforts are going on to explore alternative approaches and develop novel therapies. Based on mechanisms of action, these therapies may be classified into five broad categories: genetically modified wheat, decreasing intestinal permeability by blockage of the epithelial zonulin receptor, inducing oral tolerance to gluten with a therapeutic vaccine, microwave thermal treatment of hydrated wheat kernels, enzymatically modified wheat gluten, use of transglutaminase and cathepsin inhibitors, HLA blocker, polymeric binding and degrading immunodominant gliadin peptides using probiotics with endopeptidases or transglutaminase inhibitors (Yasoof and Makhari, 2019).

One promising approach involves enzyme supplementation of the gastrointestinal tract, to avoid the induction of immuneresponses by partially digested gluten peptide is the key antigen that binds to HLA and stimulate inflammatory cascade (Bethune et al., 2012). A small number of candidates have been tested for such purposes, mostly involving prolyl endopeptases (PEPs) or prolyl oligopeptidases (POPs). Two options in advanced testing are AN-PEP19–21, a prolyl endopeptase from *Aspergillus niger*, and ALV00322, a combination of a POP from *Sphingomonas capsulate* and a glutamine-targeting cysteine endopeptase (Gass et al., 2007). It has been shown that they are well tolerated and work perfectly at low pH. Based on clinical studies it has been demonstrated that these enzymes can attenuate intestinal injury (Seigel et al., 2012).

| Therapeutic agents | Mechanism of action |
|------------------------------------|---|
| Genetically modified gluten | Decrease gluten exposure by transamidation of gliadin |
| Zonulin inhibitor | Decreases zonulin secretion and inhibits intestinal permeability |
| Therapeutic vaccine | Creates immunetolerance to gluten fragments and desensitizes celiac disease patients to the toxic effects of gluten |
| Probiotics | Detoxify gliadin and promote intestinal healing |
| Tissue transglutaminase inhibitors | Stop tissue transglutaminases from modifying gluten fragments, a process that otherwise triggers the immune response. |
| Polymeric Binding | Binds to gluten fragments and ultimately degrade them |
| HLA blocker | Prevents binding of gluten peptides with receptor present on Antigen presenting cells (APC) |

Table.1. Novel approaches for celiac disease and their mechanism of action (Bakshi et al., 2012).

The glutenase EP-B2 (endoprotease B, isoform 2) is a glutamine specific peptidase and their active sites contain Cys-His-Asn catalytic triad. They serve to digest hordein, the analog of gliadin and secreted naturally in the acidic endosperm of germinating barley seeds (*Hordeum vulgare*). Glutenase EP-B2 shows maximum active at low pH and it is resistant to pepsin but it lysed at physiological concentrations of trypsin. This enzyme recognizes sequence QXP, which is highly abundant in the 33-mer as well as other immunotoxic gluten compounds. These factors make it a good option for therapy in CD as a gastric active enzyme (Bethune et al., 2006).

Proline specific endoproteases (PEP) from the microbes *Flavobacterium meningosepticum* (FM-PEP), *Sphingomonas capsulata* (SC-PEP), and *Myxococcus xanthus* (MX-PEP) have also been investigated as potential glutenases. They are serine proteases and each has a larger b-propeller domain and a smaller, N-terminal catalytic domain that breaks the peptide bond of proline residues at the carboxy end of the gluten protein (Gass et al., 2007). Activity of SC-PEP extends into the acidic range of pH, and is by and large, unaltered in the presence of pepsin. However, the other two PEPs are lysed by pepsin. Furthermore, FM-PEP is inactivated by the small intestinal enzyme trypsin in the presence of bile acids. MX-PEP too is unstable in the presence of bile salts (Gass et al., 2007). Considering these limitations,

SC-PEP has been explored as a more favorable candidate for therapy in CD. In order to improve its action further, mutant variants (variant 10,224 or 10,230) of SC-PEP have been developed which have 200-fold higher resistance to pepsin and 20% higher turnover at acidic pH (Ehren et al., 2007).

While SC-PEP has high specificity for gluten immunogenic epitopes, it has relatively low specificity for long peptide sequences. This is because the larger b-propeller domain preferentially allows smaller gliadin fragments into the active site, and therefore, is unable to completely eliminate the immunogenic gliadin peptides. This limitation could be overcome by combining it with other enzymes with complementary specificity. Combination of EP-B2 with SC-PEP, for instance has been explored for application in CD. The EP-B2 efficiently digests the 33 mer peptides into smaller, not necessarily non-toxic proline containing fragments. The PEP complements its action by digesting the proline- glutamine links in these smaller oligopeptides, thereby reducing their immunotoxicity (Gass et al., 2007).

Several clinical trials have been conducted to assess the effectiveness of this enzyme mixture in making dietary gluten safe for patients with CD. One of the most prominent of these has been using the enzyme cocktail ALV 003, now known as Latiglutenase. Latiglutenase is a 1:1 combination

of different types of enzymes such as EP-B2, or ALV 001 plus PEP, or ALV 002. It has been seen that ALV003 group showed significantly lower immunological activation, as found in peripheral T cell IFN- γ responses to gliadin (Tye-Din et al., 2010).

Kuma030 is an engineered glutenase developed by the Institute for Protein Design, University of Washington. Before its development, the researchers identified Kuma030 (KumaWT), a naturally occurring enzyme from the acidophilic microbe *Alicyclobacillus sendaiensis*. It is a serine endoprotease, with optimal activity over the pH range of 2–4/37 C and therefore adaptable for use in the gastric environment (Gordon et al., 2012). Based on the structure of KumaWT, an enzyme was designed, with specificity toward known gliadin peptides. The new enzyme called KumaMax or Kuma010, had 116 times higher proteolytic activity, and 877 times higher specificity for the target gliadin oligopeptides. Further modification was done in KumaMax or Kuma010 which results in several-fold higher activity against immunotoxic 33-mer and 26-mer peptides. This modified version was called Kuma030. It has been reported that Kuma030 is more efficient than SC PEP- EP B2. It works efficiently at a lesser concentration of 1:40 weight/weight (w/w) ratio, achieved >99.9% gliadin degradation thereby reducing the gluten content to 3 ppm, well-below the 20 ppm threshold for “gluten-free” labeling but the mixture of PEP-EP B2 effectively works at higher concentration i.e. 1:10 w/w ratio and achieved 84.4% gluten degradation (Wolf et al., 2015). When gluten sensitive T cells isolated from patients with CD were incubated with gliadin pre-treated with Kuma030, a dose dependent reduction in IFN- γ production and T cell proliferation was observed (Wolf et al., 2015). Based on these findings Kuma030 may hold promise in the near future.

Dipeptidyl peptidase- IV (DPP-IV) is an exopeptidase that acts on the amino-terminal side to liberate X-Pro dipeptides in gliadin. It occurs naturally in small amounts in the small intestinal brush border. It has been obtained commercially from the fungus *Aspergillus oryzae* and its potential as a glutenase has been investigated. On its own,

DPP-IV has modest efficiency as it can only act on peptides starting with X-Pro. Additionally, DPP-IV has a neutral pH optimum and hence it starts action only in the intestine. It has been investigated that DPP-IV executes higher efficiency in the presence of AN-PEP. The combination when administered as an oral mixture has been found to successfully degrade small amounts of gluten (Ehren et al., 2009). Because of non-specificity of AN-PEP and the very limited proteolytic effect of DPP-IV, the effect of this combination appears to be the best. This combination was studied as a part of STAN1, a cocktail of microbial enzymes commonly used in food supplements. However, in presence of trypsin/Ph 8.0/37 C, the enzyme is susceptible to destruction. Hence it may be effective only in the gastric digestion of wheat gluten prior to the food bolus reaching the intestine. Further invitro testing to study its efficiency as detoxifying enzyme in celiac disease is required.

Endopeptidase 40 is a novel glutenase isolated from the soil actinomycete *Actinoallomurus A8* as a secreted protein. It is active at low pH ranges 3 to 6 and shows resistance against pepsin and trypsin. The most immunogenic 33-mer as well as the whole gliadin proteins are efficiently degraded and no toxic peptides are produced during gluten digestion by E40 into the stomach, thus preventing the intestinal inflammatory reactions to occur in CD patients. Hence, E40 is proposed as a novel candidate in oral enzymatic therapy for the dietary management of gluten intolerance (Cavaletti et al., 2019).

Although all the enzymes described above have been proven effective glutenase activity under appropriate thermochemical conditions, whether these enzymes completely eliminate all immunogenic epitopes and prevent any possible immune-activation by dietary gluten is the most pertinent question. Moreover, most of the glutenases that are now in advanced stages of clinical trials, have been studied in the context of small amounts of gluten challenge, in patients who are already on the GFD. Such small challenges simulate inadvertent gluten exposure in patients that adhere to GFD, and are useful to study patients that are not responsive despite adherence to GFD. Whether these oral

enzymatic mixture would help them remains to be proven. Clinical trials with higher doses of gluten challenge are required.

Conclusions

The high incidence of CD in the worldwide population is a challenging task, imposed the negative impact of a strict gluten-free diet on the perceived quality of life of celiac patients for several reasons. A life-long adherence to gluten-free diet is not easy since gluten is the most common ingredient in the human diet. Multidirectional research efforts are currently going on to find out new treatment strategies in order to reduce sensitivity to gluten. The use of oral proteases capable of detoxifying ingested gluten and bacterial-derived endopeptidases currently represent the most advanced and promising strategies to manage CD. GFD is likely to remain the mainstay of therapy of CD in the near future, since all other treatment modalities are only in the preliminary stages of research. An ideal therapeutic agent would be one that permits a CD patient to consume gluten in usual amounts, without compromising her/his quality of life. So, Glutenases have been extensively explored as therapeutic agents and their list is continuously growing with newer discoveries. It has been shown that among these, latiglutenase had reached far away in terms of clinical trials. Based on the results of preliminary studies, Kuma030 (Type of glutenase), suggested that this enzyme may provide more promising results in future, compared to other glutenases studied so far. Finally it has been concluded that although most trials on novel therapeutics are currently in phase 2 or earlier stages, ongoing research in areas targeting various molecular pathways in CD is robust. This provides much scope to find definitive alternatives to GFD in the coming years, in order to improve the quality of life of patients with CD. Celiac patients abide by a gluten-free diet, and the supplementation of exogenous gluten-digestive enzymes (glutenases) is expected as a promising way to reduce the risk of dietary gluten boost.

