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From the Director's Desk



DeNovo provides a platform to express the talents of the students, researchers and faculty at the Institute of Science, Nirma University (ISNU). Despite the onslaught of COVID-19 pandemic, the current year has been very eventful in the history of the institute. We completed 17 years of our journey in imparting quality education to master's students in the field of Bioscience. In 2004 we started as a teaching institute, but today we have placed ourselves among the research institutes advancing the cutting-edge research. In the western zone of India, we are one of the preferred educational institutes for higher study for our commitment to the education, training and research that enable our students to succeed in the competitive world. Efforts of last 10 years by all the members of science parivar have brought lots of vibrancy not only in the institute but also in university as whole. We as an institute might be a small constituent of Nirma University, but we have played a significant role in dignifying the University. Today faculties across the campus are lot more confident and competing with established investigators in the research community. University authorities are more ambitious and are taking encouraging steps to boost the research productivity. I am sure that the students in the Institute of Science enjoy the nurturing academic environment and are dreaming big in their personal lives. This mouth piece of ISNU reflects their emotion. I congratulate one and all including editorial team, Dr. Kuldeep Verma and Ms. Zankruti Dholakia for their contributions to bring this issue of DeNovo and I am sure you will enjoy reading it.

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ADMINISTRATIVE AND LEADERSHIP PHILOSOPHY

-Dr. Sarat K Dalai

I am an immunologist with over twenty years of post-PhD research experience and a decade of academic experience. I have worked in various capacities as a scientist, researcher, teacher, and administrator. The experience I have gained all these years has enabled me to develop my ideas/vision of an academic leader that I would like to share in this narrative.

- 1. Through the statements of vision and mission each institute/organization at the time of inception sets its aspiration and intends to achieve the goal(s) through day-to-day activities. For the same, prospective and strategic plans need to be developed for a period of every 5-10 years, monitored and evaluated at regular intervals for the effective implementation. While each member of the institute has to work in-line with the mission, the leader of the institute shoulders a greater responsibility. He/she has to provide the direction, build the institute by taking the colleagues and co-workers into confidence. Recognizing the strength of individuals directly associated with the welfare of the institute is the first step in allocating them the responsibilities. While accomplishing the tasks through the diligence of colleagues is a pragmatic approach to achieving the goals of the organization, the leader must recognize their efforts and reward them appropriately. More importantly, understanding their challenges and the difficulties they face in performing their tasks, whether it is academics or research, and facilitating the process to alleviate their problems to make them more productive should be the prime focus of the leadership. Such a compassionate conservative approach to leadership has helped me achieved many daunting tasks.
- We are living in a world of inter-dependency. The inter-disciplinary approach has become an integral part of our academic and research culture. Through collaborative efforts, we can bring in diverse ideas and expertise to solve challenging problems more effectively and meaningfully. In this effort, the academic administration/leadership would play a pivotal role in reaching out to people from diverse backgrounds within and outside the university campus, facilitating team building, and ensuring the accomplishment of tasks toward achieving the goals. While the mission of the institute would remain the top priority in the mind of leadership, the interest of each collaborator needs to be safeguarded without any bias or preconceived notion. Such an approach promotes good research culture and solves societal problems much more effectively. To develop good curricula for various academic programs, a similar approach is critical for which the department chair has to play a key role in identifying the experts in various domains, and through brainstorming discussions, the syllabi would be designed with the recommendations for sets of pedagogy.
- 3. It has been observed and experimentally proven that any work-force that is very diverse in nature brings in innovations to the organizational functioning and makes people more productive. The inclusion of men and women from different cultures and ethnic backgrounds make the work environment more pleasant and conducive for growth. Understanding the challenging problem from diverse angles and developing testable ideas according to their training that is often influenced by their social background bring in many good alternative solutions. Therefore, the leadership without any ambiguity should encourage the recruitment of committed, intelligent, and well-trained people from diverse backgrounds in the work-force of the organization. I have experienced this during my training at Johns Hopkins University, and implemented the same in my

current institute leading to best research and academic productivities among the constituent institutes of Nirma University and helping the university to get many recognitions including Grade-A score during the accreditation by NAAC (National Assessment and Accreditation Council), University Grants Commission, SIRO (Scientific and Industrial Research Organization) recognition, Govt. of India, and permanent member status of the AIU (Association of Indian Universities).