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Press Release

FABA Academy Launched on 19th Feb, 2020 during BioAsia 2020

Federation of Asian Biotech Associations (FABA), a non-profit, non-government organization, is established in 2005 as registered society under the Indian Societies Act. The main objective of FABA is to provide a common platform for development of biotechnology sector across the globe, particularly in the Asian countries. BioAsia has been one of its brain child and later became the flagship event of State Government and is being organised in Hyderabad annually for the past 17 years.

FABA has been organising seminars, workshops and distinguished lectures not only in India but also in several Asian countries. These activities over the years enabled in cross-border marketing of products, technology transfers and R & D collaborations.



The Problem of Trained Manpower

FABA has recognised the non-availability of trained manpower as the biggest impediment in the growth of pharma and biotech industry as the graduates coming out of academic institutions, particularly from tier II and III towns, lack specific skills needed. It also recognised the need for appropriate career guidance among the fresh graduates to choose right career based on their strengths and interests. With a view to address this issue, FABA took the initiative and interacted with its stakeholders and came up with the idea of launching skill development courses to impart required skill sets so as to make them readily employable and career guidance workshops/webinars.

To undertake these activities the association has established 'FABA Academy' that was formally launched by Dr. M. Sivakumaran, Director of Aurobindo Pharma on 19th Feb, 2020, during BioAsia 2020. The activities of Academy will be scaled in a phased manner and will be run in close association with industry.

FABA Academy

FABA Academy Advisory Committee

In order to identify the appropriate courses and design the curricula in consultation with industry, an Advisory Committee was constituted under the Chairmanship of Dr. D. Yogeswar Rao and members drawn from the academy, industry and Government agencies. The advisory committee along with Prof. P. Reddanna, Executive President, Prof. Vijaykumar, Secretary General and other Executive Council members of FABA met for the first time on 19th February at HICC during the course of BioAsia 2020 and deliberated on various issues related to skill development and career guidance programmes.



Guest Article

Curcumin: From Extraction to bioavailability

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Introduction

Turmeric (*Curcuma longa* L.) is a herbaceous plant with thick and fleshy rhizomes and leaves in sheaths that characterize the family Zingiberaceae. *Curcuma longa* L., was originated in India and at present distributed throughout tropical and subtropical regions of the world, is widely cultivated in Southeast Asian countries. Turmeric is commonly known for its medicinal values in the Indian traditional systems of medicine. Turmeric contains 2-9% curcuminoids which are comprised of curcumin (80%), demethoxycurcumin (17%) and bisdemethoxycurcumin (3%) which all belong to the diarylheptanoids (Salem et al., 2014, and Esatbeyoglu et al., 2012). Apart from 2-9% curcuminoids turmeric also contains 2-4% essential oil and 2-3% of fixed oil and various volatile oils, including turmerone, atlantone, and zingiberone. Numbers of studies in the past have shown the medicinal application of curcumin which is not just limited to antioxidant, antimicrobial, anti-inflammatory, and anticancer actions but way more (Aggarwal et al. 2003, Menon & Sudheer 2007). Although curcumin has many health-promoting effects but still hard to find a place in mainstream drug application due to its poor bioavailability (Prasad et al., 2014); therefore to get the health-promoting effect one must need to



have a high dose of curcumin to exert the positive and health-promoting effects (Vareed et al., 2008). Curcumin is an oil-soluble pigment, sparingly soluble in water at acidic and neutral pH, and soluble in alkaline condition. It is a tautomeric compound existing in enolic form in organic solvents and as a keto form in water. The value of the turmeric products is based on their curcuminoids content and estimated based on its absorbance at 420nm.

Extraction of curcumin:

The dried root of the rhizome *Curcuma Longa* is utilized for the extraction of curcumin. The first and foremost step in the extraction process is grounding of the rhizome into a fine powder and washing with a suitable solvent to get the coloring agent selectively. The distillation process followed the first step and yields an oleoresin with coloring matter that accounts for 25-35% content with volatile oils and other resinous extractives. Further washing of oleoresin so obtained with selective solvents leads to the extraction of curcumin from the oleoresin. This process leads to a purified yellowish powder with over 90% curcumin and very little amount of volatiles and natural matter. Various solvents which are being utilized in curcumin extraction process one or other way are Isopropanol (purifying curcumin), Ethyl acetate (quality of product), Acetone (manufacturing process), Methanol (for purification) other are Hexane, ethanol, CO₂. Although curcumin is extracted from a natural source, chemical synthesis is also being available (Lampe and Milobedzka, 1913).

Extraction Methods of Curcumin-

In all the conventional extraction methods, maceration and soxhlet extraction are suitable for the extraction of curcumin. However, maceration is the most effective method to extract compounds from plants. It is also reported that the maceration extraction of Curcuminoids has about two times higher yield than the other extraction methods. Soxhlet extraction can be quite time-consuming than maceration, taking from a few hours up to days, and consume large volumes of solvent. Its main advantage is that the material is extracted continuously. The disadvantage is that the extract is constantly heated at the boiling point of the solvent used, which can damage thermolabile compounds.

In the case of the modern extraction methods including microwave-assisted, ultrasound-assisted and enzyme-assisted extractions do not show high extraction yields as high as Soxhlet method, but their highlighted advantages such as low extraction temperature, short extraction time and use of a very small volume of solvent make them more favorable extraction methods.

| S.No. | Extraction Methods | Efficiency/Yield of curcumin extraction | Reference | Remarks |
|--------------------------------|--|---|-------------------------------------|---|
| A. Conventional methods | | | | |
| 1. | Homogenization | Low | Gonçalves <i>et al.</i> , 2014 | Maceration and Soxhlet extraction methods are efficient |
| 2. | Single extraction | Low | Revathy <i>et al.</i> , 2011 | |
| 3. | Sequential extraction | Low | Quitschke, 2008 | |
| 4. | Maceration | High | Chaves and Costa., 2008 | |
| 5. | Subcritical solvent extraction | Low/4.94% | Kwon and Chung, 2015 | |
| 6. | Soxhlet extraction | High/6.9% | Shagufta Nazet <i>et al.</i> , 2010 | |
| B. Modern methods | | | | |
| 7. | Microwave-assisted extraction | High/3.72% | Mandal <i>et al.</i> , 2007 | MAE method is efficient compared to others |
| 8. | Ultrasound-assisted extraction | Low/3.92% | Costa <i>et al.</i> , 2011 | |
| 9. | Enzyme-assisted extraction | Low/4.1% | Kurmudleet <i>et al.</i> , 2013 | |
| 10. | Supercritical CO ₂ Extraction | Low | Santana <i>et al.</i> , 2011 | |

Table 1 : Different extraction methods are known for the extraction of curcumin.

Storage

Turmeric color properties are everlasting but flavor and aroma are lost quickly if not stored properly. Store it in airtight containers away from sunlight. Store it in cool, dark and dry places.

Bioavailability

Various studies have evident proof that curcumin has low bioavailability as well as low pharmacokinetics. Vareed et al. 2008 in his study have found that even after a single oral dose of 10 or 12 g of curcumin, it was barely detected in human plasma. Numerous factors are accountable for the low bioavailability of curcumin that includes low solubility in aqueous gastrointestinal fluids, low chemical stability at physiological pH, low absorption in the gastrointestinal tract (GIT), and rapid metabolism in the GIT and liver.

Since curcumin is known to possess multiple therapeutic effects, therefore, considering the utmost importance of this polyphenol, plentiful approaches

have been tried to boost up the bioavailability of curcumin. Recently reported approaches that are being used to enhance the bioavailability of curcumin are-

Toxicity of curcumin

Some reports suggest that curcumin may be toxic under some specific conditions. For example, time- and dose-dependent induction of chromosomal aberration in mammalian cell lines was reported at a concentration of 10 g mL⁻¹ of turmeric. Similarly, curcumin at the concentrations of 5 g mL⁻¹ and 2.5 g mL⁻¹ were shown to induce nuclear and mitochondrial DNA damage. Toxicology and carcinogenesis studies on turmeric oleoresin revealed that ingestion of turmeric oleoresin resulted in an increased incidence of inflammation, hyperplasia, and ulcers of caecum and colon in male rats and thyroid gland follicular cell hyperplasia in the female rats. Similarly, in one of the studies, it was reported that curcumin can promote lung cancer in mice.

| S.No. | Cause for the low bioavailability | Data | Reason attributed | Reference |
|-------|--|--|--|--|
| 1. | Low solubility in aqueous gastrointestinal fluids | N/A | Highly hydrophobic nature | Tønnesen & Karlsen 1985). |
| 2. | Low chemical stability at physiological pH | At pH of 3–6.5 half-life ~100–200 minutes. At pH of 7.2–8.0 half-life 1–9 minutes | Radical-dependent oxidation process | Gordon et al. 2015; Griesser et al. 2011, Nimiya et al. 2016; Schneider et al., 2015 |
| 3. | low absorption in the gastrointestinal tract (GIT) | main absorption site of curcumin in the GIT is in the small intestine | Lipophilic phenolic compound and rapid metabolism and conjugation | Prasad et al. 2014 |
| 4. | Rapid metabolism in the GIT and liver | N/A | two phenolic groups, making it susceptible to detoxification enzymes | Sanidad et al. 2019 |

Methods to increase the bioavailability

| | |
|-----------------------|--------------------------|
| Nano suspension | Liposome |
| Polymer conjugates | Nanoemulsion |
| Magnetic nanoparticle | Polymeric nanoparticle |
| Micelles | Solid lipid nanoparticle |
| Nano hydrogel | |

In fact, the number of reports showing a positive effect of curcumin is much higher than those showing the toxic effect, which may be due to the fact that more scholars are busy evaluating the positive effect of curcumin than its toxicity. It is the opinion that future research is needed to establish the benefit-to-risk ratio of curcumin.

Conclusion

Curcumin is listed with numerous applications such as food colorants, medicinal and other health benefits. But still, it is hard to find a direct application in medicine due to its low bioavailability. Although numerous methods have been evolved to increase bioavailability still it is necessary to find out the best suitable method which is effective and economical. One area of further research in curcumin is to validate the health benefits along with its toxicity nature which is also being reported by some researchers.

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News in Focus

34th DBT Foundation Day Celebrated



Department of Biotechnology, Ministry of Science & Technology, today celebrated its 34th Foundation Day at the National Institute of Immunology (NII), New Delhi.

Calls upon all scientists to engage themselves in innovative ideas for “India@ 75” Dr. Harsh Vardhan Announces launching of “M K Bhan Young Investigators’ Research Award” by DBT Gives away DBT BRITE Awards to 34 scientists India rated among top 12 biotechnology destinations in the world

Speaking on the occasion, the Chief Guest, Minister for S&T, Earth Sciences and MoH&FW, Dr. Harsh Vardhan congratulated the Department of Biotechnology for its pioneering work over the years and called upon all scientists to engage themselves in innovative ideas and work to meet new challenges by the time the nation celebrates its 75 years of independence in 2022 to realise the vision of the Prime Minister Shri Narendra Modi of a new India. Dr. Harsh Vardhan also called upon young scientists and awardees to come up with new solutions for the event which he called as 'India @ 75'.

The Minister acknowledged the immense contribution made by former Secretary DBY, Prof. M K Bhan whom we had lost very recently. He announced launching of "M K Bhan Young Investigators' Research Award" in Prof. Bhan's memory by DBT to promote young investigators working in challenging areas of research.

Dr. Harsh Vardhan praised the Department's efforts in launching three New National Level Initiatives as a part of the 100 Day Programme:

- Launch of Genome India;
- Biotech KISAN hub in all Aspirational Districts and
- Waste to value technologies

The Minister also gave away the Awards to 34 recipients on the occasion. Department since its inception has instituted various awards to encourage and recognize the contribution of scientists working in various research institutes, universities, scientific organizations, national laboratories etc at different levels across the country. Various awards instituted by DBT are now considered under an overarching umbrella as DBT BRITE Awards [Biotechnology Research Innovation and Technology Excellence Awards]. The Department has renamed few awards in honour of outstanding scientists of our country who have immensely contributed to the Indian Science and been an inspiration to scientific fraternity across the globe.

DBT BRITE Awards constitutes the following awards hosted by DBT:

- Har Gobind Khorana-Innovative Young Biotechnologist Award
- S. Ramachandran-National Bioscience Award for Career Development
- Janaki Ammal National Women Bioscientist Award
- Tata Innovative Fellowship Award
- Biotechnology Social Development Award
- Eminent scientist Padma Shri Dr. D Balasubramaian, Emeritus Director, LV Prasad Eye Institute, Hyderabad delivered the DBT Foundation day lecture.

The Minister also released a publication by the Department "Biotechnology- Contributing to Growing Bioeconomy".

The biotechnology sector in India has evolved over the last three decades and has made significant contribution in various sectors especially health, agriculture etc. Due to enormous support received both from government & private sector biotechnology sector has seen a rapid growth amounting to an annual growth rate of nearly 20%. India is rated among top 12 biotechnology destinations in the world.

It is the demand for biotechnology products and services that has been the fulcrum for setting an ambitious target of US\$150 billion by 2025. Looking at the growth prospects, biotech sector plays a significant role in addressing major global challenges in sectors like health care, agriculture, energy, live stock etc.

Karnataka to set up nano technology park, to come out with new S&T policy



The Karnataka government has plans to develop a nano park here and also come out with a new science and technology policy. In his inaugural address to the eleventh edition of Bengaluru India Nano 2020, Chief Minister B S Yediyurappa said the proposed park would be in collaboration with the Government of India.

Deputy Chief Minister C N Ashwath Narayan said the nano park proposal is being discussed with Prof C N R Rao, National Research Professor, Honorary President, Jawaharlal Nehru Centre for Advanced Scientific Research and Chairman of Karnataka's Vision Group of Nanotechnology.

"we expect many of the research centres to be established in Bengaluru to promote the (nano technology) ecosystem, to strengthen this industry," Ashwath Narayan, who holds the IT, BT and S&T portfolios, said. He also said the government plans to come out with a new

science and technology policy to promote research and development and related industries.

The two-day Bengaluru India Nano 2020 is a premium event of the Karnataka's Department of IT, BT and S&T, and is being held in association with the Vision Group.

Cabinet clears abortion, surrogacy, assisted reproductive tech Bills; Champions women's rights

The Union Cabinet chaired by Prime Minister Narendra Modi has approved the Assisted Reproductive Technology Regulation Bill, 2020, a historic Bill for the welfare of women in the country. This follows the introduction in Parliament of the Surrogacy Regulation Bill, 2020, and the approval of the Medical Termination of Pregnancy (Amendment) Bill, 2020. These legislative measures are steps to protect women's

reproductive rights.

The National Board shall lay down a code of conduct to be observed by persons working at clinics, to set the minimum standards of physical infrastructure, laboratory and diagnostic equipment, and expert manpower to be employed by clinics and banks.

The Bill provides for the National Registry and Registration Authority to maintain a central database and assist the National Board in its functioning, and proposes for a stringent punishment for those practising sex selection, sale of human embryos or gametes, and running agencies, rackets, or organisations for such unlawful practices.

The major expected benefit of the Act will be that it will regulate the assisted reproductive technology (ART) services in the country. Consequently, infertile couples will be more ensured and confident of the ethical practices in ARTs.

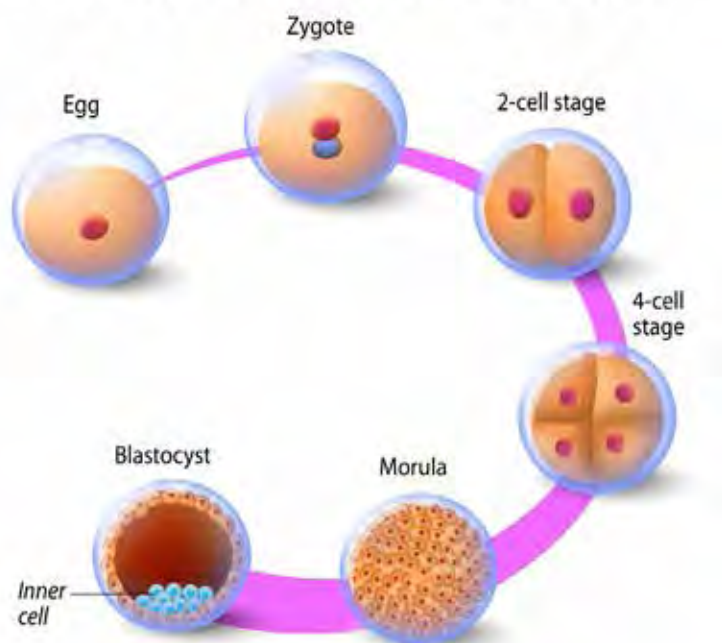
The Surrogacy (Regulation) Bill, 2020, proposes to regulate surrogacy in India by establishing a National Board at the central level, and State Boards and appropriate authorities in the states and Union Territories. The Bill has been examined by the Select Committee and the report has been tabled in the Rajya Sabha on 5 February.

The major benefit of the Act is that it will regulate the surrogacy services in the country. While commercial surrogacy will be prohibited – including sale and purchase of human embryos and gametes – ethical surrogacy to Indian married couples, Indian-origin married couples, and Indian single women (only widows or divorcees) will be allowed on fulfillment of certain conditions. As such, it is expected to control unethical practices in surrogacy, prevent commercialization of surrogacy, and prohibit potential exploitation of surrogate mothers and children born through surrogacy.

The Medical Termination of Pregnancy Act, 1971 (34 of 1971), was enacted to provide for the termination of certain pregnancies by registered medical practitioners and for connected or incidental matters. The Act recognised the importance of safe, affordable, and accessible abortion services to women who need to terminate pregnancy under certain specified conditions. Besides this, several writ petitions have been filed before the Supreme Court and various High Courts seeking permission for aborting pregnancies at gestational age beyond the present permissible limit on the grounds of foetal abnormalities or pregnancies due to sexual violence faced by women.

Taken together, the Govt says the three proposed legislations create an environment of safeguards for women's reproductive rights, addressing changing social contexts and technological advances.

DEVELOPMENT OF THE EMBRYO



Thermo Fisher Expands Diagnostics Capabilities with \$11.5 Billion Takeover of Qiagen

Waltham, Massachusetts-based Thermo Fisher Scientific is acquiring QIAGEN N.V., based in Venlo, The Netherlands. Thermo Fisher is offering 39 euros per share in cash for a transaction total of about \$11.5 billion. It is also taking on \$1.4 billion of net debt.

In March 2019, Thermo Fisher acquired Brammer Bio, a gene and cell therapy manufacturer, for \$1.7 billion in cash. Brammer Bio is a contract development and manufacturing organization (CDMO) focused on manufacturing viral vectors for gene and cell therapies. In July of last year, Amicus Therapeutics inked a strategic manufacturing deal with Brammer.

This announcement makes it one of Thermo Fisher's largest deals after the 2014 acquisition of Life Technologies Corp. for \$13.6 billion. That deal allowed Thermo Fisher to pick up Life Tech's DNA-testing capabilities.

Qiagen's Peer Schatz, who had been the company's chief executive officer for 15 years, stepped down in October 2019. The company explored possible sale options after receiving approaches from buyers, then halted them in December, stating they weren't compelling enough. However, Qiagen indicates its board backs the Thermo Fisher deal.