- In my personal opinion mentoring is a natural trait of any leader. Mentoring is essential for professional 4. development of any individual. Often colleagues and coworkers might be in doubt or looking for best possible solution to a given problem. Sharing the wisdom and experience combined with some useful suggestions for way-out greatly motivates and makes them very productive. It creates a good work culture and brings in more commitment and loyalty among colleagues and coworkers that is critical to the success of any good institute. Here I would like to share my own experience. Being a senior faculty member and director of the Institute, my role has been multifaceted. Besides my stipulated responsibilities, mentoring my faculty colleagues as well as the colleagues from the other institutes inside the university campus has become my spontaneous habit. Almost 50% of my colleagues are women and >60% of our students are girls in some programs. In the last 10 years of joining the current institute, my role of mentoring has incredibly helped create a good research ambiance at the Nirma University. Being a member of Board of studies of various colleges and universities in the state of Gujarat, I am helping improve their course curricula and pedagogy of teaching. Often, I take lectures to help the undergraduate students in the state of Gujarat to prepare them for various national level entrance tests for their higher studies. These efforts have directly or indirectly helped my institute in developing collaboration for research or recruiting good students for our academic programs.
- 5. Biological research is costly and resource demanding. It requires varieties of infrastructure and manpower with diverse technical expertise. The Academic program might run with the collection of fees from the students and contributions from the promoters/managing trustee. Since university academic programs are intractably associated with research programs, there is a huge need of funds to run successful academic and research programs. While government funding agencies are expected to play a major role in supporting the university activities, the fundraising from other sources including industries is very critical. In this effort, the university administration and leadership including the department chair have to work diligently. While fund mobilization is one of the prime responsibilities of leadership, fiscal conservative approach of avoiding wasteful spending on the part of administration is required to manage the budgets effectively; this will help to build and expand the necessary infrastructure for research and ensure the financial benefits to the employees.
- 6. While monitoring/overseeing the research progress of faculty colleagues becomes a prime focus of the department chair, academic delivery of faculty in their classroom teaching and providing good practical training to the students at various levels cannot be given low priority. Career counseling and facilitating the placement of students through proper placement-cell of university should be considered a top priority in the minds of administration to enhance the image and brand building of the programs.

In summary, the leaders whether department chair, vice-chair, dean, or CEO of the university should be flexible, approachable, and must adopt open door policy with a vision to take the organization to greater heights.



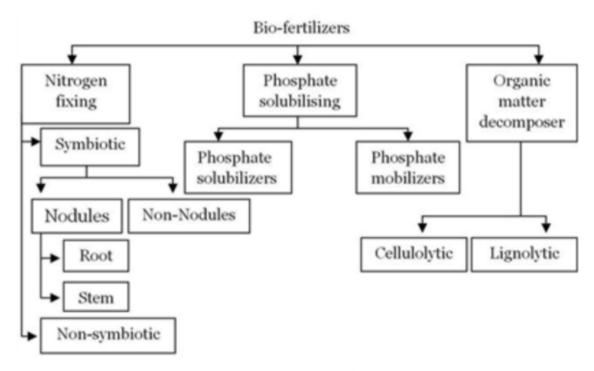
HARNESSING MULTI-POTENTIAL PLANT GROWTH PROMOTING RHIZOBACTERIA FOR IMPROVED PLANT NUTRITION

-Dr. Shalini Rajkumar

The evolution of life greatly relies on the soil quality and diversity as the dynamic nature of soil is a clear consequence of the synergistic effects of community composition, eco-system functioning and other environmental components. Increase in the world's population has amplified the demand for agricultural yield, forcing us to rely heavily on chemical fertilizers for meeting the food demands. The use of fertilizers and pesticides in the agricultural fields has greatly degraded the soil quality and fertility, forcing the researchers and scientists to shift their attention from harmful chemical fertilizers to safer, eco-friendly and productive means of agricultural practices.