Qiagen employs about 5,100 staffers at 35 sites in more than 25 countries. In 2019, it brought in \$1.53 billion in revenue. Thermo Fisher will benefit from the company's molecular diagnostics technology, including infectious disease testing, as well as its innovative sample preparation, assay and bioinformatics technologies. Thermo Fisher has a market capitalization of more than \$122 billion.



World's Largest Stem Cell Bio-Bank Launched at Lund University

To increase the understanding of how these diseases arise, a new biobank, the world's largest stem cell biobank was launched at Lund University in Sweden. This biobank had stem cells from both healthy and affected individuals. Professor of molecular neurogenetics at Lund University, Johan Jakobsson says, "We will be able to study the consequences of human genetic variation and how this contributes to disease using this biobank."



At Lund University, this initiative is a collaboration between the Stem Cell Center and Diabetes Centre. Researchers from all over the world can apply for and gain access to the biobank, which will include around 100 stem cell lines.

Hindrik Mulder says, "Researchers who are working to control or contribute to the development of major global diseases by working on fundamental questions relating to genetic, cellular, biochemical and molecular processes will have the access to the stem cell lines."

First, a skin biopsy or a blood sample is used. Then, the blood cells or the skin cells are reprogrammed into iPS cells or pluripotent stem cells. Almost any mature cell type in the body can be developed by these cells; muscle cells, liver cells, nerve cells, insulin cells, etc. The type of cell required depends on what the research study is.

At Lund University, the researchers plan to map DNA's genetic code by extracting DNA from the iPS cells and analyzing them. By doing so, we can identify the majority of all genetic variants in the individual's genetic material and we can investigate their significance for disease emergence. Hindrik Mulder and Johan Jakobsson, both use the gene-editing technology CRISPR in their research.

Hindrik Mulder concludes, "A gene variant that causes a disease can be changed to one that does not have a negative impact by using CRISPR. The mature cells created from stem cells can be compared with and without disease-generating gene variants. For example, we can predict which drugs are potential treatments by testing new drugs in these different cells."

University of Hyderabad life sciences incubator ASPIRE BioNEST among top 10: According to a survey



ASPIRE-BioNEST of University of Hyderabad (UoH) was placed in sixth position among life sciences incubators in the country in a survey conducted by BioSpectrum India, a leading B2B media platform in life sciences. The survey focused on BioIncubators, both private and public, based on their achievements in the past financial year.

Four parameters — number of incubatees, funds raised, space available and pacts signed by BioIncubator with other agencies to attract enterprises/ entrepreneurs — were considered for the rankings. ASPIRE-BioNEST located in the School of Life Sciences of UoH is a 20,000-sq.ft. facility dedicated deep science incubation space.

The facility was inaugurated on February 28, 2018, and presently has 21 incubatees in diverse areas of life sciences such as agri-biotech, biologics, healthcare, pharmaceuticals and IT for life sciences.

“It is a matter of pride to figure in the top 10 of the Life Sciences incubators in the country, but we should not rest on these laurels and strive for higher goals,” said UoH Vice-Chancellor Appa Rao Podile.

The life sciences school has over 60 faculty members, 60 post docs, 350 Ph.D scholars and 300 PG students. It has two more incubators — Technology Business Incubator focused on chemicals, materials, energy etc., supported by Department of Science and Technology, and Technology Incubation and Development of Entrepreneurs focused on electronics and IT and ITeS, supported by Ministry of Electronics and IT.

Union Budget 2020: How much allocated for science

The Department of Biotechnology (DBT) posted the largest increase, with an outlay of ₹2,786 crore, a 17% increase from the ₹2,381 crore it spent last year.



The Department of Science and Technology got a 14% hike, at ₹6,301 crore, over its expenditure last year, the Earth Sciences Ministry posted a 14% hike at ₹2,070 crore and the Council of Scientific and Industrial Research got a 10% hike at ₹5,385 crore.

Overall, the science Ministries received ₹16,542 crore, 13% more than what was spent last year. In previous years, science departments generally posted percentage hikes that were in the single digits, and this is the first time in at least three years that all departments have posted double digit percentage hikes.

“Generally, the hikes revolve round 7%, but this time there’s been a significant signal of the government’s encouragement to scientific endeavours,” said Renu Swarup, Secretary, Department of Biotechnology, “The genomics initiatives as well as encouragement to set up knowledge transfer clusters are among the key sectors that have got a boost.”

The DBT has embarked on projects to map the genes of Indians as well the genetic structure of every plant variety. Another official said the government’s expenditure on science had nearly doubled since 2014.

NEWS: Govt. & Industry

Abbott India launches vaccine against 4 strains of influenza virus

Abbott India on Monday announced the launch of an inactivated vaccine in India against four strains of influenza virus.

“It is the only 0.5 ml quadrivalent flu vaccine in India that has been approved for use in children below 3 years. In fact, it can be given to children from 6 months onwards, and to adults,” the company said in a statement.

An inactivated influenza vaccine is beneficial in high risk population, since it can be given to a larger set of people, such as pregnant women, children below 2 years, older adults and immunocompromised patients, the company said.

“We are excited with the launch of the quadrivalent version of our flu vaccine, which can be offered to both children above 6 months and adults. This particular type of vaccine provides good immune response with less side-effects,” Abbott India medical director Srirupa Das was quoted as saying in the release.

Quoting a recently published study Abbott India claimed that the tetravalent vaccine demonstrated immune response compared with the some B-strains trivalent vaccines against influenza, with comparable safety.

Influenza A and B are the two strains of viruses that cause human disease, with B strain of viruses estimated to be associated with 25% of all influenza related mortality, as per the release.



Jawed Zia quits Abbott India

Almost two years after he joined Abbott India Ltd NSE 7.92 % (AIL) as Vice President established pharmaceuticals, Jawed Zia, quit Abbott, the company confirmed. Sources told ET that he is leaving due to “personal reasons” and his last day is February 29.

Jawed had joined Abbott, India’s second largest drug maker in June 2018.

Prior to Abbott, he was the Country President, Novartis India, as well as the Pharma Division Head of Novartis Pharmaceuticals.



He had joined Novartis in 1987. During his stint in Novartis he held various functions, including market research, brand management, marketing, division and area management, in countries across the globe such as Ireland, Saudi Arabia, Turkey, Singapore, Canada, Switzerland, and India.

Jawed, a graduate of Clinical Pharmacology from the All India Institute of Medical Sciences (AIIMS) studied Business Administration from Trinity College, Dublin, Ireland. His experience includes roles in pharmaceuticals, consumer health and devices.

Ambati Venu will take over as the Vice President of Abbott’s pharmaceutical business in India beginning March 1, 2020. Venu replaces Jawed Zia, who is leaving Abbott effective February 29,” the company said in a statement.

Prior to this role, Ambati Venu was the Managing Director of Abbott’s listed entity, Abbott India Limited, it further said.

The company will announce Venu’s successor at a later stage.

Biological E Inaugurates its Hyderabad Plant and Unveils New Typhoid Conjugate Vaccine

K T Rama Rao, Minister for Information Technology, Industries & Commerce, Municipal Administration and Urban Development, Government of Telangana, inaugurated Biological E. Limited’s (BE) Plant and unveiled its new Typhoid Conjugate Vaccine (TCV) in the Special Economic Zone at Genome Valley in Kolthur Village on the outskirts of Hyderabad.

Mahima Datla, Managing Director, Biological E. Limited, said: “BE has invested around Rs.300 crore for building this plant, which is now ready for commercial production, on about 29 acres of land. This Plant would generate employment opportunities for around 1000 people. This new facility will help our existing Vaccines Plant enhance the production and manufacture new products, which are in the pipeline.”



Recently, BE received the authorisation from the health regulatory authorities of India to license and market a new Typhoid Conjugate Vaccine. The approval from the Central Drugs Standard Control Organisation (CDSCO) is based on a thorough assessment of the vaccine's efficacy and safety profile.

TCV is an injectable single-dose vaccine to be administered to children from 6 months old as well as adults and it contains Vi Polysaccharide derived from *C. Freundii* conjugated to CRM197 protein. The clinical studies conducted in India demonstrated that the safety and immunogenicity profiles of this vaccine are comparable to the other licensed and WHO Pre-qualified Typhoid conjugate vaccine.

This vaccine was developed in partnership with the GSK Vaccines Institute for Global Health, based in Si-

ena (Italy), which first developed the asset and transferred it to BE in 2013.

Subsequent developmental work on the vaccine was done by BE, including manufacturing process optimization and scale up, pre-clinical studies and full clinical trials in India. This vaccine will be manufactured in BE's GMP manufacturing facilities in Hyderabad, India and could be commercially available within 3 months.

With this authorization from CDSCO the vaccine is now approved to be marketed in India, and it also allows BE to submit the vaccine for WHO pre-qualification (PQ) and registration in several other countries. This will help to expand its current portfolio of seven WHO PQ vaccines.

Biogen and Sangamo Ink \$2.7 Billion+ Neurodegeneration Deal



Biogen and Sangamo Therapeutics announced a broad global licensing collaboration deal to develop and commercialize several compounds for a range of neurological and neuromuscular diseases.

Under the deal they will work to develop and commercialize ST-501 for tauopathies, diseases caused by abnormal tau proteins, such as Alzheimer's disease, and ST-501 for synucleinopathies, neurodegenerative diseases marked by abnormal accumulation of alpha-synuclein proteins, such as Parkinson's disease.

They will also work on a third undisclosed target for neuromuscular disease and up to nine more undisclosed neurological disease targets. The agreement revolves around using Sangamo's proprietary zinc finger protein (ZFP) technology that is delivered by way of adeno-associated virus (AAV). In other words, it is a

type of gene therapy.

"As a pioneer in neuroscience, Biogen will collaborate with Sangamo on a new gene regulation therapy approach, working at the DNA level, with the potential to treat challenging neurological diseases of global significance," said Alfred Sandrock Jr., executive vice president, Research and Development, at Biogen. "We aim to develop and advance these programs forward to investigational new drug applications."

Biogen is plunking down \$350 million up front, with \$125 million a license fee payment and \$225 million in new Sangamo stock, coming to about 24 million shares at \$9.21 per share. Sangamo will be eligible for up to \$2.37 billion in various milestone payments, including up to \$925 million in pre-approval milestone payments and up to \$1.445 billion in first commercial sale and other sales-based milestone payments. Sangamo will also be eligible for tiered high single-digit to sub-teen double-digit royalties on any sales of products coming out of the partnership.

Biogen gains exclusive global rights to ST-501 for tauopathies and ST-502 for synucleinopathies, as well as the third undisclosed target, and up to nine more undisclosed targets for five years. Sangamo will handle early research activities and the expenses will be shared by the companies. Biogen will then take over responsibility and costs for investigational new drug-enabling research, clinical development, regulatory submissions and global commercialization.

Sangamo will handle GMP manufacturing operations for the initial clinical trials for the first three products, with expectations of using its in-house manufacturing capabilities. Then Biogen will take over GMP manufacturing activities beyond the first clinical trial.

In preclinical research, ST-501 and ST-502 have repressed both the proteins tau and alpha synuclein, respectively. It's a very long ways from preclinical work and effective medications for these types of neurodegenerative diseases, however. Still, investors seem pleased with it, with Sangamo shares climbing 39% at the news.

FDA to Study Instagram and Social Media Influencers



The U.S. Food and Drug Administration (FDA)'s Office of Prescription Drug Promotion (OPDP) is interested in how social media affects the public's perception of drugs. So the agency is running two studies, one that will focus on Instagram influencers while the other will study print direct-to-consumer (DTC) advertising.

Notoriously, Kim Kardashian West in 2015 received an FDA warning letter after she promoted Diclegis, a so-called morning sickness pill, on her Instagram feed. The letter indicated that she had failed to mention any safety issues associated with the drug.

As part of the study, the FDA will evaluate two different forms of disclosure language, one "direct and more consumer-friendly" and the other "less direct."

The FDA, at least for the purposes of the study, defined an "influencer" as "a 'regular' person who gained a following on a blog, a Twitter feed or other social media medium."

The agency expects to recruit 654 people from the general population who report familiarity with the celebrity for a fictitious acne product, although the agency has not divulged that person's identity.

The people chosen will be randomly assigned to see one of the endorsements and to see the advertisement with or without the payment disclosure, which the agency indicates will be something along the lines of "[Endorser] has been paid to appear in this ad for Drug X."

The second study will evaluate two endorser types, patient and Internet influencer in addition to "the explicitness of the payment disclosure." To do so they will use a direct disclosure, such as "Paid Ad", indirect, such as #sp for "sponsored," or no disclosure. This will be on Instagram for a fictitious endometriosis product.

For this study, a subset of 698 people who follow the Instagram influencer will be recruited. They indicate that this Instagram influencer has more than 500,000 followers.

The FDA stated, "In both studies, we are interested in the role of endorsement and payment status on participants' recall, benefit and risk perceptions and behavioral intentions," including "attention to disclosure statement and risk/benefit information; retention of risk/benefit information; recognition of piece as promotion and endorser as paid; perceived benefits and risks, attitudes toward the product, endorser and ad; and behavioral intentions such as asking a doctor about the drug."

Gilead to Acquire Forty Seven for \$4.9 Billion



Gilead Sciences, Inc. (Nasdaq: GILD) and Forty Seven, Inc. (Nasdaq: FTSV) announced that the companies have entered into a definitive agreement pursuant to which Gilead will acquire Forty Seven for \$95.50 per share in cash. The transaction, which values Forty Seven at approximately \$4.9 billion, was unanimously approved by both the Gilead and Forty Seven Boards of Directors and is anticipated to close during the second quarter of 2020, subject to regulatory approvals and other customary closing conditions.

Through the addition of Forty Seven's investigational lead product candidate, magrolimab, the acquisition will strengthen Gilead's immuno-oncology research and development portfolio. Magrolimab is a monoclonal antibody in clinical development for the treatment of several cancers for which new, transformative medicines are urgently needed, including myelodysplastic syndrome (MDS), acute myeloid leukemia (AML) and diffuse large B-cell lymphoma (DLBCL). The investigational therapy targets CD47, a "do not eat me" signal that allows cancer cells to avoid destruction thereby permitting the patient's own innate immune

system to engulf and eradicate those cancer cells. Forty Seven presented promising results of a Phase 1b study of magrolimab in patients with MDS and AML at the American Society of Hematology meeting in December 2019. Magrolimab has the potential to be a first-in-class therapy.

"This agreement builds on Gilead's presence in immuno-oncology and adds significant potential to our clinical pipeline," said Daniel O'Day, Chairman and Chief Executive Officer of Gilead Sciences. "Magrolimab complements our existing work in hematology, adding a non-cell therapy program that complements Kite's pipeline of cell therapies for hematological cancers. With a profile that lends itself to combination therapies, magrolimab could potentially have transformative benefits for a range of tumor types. We are looking forward to working with the highly experienced team at Forty Seven to help patients with some of the most challenging forms of cancer."

"This is an exciting day for patients who may one day benefit from future anti-CD47 therapies and other immuno-oncology treatments based on our research and an exciting time for Forty Seven as this allows us to achieve our vision of helping patients defeat their cancer," commented Mark McCamish, MD, PhD, President and Chief Executive Officer of Forty Seven. "We are pleased to join Gilead and believe that by combining our scientific expertise with Gilead's strength in developing treatments that modify the immune system, we will be able to more rapidly advance our therapies."

Under the terms of the merger agreement, a wholly-owned subsidiary of Gilead will promptly commence a tender offer to acquire all of the outstanding shares of Forty Seven's common stock at a price of \$95.50 per share in cash. Following successful completion of the tender offer, Gilead will acquire all remaining shares not tendered in the offer through a second step merger at the same price as in the tender offer.

Consummation of the tender offer is subject to a minimum tender of at least a majority of outstanding Forty Seven shares plus Forty Seven shares underlying vest-

ed options, the expiration or termination of the waiting period under the Hart-Scott-Rodino Antitrust Improvements Act and other customary conditions.

Gilead plans to pay all cash consideration for the transaction. The tender offer is not subject to a financing condition.

Citi and J.P. Morgan are acting as joint financial advisors to Gilead. Centerview Partners LLC is acting as the exclusive financial advisor to Forty Seven. Skadden, Arps, Slate, Meagher & Flom LLP is serving as legal counsel to Gilead and Cooley LLP is serving as legal counsel to Forty Seven.

Merck and AMCM / EOS Cooperate in 3D Printing of Tablets

Merck, a leading science and technology company and AMCM, Starnberg, Germany, today announced a cooperation agreement on the 3D printing of tablets. AMCM offers customized additive manufactur-

ing solutions and is a sister company of 3D printing worldmarket leader EOS. The cooperation targets GMP-conform (Good Manufacturing Practice) tablet formulation development and production for clinical trials in a first step and later also commercial manufacturing services.

“Our partnership with AMCM / EOS has the potential to revolutionize the way tablets are produced. It will be a massive move towards digitalization of the industry,” said Isabel de Paoli, Chief Strategy Officer at Merck. “Our goal is to develop the industrial application of this technology, which we will make available for clinical trials first, and then move to full digital solutions at commercial scale.”

Marie Langer, CEO of EOS, added, “We are excited to support Merck on its innovation journey. This cooperation combines Merck’s formulation competences in Healthcare as well as its excipient expertise in Life Science with our long-standing additive manufacturing know-how. Together, we will help make drug development more flexible and faster.”

Through this partnership, a novel, simplified process in clinical development of drugs can be enabled by using powder bed fusion methods, whereby a laser melts and fuses powder together layer by layer. In addition, 3D printing allows for API (active pharmaceutical development) formulation to be scalable while avoiding costly reformulations throughout the entire pharmaceutical development and commercial production processes. As a result tablet manufacturing can become faster and cheaper.

Beyond the aforementioned objectives, the vision is to allow flexible and sustainable local tablet production according to specific market requirements as well as adaptation to patient needs.

Next-generation tablet manufacturing through 3D printing is a project in the Innovation Center at Merck headquarters in Darmstadt, Germany. Here, project teams work on developing and upscaling ideas to create new businesses between and beyond the three Merck business sectors of Healthcare, Life Science and Performance Materials.



Second patient has been cured of HIV, study suggests



A study of the second HIV patient to undergo successful stem cell transplantation from donors with a HIV-resistant gene, finds that there was no active viral infection in the patient's blood 30 months after they stopped anti-retroviral therapy, according to a case report published in *The Lancet HIV* journal and presented at CROI (Conference on Retroviruses and Opportunistic Infections).

Although there was no active viral infection in the patient's body, remnants of integrated HIV-1 DNA remained in tissue samples, which were also found in the first patient to be cured of HIV. The authors suggest that these can be regarded as so-called 'fossils', as they are unlikely to be capable of reproducing the

virus.

In 2011, another patient based in Berlin (the 'Berlin patient') was the first HIV patient to be reported cured of the virus three and half years after undergoing similar treatment. Their treatment included total body irradiation, two rounds of stem cell transplant from a donor who carried a gene (CCR5 Δ 32/ Δ 32) that is resistant to HIV, and a chemotherapy drug regimen. The transplant aims to make the virus unable to replicate in the patient's body by replacing the patient's immune cells with those of the donors, whilst the body irradiation and chemotherapy targets any residual HIV virus.

The patient reported in this study (the 'London patient'), underwent one stem-cell transplantation, a reduced-intensity chemotherapy drug regimen, without whole body irradiation. In 2019, it was reported that their HIV was in remission, and this study provides follow-up viral load blood test results at 30-months and a modelling analysis to predict the chances of viral re-emergence.