Plant roots communicate chemically with the microbes in a sophisticated manner through the process of root exudation. Many of the microorganisms that reside on plant surfaces (termed as epiphytes) or within plant tissues (termed as endophytes) do not cause any harm to the plant. They often contribute appreciably to the nutrient supply of their host plant and help the plant to overcome an array of biotic and abiotic stress. The yield potential of any particular plant depends, not only on the phytobeneficial traits which improve their adaptation to multiple stressful environments but also on the potential of the plant microbiome that facilitates plant growth under such adverse conditions. There is an ever-increasing interest to investigate in detail the mechanism underlying these beneficial plant-microbe interactions, as the activities of these microbial communities critically influence the plant growth, especially under stress conditions. Such studies may also lead to the development of novel strategies to improve yield and stress resistance of agronomically important crops.

In order to take maximal advantage of the potent PGPR strains, it is necessary to formulate the inoculum i.e. microbial fertilizer or bio-fertilizer which contains living organisms capable of successfully colonizing the rhizosphere and improving plant growth. Bio-fertilizer development involves multiple steps: a) isolation of effective organism, b) characterization of the chosen organism on appropriate growth medium under proper conditions, c) mass multiplication of microbes, d) choice of the carrier, e) inoculum formulation, f) field studies, g) large scale studies and industrial mass production, h) constructing a quality control and storage system. Each of the steps is equally important as only the appropriate execution of all the steps with utmost attention will result in a microbial fertilizer of desired quality. Multiple researchers have confirmed the beneficial effects of PGPR on plants. Biofertilizers with multiple combinations of tested microorganisms are currently available in the market and are mainly employed for the purpose of improving soil N nutrition, P nutrition and for decomposition of organic matters using symbiotic or non-symbiotic bacteria. Our lab focuses on the employment of both symbiotic and non-symbiotic bacteria for accomplishing the dual purpose of improving plant N and P nutrition.



Common classes of bio-fertilizers

Previous and recent studies have proved that microbial fertilizers are not greatly accepted by the agricultural producers as it is highly difficult to replicate the results of in vitro studies in vivo. Most bio-fertilizer components available in the market have reduced the rhizospheric colonization of the beneficial bacteria and reduced the number of viable cells, badly affecting the overall performance. Studies have also reported contamination of the bio-inoculants leading to lack of trust in a bio-fertilizer. There is also a notion that the natural microbiome of each plant will directly influence the type and concentration of different metabolites present in its rhizosphere which makes the study of the plants' natural microbiome very vital for effectively choosing an appropriate bio-fertilizing agent. The current focus is therefore on developing bio-fertilizers enriched with different metabolites in addition to the microorganisms, as per the plants requirements.

Microbial fertilizers have been in the research focus for the longest time as they are currently the only ecologically acceptable alternative to chemical fertilizers and agrochemicals whose overuse has harmed the environment beyond imagination. Although this idea is not brand new and has been the focus of ample researchers and scientific papers for several decades, there are many unanswered questions with a lot of place for improvement. The production of microbial fertilizers demands detailed knowledge and understanding of the physiology of plants and microorganisms, the fermentation and scale-up process, formulations, the population of microorganisms and their system of release. Thus, the development of a stable bio-fertilizer is possible only by combining the knowledge from microbial and technical aspects. Our lab sincerely focuses on all the critical technical aspects and also tries to address and overcome the gap between the microbial and technical aspects.