Ultrasensitive viral load sampling from the London patient's cerebrospinal fluid, intestinal tissue, or lymphoid tissue was taken at 29 months after interruption of ART and viral load sampling of their blood at 30 months. At 29 months, CD4 cell count (indicators of immune system health and stem cell transplantation success) was measured, and the extent to which the patient's immune cells have been replaced by those derived from the transplant.

Results showed no active viral infection was detected in samples of the patient's blood at 30 months, or in their cerebrospinal fluid, semen, intestinal tissue, and lymphoid tissue 29 months after stopping ART.

The patient had a healthy CD4 cell count, suggesting they have recovered well from the transplant, with their CD4 cells replaced by cells derived from the HIV-resistant transplanted stem cells.

Furthermore, 99% of the patient's immune cells were derived from the donor's stem cells, indicating the stem-cell transplant had been successful.

First coronavirus vaccine trial in the US is recruiting volunteers



Researchers in Seattle have begun recruiting healthy volunteers to participate in a clinical trial for an experimental COVID-19 vaccine, according to news reports.

Massachusetts-based Moderna shipped its first batch of mRNA-1273, a vaccine against the virus, for a planned Phase I clinical trial in the U.S. mRNA-1273 is a mRNA vaccine that encodes for a prefusion stabilized form of the Spike (S) protein.

The vaccine, developed by the biotechnology company Moderna Therapeutics, was initially sent to the National Institute of Allergy and Infectious Diseases (NIAID) in Maryland on Feb. 24, according to The Wall Street Journal. The agency anticipates launching a clinical trial by the end of April and will sponsor the Kaiser Permanente Washington Health Research Institute to conduct the testing, NIAID Director Anthony Fauci told The Wall Street Journal.

Forty-five healthy volunteers between the ages of 18 and 55 will be enrolled in the initial trial, which aims to determine whether the vaccine triggers an immune response, and whether the given dose causes adverse

side effects, according to a description on ClinicalTrials.gov.

Takeda Acquires Celiac-Focused PVP Biologics in Deal Worth \$330 Million

Three years after Takeda and San Diego-based PVP Biologics inked a \$35 million deal to develop a novel treatment for celiac disease, the Japanese pharma company has exercised its option to acquire the company for \$330 million.

Takeda and PVP will enter into the agreement following the conclusion of the Phase I trial for TAK-062 (also known as Kuma062), which is being developed for uncontrolled celiac disease. In 2018, PVP initiated its first-in-human clinical studies for Kuma062, a uniquely engineered, recombinant enzyme that is active under acidic stomach conditions and has high specificity for the parts of gluten that cause the au-



to immune reaction leading to celiac disease. In its announcement, Takeda said TAK-062 is a potential best-in-class treatment that was computationally engineered to treat celiac disease.

The acquisition of PvP will enhance Takeda's commitment to developing treatments for gastrointestinal disorders. TAK-062 represents the second celiac-focused product in the company's arsenal. In October, Takeda acquired the license for a first-in-class celiac treatment from COUR Pharmaceuticals.

TAK-101 is an immune modifying nanoparticle-containing gliadin proteins. The company struck the deal with COUR following positive Phase IIa proof-of-concept. In the study, TAK-101 demonstrated T-cell response suppression, suggesting that it may induce tolerance to gluten in patients with celiac disease by immune uptake of proprietary nanoparticles loaded with gliadin proteins, a disease-specific antigen.

When the acquisition of PvP is complete, Takeda plans to initiate a Phase IIb efficacy and dose-ranging trial for TAK-062 in celiac patients who maintained a gluten-free diet. The company also plans to submit data from the Phase I safety and tolerability study for presentation at an upcoming medical congress.

"PvP Biologics' work demonstrated that TAK-062 is a highly targeted therapy that could change the standard of care in celiac disease. We are now applying our deep expertise in gastrointestinal diseases to advance the clinical study of TAK-062 and TAK-101, two programs with different modalities that have both demonstrated clinical proof of mechanism," Parikh said in a statement.

TAK-062 works by enzymatically digesting gluten. It is designed to degrade the immune-reactive parts of gluten before they exit the stomach in order to prevent the immune response to gluten and eliminate the symptoms and intestinal damage caused by celiac disease.

The medication has demonstrated enhanced catalytic activity compared to other glutenases, Takeda said.

The Median Cost of Bringing a Drug to Market is \$985 Million, According to New Study



The study notes that estimates have ranged from \$314 million to \$2.8 billion. The authors were Oliver Wouters, an assistant professor of Health Policy at the London School of Economics and Political Science, Martin McKee, professor of European Public Health at the London School of Hygiene & Tropical Medicine, and Jeroen Luyten an associate professor of the Faculty of Medicine at the Department of Public Health and Primary Care with the Leuben Institute for Healthcare Policy.

The research included 63 of 355 new therapeutic drugs and biologics approved by the U.S. Food and Drug Administration (FDA) between 2009 and 2018. They note that data was mainly found for smaller companies, products in specific therapeutic areas, orphan drugs, first-in-class drugs, and drugs that received accelerated approval. The data came from 47

disease (COVID-19) pneumonia



different companies.

They found that the estimated median capitalized research and development cost per therapeutic product was \$985 million.

The authors wrote, “After accounting for the costs of failed trials, the median capitalized research and development investment to bring a new drug to market was estimated at \$985 million (95% CI, \$638.6 million - \$1228.9 million), and the mean investment was estimated at \$1335.9 million (95% CI, \$1042.5 million - \$1637 million) in the base case analysis.”

The median estimates for therapeutic areas that had five or more drugs ranged from \$765.9 million for nervous system therapeutics to \$2.7716 billion for cancer and immunomodulating drugs.

The authors note that the primary difference for their study from others available is they relied on publicly available data.

A study published by the Tufts Center for the Study of Drug Development published in the Journal of Health Economics in May 2019, gave an estimated cost of \$2.6 billion. That study broke down the number to include approximate average out-of-pocket costs of \$1.4 billion and time costs of \$1.2 billion.

The Tufts study evaluated the R&D costs of 106 randomly chosen new drugs from a survey of 10 pharmaceutical companies. The drugs were approved from 1995 to 2007. They then calculated the average pre-tax cost of new drug and biologics development. They also included the costs related to abandoned trials and development. They also found that adding an estimate of post-approval R&D costs increased the cost estimate to \$2.870 billion in 2013 dollars.

Chest CT findings in coronavirus

A multi-center study (n=101) of the relationship between chest CT findings and the clinical conditions of coronavirus disease (COVID-19) pneumonia -- published ahead-of-print and open-access in the American Journal of Roentgenology (AJR) -- determined that most patients with COVID-19 pneumonia have ground-glass opacities (GGO) (86.1%) or mixed GGO and consolidation (64.4%) and vascular enlargement in the lesion (71.3%).

In addition, lead authors Wei Zhao, Zheng Zhong, and colleagues revealed that lesions present on CT images were more likely to have peripheral distribution (87.1%) and bilateral involvement (82.2%) and be lower lung predominant (54.5%) and multifocal (54.5%).

Zhao, Zhong, et al. collected their 101 cases of COVID-19 pneumonia across four institutions in China's Hunan province, comparing clinical characteristics and imaging features between two groups: nonemergency (mild or common disease) and emergency (severe or fatal disease).

Accordingly, most of the cohort (70.2%) were 21-50

years old, and most patients (78.2%) had fever as the onset symptom. Only five patients showed disease associated with a family outbreak.

While the emergency group patients were older than the patients in the nonemergency group, the rate of underlying disease was not significantly different in the two groups -- suggesting that viral load could be a better reflection of the severity and extent of COVID-19 pneumonia.

As Zhao and Zhong explained further: "Architectural distortion, traction bronchiectasis, and pleural effusions, which may reflect the viral load and virulence of COVID-19, were statistically different between the two groups and may help us to identify the emergency type disease."

The authors of this AJR article also noted that CT involvement score can help evaluate the severity and extent of COVID-19 pneumonia.

Journal Reference:

Wei Zhao, Zheng Zhong, Xingzhi Xie, Qizhi Yu, Jun Liu. Relation Between Chest CT Findings and Clinical Conditions of Coronavirus Disease (COVID-19) Pneumonia: A Multicenter Study. American Journal of Roentgenology, 2020; 1 DOI: 10.2214/AJR.20.22976

Egg stem cells do not exist, new study shows

Researchers at Karolinska Institutet in Sweden have analysed all cell types in the human ovary and found that the hotly debated so-called egg stem cells do not exist. The results, published in Nature Communications, open the way for research on improved methods of treating involuntary childlessness.

The researchers used single-cell analysis to study more than 24,000 cells collected from ovarian cortex samples of 21 patients. They also analysed cells collected

from the ovarian medulla, allowing them to present a complete cell map of the human ovary.

One of the aims of the study was to establish the existence or non-existence of egg stem cells. "The question is controversial since some research has reported that such cells do exist, while other studies indicate the opposite," says Fredrik Lanner, researcher in obstetrics and gynaecology at the Department of Clinical Science, Intervention and Technology at Karolinska Institutet, and one of the study's authors.

The question of whether egg stem cells exist affects issues related to fertility treatment, since stem cells have properties that differ from other cells.

The new study substantiates previously reported findings from animal studies -- that egg stem cells do not exist. Instead, these are so-called perivascular cells. The new comprehensive map of ovarian cells can contribute to the development of improved methods of treating female infertility, says Damdimopoulou.

"The lack of knowledge about what a normal ovary looks like has held back developments," she says. "This study now lays the ground on which to produce new methods that focus on the egg cells that already exist in the ovary. This could involve letting egg cells mature in test tubes or perhaps developing artificial ovaries in a lab."

The results of the new study show that the main cell types in the ovary are egg cells, granulosa cells, immune cells, endothelial cells, perivascular cells and stromal cells.

Journal Reference:

Magdalena Wagner, Masahito Yoshihara, Iyadh Douagi, Anastasios Damdimopoulos, Sarita Panula, Sophie Petropoulos, Haojiang Lu, Karin Pettersson, Kerstin Palm, Shintaro Katayama, Outi Hovatta, Juha Kere, Fredrik Lanner, Pauliina Damdimopoulou. Single-cell analysis of human ovarian cortex identifies distinct cell populations but no oogonial stem cells. Nature Communications, 2020; 11 (1) DOI: 10.1038/s41467-020-14936-3

Remdesivir prevents MERS coronavirus disease in monkeys

The experimental antiviral remdesivir successfully prevented disease in rhesus macaques infected with Middle East respiratory syndrome coronavirus (MERS-CoV), according to a new study from National Institutes of Health scientists. Remdesivir prevented disease when administered before infection and improved the condition of macaques when given after the animals already were infected.

The new report from NIH's National Institute of Allergy and Infectious Diseases (NIAID) appears in the Proceedings of the National Academy of Sciences.

MERS-CoV is closely related to the 2019 novel coronavirus (SARS-CoV-2, previously known as 2019-nCoV) that has grown to be a global public health emergency since cases were first detected in Wuhan, China, in December.

Remdesivir has previously protected animals against a variety of viruses in lab experiments. The drug has been shown experimentally to effectively treat monkeys infected with Ebola and Nipah viruses. Remdesivir also has been investigated as a treatment for Ebola virus disease in people.

The current study was conducted at NIAID's Rocky Mountain Laboratories in Hamilton, Montana. The work involved three groups of animals: those treated with remdesivir 24 hours before infection with MERS-CoV; those treated 12 hours after infection (close to the peak time for MERS-CoV replication in these animals); and untreated control animals.

The scientists observed the animals for six days. All control animals showed signs of respiratory disease. Animals treated before infection fared well: no signs of respiratory disease, significantly lower levels of virus replication in the lungs compared to control

animals, and no lung damage. Animals treated after infection fared significantly better than the control animals: disease was less severe than in control animals, their lungs had lower levels of virus than the control animals, and the damage to the lungs was less severe.

The scientists indicate that the promising study results support additional clinical trials of remdesivir for MERS-CoV and COVID-19, the disease that SARS-CoV-2 causes. Several clinical trials of remdesivir for COVID-19 are under way in China, and other patients with COVID-19 have received the drug under a compassionate use protocol.

The Biomedical Advanced Research and Development Authority (BARDA), part of the U.S. Department of Health and Human Services, also provided support for this study. Gilead Sciences, Inc., developed remdesivir, also known as GS-5734, and collaborated in the research.

MERS-CoV emerged in Saudi Arabia in 2012. Through December 2019, the World Health Organization had confirmed 2,499 MERS-CoV cases and 861 deaths (or about 1 in 3). Because about one-third of MERS-CoV cases spread from infected people being treated in healthcare settings, the scientists suggest that remdesivir could effectively prevent disease in other patients, contacts of patients, and healthcare workers. They also note the drug might help patients who are diagnosed with MERS or COVID-19 if given soon after symptoms start.

Journal Reference:

Emmie de Wit, Friederike Feldmann, Jacqueline Cronin, Robert Jordan, Atsushi Okumura, Tina Thomas, Dana Scott, Tomas Cihlar, Heinz Feldmann. Prophylactic and therapeutic remdesivir (GS-5734) treatment in the rhesus macaque model of MERS-CoV infection. Proceedings of the National Academy of Sciences, 2020; 201922083 DOI: 10.1073/pnas.1922083117

XVII Convention of BRSI: International Conference on Biotechnology for Sustainable Agriculture, Environment and Health (BAEH-2020)



November 8-11, 2020 Jaipur
Details: <http://brsi2020jaipur.in/>



The event will be jointly organized by the MNIT, Jaipur; CDC India, Jaipur, BISR, Jaipur and NIT-Uttarakhand in association with the International Solid Waste Association (ISWA), The Institute of Chartered Waste Managers (ICWM) and B Lal Institute of Biotechnology, Jaipur. This will be supported by the International Bioprocessing Association, France; Centre for Energy and Environmental Sustainability (CEES)-India and Amity University, Jaipur. The event will be held at BISR, Jaipur. Prof TP Singh, Prof AB Gupta and Dr Vivek Agarwal are conference chairs. Dr V Vivekanand is the convener of BAEH-2020 and Dr P Binod, COE, BRSI; Dr Krishna Mohan, BISR, Jaipur and Dr B Lal, BIB, Jaipur, Dr Rakesh Kumar Mishra, NIT-Uttarakhand are its co-conveners. Details can be found at <http://brsi2020jaipur.in/>

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NOTICES

Nominations are Invited for Shanti Swarup Bhatnagar Prize for Science and Technology 2020



The Council of Scientific and Industrial Research (CSIR) invites nominations for the Shanti Swarup Bhatnagar (SSB) Prizes in Science and Technology for the year 2020. The SSB Prizes are to be given for research contributions made primarily in India during the past five years. The age of the nominee for the SSB Prize 2020 should not be more than 45 years as on 31 December 2019.

The SSB Prizes are awarded for notable and outstanding research, applied or fundamental, in the following disciplines: (1) Biological Sciences, (2) Chemical Sciences, (3) Earth–Atmosphere–Ocean– Planetary Sciences, (4) Engineering Sciences, (5) Mathematical Sciences, (6) Medical Sciences and (7) Physical Sciences.

The SSB Prize carries a cash award, a citation and a plaque for each scientist selected for the award. Nominations addressed to The Scientist Incharge – SSB YSA Unit, Human Resource Development Group, CSIR Complex, Library Avenue, Pusa, New Delhi 110 012 should be sent as per the prescribed proforma along with reprints of significant publications of the last 5 years period on or **before 31 March 2020**. PDF version of duly filled proforma, significant publications and photograph of the proposed nominee are also required in USB/Pen drive.

The details of the SSB Prize and the prescribed proforma for nomination may be obtained from the above address or may also be downloaded from the website: www.csirhrdg.res.in



Call for 2020 applications is now open!

Apply to be a Young Investigator

Applications to the EMBO Young Investigator Programme are accepted annually in a two-stage process and must be submitted through an online system

Application process

- The deadline for pre-applications is 1 April 2020, 14:00 CEST.
- The Young Investigator Committee invites selected candidates to submit a full application and attend an interview.
- The deadline for full applications is 2 July 2020, 14:00 CEST.
- All invited candidates will be interviewed by the Young Investigator Committee on 5 or 6 November 2020.
- The final decision will be made at the Young Investigator Committee meeting.
- All applicants will be informed of the outcome of their application by email.

Required documentation

The complete application for the Young Investigator Programme consists of:

- CV
- Synopsis of recent work
- Outline of the research programme
- Short summary of research
- Publication list and list of three best papers
- Three letters of reference
- List of grants and pending grant applications
- ORCID

*Applicants must have published at least one last author research paper in an international peer reviewed journal from independent work carried out in their own laboratory. EMBO will consider papers published on preprint servers (arXiv, BioRxiv, PeerJ., etc), but a last author publication in an international peer reviewed journal is still a requirement. Your last author paper should have "accepted" status by the time of the interview (05 or 06 November 2020).

Do NOT indicate the journal impact factor. EMBO is a signatory of the San Francisco Declaration on Research Assessment (DORA), which recommends “not to use journal based metrics, such as Journal Impact Factors, as a surrogate measure of the quality of individual research articles, to assess an individual scientist’s contributions, or in hiring, promotion, or funding decisions”.

For detailed information on the application process, key dates and required documentation, please consult the application guidelines (pdf).

***For detail information please visit following link:**

<https://www.embo.org/funding-awards/young-investigators/apply#application>



ICMR Inviting application for Directors' Posts (3)

Last Date: 14th April 2020

Indian Council of Medical Research (ICMR), an Autonomous Organization under Department of Health Research, Ministry of Health & Family Welfare invites application(s) up to **14th April, 2020** till 5.30 PM for three Posts of Director at the following Institutes in Level 14 of Pay Matrix (Rs.1,44,200-2,18,200) (7th CPC Scale) and usual allowances as admissible to ICMR employees:-

- 1) National Institute of Pathology, New Delhi
- 2) National Institute for Implementation Research on Non-Communicable Diseases, Jodhpur (formerly known as Desert Medicine Research Centre (DMRC), Jodhpur)
- 3) National Institute for Research in Tuberculosis, Chennai

Indian Council of Medical Research deals with health research in various areas in collaboration with national/ international agencies through its 27 Institutes/Centres and a large number of field stations situated all over the country.

The posts are with all India transfer liability under the Council.

Essential Qualification & Experience:

i) MD/MS/DNB or equivalent degree* recognized by MCI

OR

First Class Master's degree with Ph.D from a recognized University in subjects mentioned in Annexure I

ii) 16 years R&D experience in the relevant areas (mentioned in Annexure I) from a recognized institute, (preferably 5 years in a managerial position to handle R&D projects independently) including 2 years regular service in the Pay matrix level-13-A or equivalence as per DoPT guidelines as amended from time to time**.

Out of above experience, five years should be in Managerial Research position viz., PI or Co-PI of Scientific studies.

How to apply:

Candidates should apply in the prescribed format available in ICMR website (<http://www.icmr.nic.in->Employment>permanent posts> detailed advertisement for the post of Director>)

Following self attested required documents are to be enclosed with the application :-

- a) Proof of Date of Birth
- b) Educational qualifications
- c) Experience

Filled Application duly signed by the candidate and recent passport size photograph affixed on it along with Demand Draft towards application fee and all required documents should be sent to the Dy. Director-General(Admn.)(Room No.418), Indian Council of Medical Research, P.O. Box No. 4911, V.Ramalingaswami Bhawan, Ansari Nagar, New Delhi- 110029 (India) on or before **14th April, 2020** till 5.30 PM. The name of the post and Institute/Centre for which the candidate applies must be mentioned on the top of the envelope.

AIIMS Delhi- VACANCY FOR A POST OF SENIOR RESEARCH FELLOW



Applications are invited from Indian Citizens for a temporary post of Senior Research Fellow under an DST-supported research project entitled “Contribution of glial gap junctions towards morphine tolerance in rats” in the Department of Anatomy, All India Institute of Medical Sciences, New Delhi.