The major focus of my lab is the separation and characterization of crop-specific highly efficient PGPR strains from the soil and plant organs called root nodules. Greater emphasis has been given to the nitrogen fixing and phosphate solubilizing bacteria as nitrogen and phosphorous are the most vital macronutrients for plant growth and their deficiency badly impairs plant growth. Multiple PGP activities of bacteria belonging to different genera like Rhizobium, Klebsiella,

Acinetobacter, Erwinia, Pseudomonas, etc. have been investigated in detail. The efficiency of such strains in promoting growth of the host and the non-host plants under natural soil conditions amidst indigenous soil microbiota have also been investigated. Multiple factors affecting the soil performance of such PGPR strains and attempts to attenuate the harmful soil factors for enhanced action using genetic engineering approaches are also being practised. The bacterial groups currently being investigated are the members of Klebsiella sp., Rhizobium sp. and Acinetobacter sp. for improving plant nitrogen and phosphorous acquisition. Detailed investigations of the mechanisms underlying the process of improving plant nutrition are being carried out. Recent investigations have focused on the individual and combinatorial abilities in improving the growth of important crop plants. There is a great gap in the in vitro and in vivo performance of PGPR which may be directly attributed to various environmental factors that might affect their growth and proliferation in the plant rhizosphere. Attempts have been made to address these gaps and limitations using modern approaches and techniques of high throughput sequencing (HTS) and by the study of gene-specific mutants. The long-term goal of such studies is to replace or to at least reduce the erratic consumption of chemical fertilizers, for improving the crop yield and the soil quality through environment-friendly approaches. Such studies have greater importance in a country like India which is one of the major agricultural country ranking second globally, in the use of chemical fertilizers for agricultural purposes next to China.

Many researchers have addressed the effect of PGPR on growth and nutrient uptake of plants. There is now increasing evidence that using beneficial microbes can enhance plants' resistance to adverse environmental stress like drought, halo-tolerance, nutrient deficiency, heavy metal contaminations, etc. Integrating the mechanisms of interactions of bacterial strains in the plant rhizosphere is inevitable to improve the performance and reliability of plant growth stimulation by PGPR. The basic mechanisms by which the PGPR improve the plant nutrient uptake are nitrogen fixation and phosphate solubilization. The additional phytobeneficial mechanisms include biosynthesis of phytohormones, siderophores, cyanides, lytic enzymes, etc. Understanding the integration of bacterial strains in the plant rhizosphere and the mechanisms of their interactions are widely recognized as a key to improving the level and reliability of plant growth stimulation by PGPR.

Keeping in view the importance of bio-fertilizer for sustainable agriculture, the Government of India (GOI) has ensured production of quality bio-fertilizers under Section 3 of essential commodities, Act 1955. The government also issued a fertilizer (control) amendment order (FCO), 2006 with the gazette notification, S.O. 391 (E), dated on March 24, 2006, for bio-fertilizer production. After the enforcement of this order, four fertilizers i.e. Rhizobium, Azotobacter, Azospirillum and phosphate solubilizing bacteria (PSB) came under FCO. Even though biofertilizers exert a very slow influence on crop production, their long-term utilization will curtail the use of chemical fertilizers and improve the soil nutrition in an eco-friendly manner. Bio-fertilizer development has seen a great increase in the last two decades with the wide employment of PSBs among the farming community.