Duration of project: 1 year (extendable up to 2 years more)

Stipend : Rs. 35,000 + HRA as admissible

Qualifications: Candidate should have M.Sc. in life sciences preferably, Biochemistry or Genetics with 2 years of research experience

Desirable: Knowledge in Western blotting, RT-PCR and imaging techniques like Image J, Image Proplus etc. Having research publications on these topics will be an added qualification.

Age limit : 35 years

Interested candidates may send their applications along with detailed CV and proof of research experience to the undersigned on or **before April 15, 2020**. Only short-listed candidates will be intimated via email. No TA or DA will be paid for attending the interview.

BUREAU OF INDIAN STANDARDS

Ministry of Consumer Affairs, Food & Public Distribution, (Department of Consumer Affairs), Govt. of India, Manak Bhawan, 9 Bahadur Shah Zafar Marg, New Delhi-110002



BIS provides excellent career opportunities to bright, young dynamic persons for the post of Scientist-‘ B’ in the specified disciplines and also categories. These posts are in the Pay Level 10 as per the Seventh Central Pay Commission plus allowances as suitable. The gross emoluments at the time of joining will be approximately Rs. 87,000/- at Delhi at present.

HOW TO APPLY:

Applicants are required to apply On-Line from **02.03.2020 to 31.03.2020** through BIS website www.bis.gov.in. No other means/mode of submission of applications will certainly be accepted under any circumstances.

Educational & Other Qualifications required:

Biotechnology (01 post):

- 1) Bachelor’s Degree in Engineering or Technology or equal with not less than 60% marks in aggregate (50% for SC/ST applicants).
- 2) Having valid GATE (Grad Aptitude Test in Engineering) score of 2018/2019/2020. The GATE score has to be valid as on 31.03.2020 (closing date of application).

Notice

Award of DBT-Research Associateship in Biotechnology & Life Sciences

Applications are invited from Indian Nationals for the award of “**DBT-Research Associateship**” for pursuing research in frontier areas of Biotechnology and Life Sciences. **The Associateship is tenable in Premier Research Institutions/Universities including non-profit R&D Institutions within India. The Associateships are awarded under a program sponsored by the Department of Biotechnology, Ministry of Science & Technology, Govt. of India.**

A hard copy of the Application with necessary documents should be Speed-posted to: **The National Program Coordinator, DBT-Research Associateship Program, Department of Molecular Reproduction, Development & Genetics, New Biological Sciences Building, Indian Institute of Science, Bangalore - 560012.**

Write “**Application for DBT-RA Fellowship (National)**” on the envelope. Detailed information and relevant application format may be obtained from: <https://mrdg.iisc.ac.in/dbt-ra-program/about-dbt-ra-program/>..The last date for receiving the completed application at Indian Institute of Science, Bangalore, is **March 20, 2020.**

Award of DBT-Research Associateship In Biotechnology & Life Sciences for Candidates of North –East Region

Applications are invited from Indian Nationals of North-East Origin/Region for the award of “**DBT-Research Associateship**” for pursuing research in frontier areas of Biotechnology and Life Sciences. **The Associateship is tenable in Research Institutions/Universities including non-profit R&D Institutions within India. The Associateships are awarded under a program sponsored by the Department of Biotechnology, Ministry of Science and Technology, Govt. of India.**

A hard copy of the Application with necessary documents should be Speed-posted to: **The National Program Coordinator, DBT-Research Associateship Program, Department of Molecular Reproduction, Development & Genetics, New Biological Sciences Building, Indian Institute of Science, Bangalore-560012.**

Write “**Application for DBT-RA Fellowship (North-East)**” on the envelope. Detailed information and relevant application format may be obtained from: <https://mrdg.iisc.ac.in/dbt-ra-program/about-dbt-ra-program/>.. The last date for receiving the completed application at Indian Institute of Science, Bangalore, is **March 20, 2020.**

ALL INDIA INSTITUTE OF MEDICAL SCIENCES JODHPUR

Basni Phase-II, Jodhpur-342005 (Raj)

Website: <http://www.aiimsjodhpur.edu.in>

Applications in the prescribed format are invited for the following posts on purely temporary basis for the Research Project titled “DHR-ICMR Advance Medical Oncology Diagnostic Services (DIAMONDS) under HTA In, Pilot Research Project” under Principal Investigator Dr. Sanjeev Misra & Co-Investigator Dr. Poonam Elhence, Professor & Head, Department of Pathology, AIIMS, Jodhpur as per the details given below:

Name of the Post Research Assistant

Name of the Post Scientist-C

Laboratory Technician-III

All candidates should submit the filled application in the prescribed format and Bio-data on the day of Walk-In-Interview and should appear in person for Walk-In-Interview along with all relevant original documents and one set of self-attested photocopies of documents regarding age, qualifications and relevant experience, on March 26 & 27, 2020 at 09:00 AM at the following address:

Research Section, Room No. C-116, First Floor, Medical College Building, All India Institute of Medical Sciences, Jodhpur.





School of Innovation in Biodesign (SiB) Inter-institutional Biodesign Centers

DEPARTMENT OF BIOTECHNOLOGY, GOVERNMENT OF INDIA
www.dbtindia.gov.in

A call for proposals under the DBT Biomedical engineering division



The applications must be submitted online no later than 15th April, 2020.

NATIONAL INSTITUTE OF IMMUNOLOGY NEW DELHI

(an autonomous research institute)

Aruna Asaf Ali Marg,
New Delhi-110067

'Applications are invited for Emeritus Scientist'

The National Institute of Immunology invites applications from superannuated scientists of repute who have significant pre-retirement accomplishments in the areas of immunology for engagement as Emeritus Scientist on contractual basis. The tenure of contract shall initially be for 03 years which shall be reviewed on annual basis. The tenure may further be extended beyond 03 years by 02 more years on a year to year basis subject to assessment by a Review Committee. In case of premature cessation of tenure by either party (ES or NII), a notice of one month would be required.

The conditions such as eligibility, remuneration etc. will be as under:

1. Eligibility:

- i. Should have superannuated or due to superannuate from the post of Scientist in Level-14 of Pay Matrix or above;
- ii. Should have outstanding track records during the last 5 years as evidenced by publications in reputed journals, technology transferred to industry, consultancies offered to external bodies etc;
- iii. Recognition of scientific contributions by at least two Scientific Academies or election to prestigious professional societies/forums or recipient of prestigious awards or track records of involvement in scientific advisory bodies or eloquence in science narration;
- iv. Proven leadership quality
- v. At least 25 years of research experience.

2. Remuneration: Consolidated monthly remuneration of Rs.1,00,000/- p.m. No other allowances/perquisites are permissible.

3. Duties and responsibilities:

- a) Help in fortifying the Institute's capabilities in the areas of basic and applied immunology particularly in the area of T Cell Therapy/Cancer Immunotherapy/Regenerative Medicine;
- b) Contribute towards the Institute's academic activities by way of teaching and other relevant assignments;
- c) Assist the Institute in implementation of Immuno-Engineering Programme;
- d) Assist the Institute in expanding its outreach in the areas of popularizing Science and Bio-technology with school and college students;
- e) Any other work assigned by the Director;

Eligible and interested scientists may submit their applications, with detailed curriculum vitae containing details of qualifications, positions held, professional experience/distinctions, list of notable publications/achievements, proposed research plan (2 pages) and names and contact information of three potential referees, latest by 31.03.2020 to the Director, National Institute of Immunology, Aruna Asaf Ali Marg, New Delhi-110067 or e-mail it to diroffice@nii.ac.in/dirsec@nii.res.in. The Institute reserves the right to cancel the advertisement at any time.

Jawaharlal Nehru University Entrance Examination JNUEE 2020-21



ABOUT JNUEE (JNU ENTRANCE EXAMINATION)

Admission to JNU is based on the performance of candidates in the All India Level Entrance Examination. The final selection is based upon the performance of candidates in the CBT for all programmes of study, except M.Phil. and Ph.D. For Selection in M.Phil. and Ph.D through CBT mode, candidates are called for Viva voce and final merit list is made with 70% weightage to CBT score and 30% weightage to Viva. For details kindly refer to JNU e-prospectus 2020-21 available at <https://jnu.ac.in/admission/e-prospectus-2020-20.pdf>.

SCHOOL OF LIFE SCIENCES (Eligibility)

M.Sc.

Bachelor's (B.Sc. or B.Tech or equivalent) in Biological, Physical or Agricultural Sciences or Biotechnology under the 10+2+3 pattern of education with at least 55% marks

Ph.D.

Master's degree or equivalent with at least 55% marks or equivalent Grade 'B' in UGC 7-point scale (or an equivalent Grade in a point scale wherever Grading system is followed) in Life Sciences/Biological, Physical, Chemical, or Agricultural Sciences/ Biotechnology/Botany/Zoology/Bioinformatics/Genetics/Microbiology /Systems Biology/ any other branch of biological sciences with 55% marks or equivalent. OR Master's degree in the fields given above with 55% marks (or equivalent) and obtained 2 years M.Phil Degree with at least 55% marks (or equivalent) of a recognized University/Institution (with dissertation/seminar/viva) or one year M.Phil with 55% marks (or equivalent) with additional one year research experience of a recognized University/Institution and one publication

Relaxation to SC/ST/OBC (Non creamy layer)/Differently abled as per the UGC Regulations 2016.

P.G. holders of AYUSH related subjects are also eligible to apply.

IMPORTANT DATES:

Online Submission of Application Form 02 March to 31 March, 2020 (up to 5:00 pm)

Last Date of Successful Transaction of Fee through Credit/Debit Card/Net-Banking/UPI 31 March, 2020 (up to 11:50 pm)

Dates of Examination 11, 12, 13 and 14 May, 2020 (15 May as Reserve Day)

More Info: <https://jnuexams.nta.nic.in/WebInfo/Public/Home.aspx>



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