DIET ALTERS MICROFLORA: ALTER MICROFLORA TO CURE DIABETES

-Dr. Sriram Seshadri -Dr. Sweta Patel

Type 2 Diabetes (T2D) is now a major risk factor for Indian population. Diabetes is a lifestyle disorder linked with change in diet pattern with minimum physical exercise. According to a survey done by the International Diabetes Federation our country is at 2nd position with T2D risk. T2D is a multifunctional disorder. Our gut contains trillions of bacteria which are healthy for the digestive system, known as 'Gut microflora'. The spread of microbiota over Gastro-Intestinal tract is different and each region has specific micro-environment and output. This microflora is of two types: Gram-positive and Gram-Negative bacteria. Out of which Gram-Negative bacteria are considered pathogenic bacteria. Over eating of junk food and no exercise lead to change in the composition of gut microflora that increases Gramnegative bacterial population. It is a well-known fact that due to high energy diet (diet containing excess amount of fat, carbohydrates) Gram-negative population increases, consequently Lipopolysaccharides (cell wall component of Gramnegative bacteria) in blood also increases which lead to inflammation and lead to insulin resistance. Thus, in Type 2 diabetic patient's blood glucose remains high with low levels of inflammation. Prolonged conditions cause damage to liver, kidney and eye vision etc. It is an emerging idea to modulate gut microflora towards a healthy state to cure type 2 diabetes. To target Gram-negative microbiota, an antibiotic against gram-negative bacteria (here, cefdinir) was used. Microsphere formulation of antibiotics was prepared to have specific release of drug in different regions of GI tract. Here the targets were the small intestine and colon as the major digestion process happens in these regions. The T2D pathogenesis was mimicked in animal models with preventive and treatment strategies.

Here we found that the killing of Gram-negative bacteria reduced inflammation in blood, liver and improved insulin sensitivity of cells. Liver is a major organ which regulates blood glucose level via insulin hormone. Due to active inflammation, receptors on liver cells could not sense insulin. This condition is known as insulin resistance; thus, glucose level could not be maintained. All pathways are interconnected in our body. Altered metabolic pathway and presence of LPS activate inflammatory cells. Microflora alteration in colon successively alters liver immune cells and also helps in regulating metabolism. Here, we conclude that colonic bacteria are the important bacteria and location to target to overcome T2D pathogenesis and improve insulin sensitivity. Probiotics can also be used to reduce pathogenic bacterial growth in the gut. Type 2 diabetes can be overcome by eating a healthy diet, taking probiotics to improve gut microflora and do exercise to burn excess energy.

INSTITUTE OF SCIENCE, NIRMA UNIVERSITY



COMBATING THE ANTIBIOTIC-RESISTANT BACTERIAL INFECTIONS: TWO DIFFERENT APPROACHES - AYURVED AND SONIC THERAPY

-Dr. Vijay Kothari

Discovery of antibiotics in the twentieth century greatly helped us reduce the morbidity and mortality owing to infectious microorganisms. However, acquisition and spread of the antibiotic- resistance trait among pathogenic bacterial populations has made Antimicrobial Resistance (AMR) a major global health threat of the 21st century. Discovery of new antibiotics could not match pace with appearance of resistant phenotypes of pathogenic bacteria, and there is an urgent need to find novel alternative approaches, particularly against those listed as 'priority pathogens' by WHO (World Health Organization) and CDC (Centers for Disease Control):

https://www.who.int/news-room/detail/27-02-2017-who-publishes-list-of-bacteria-for-which-new-antibiotics-are-urgently-needed

https://www.cdc.gov/drugresistance/biggest-threats.html

One such approach is mining the wisdom of Traditional Medicine (TM) systems like *Ayurved* for tackling the AMR problem. Our experiments [https://rdcu.be/bhokn; https://goo.gl/6JiWPc] with *Ayurvedic* formulations like *Panchgavya*, *Triphala*, *Panchvalkal*, and extracts of pomegranate peel mentioned in classical texts (e.g. *Charak Samhita*), and few folklore extracts have shown how these extracts/ formulations can attenuate bacterial virulence without necessarily killing them. Interestingly, these extracts work by interfering intercellular communication among bacteria. Molecular mechanisms underlying the anti-infective efficacy of some of these extracts has also been investigated by us, which has enabled us to identify few novel potential targets for development of new anti-infectives. Building on this, we are initiating a collaborative research effort with Atomwise Inc., USA through their AIMS (Artificial Intelligence Molecular Screen) award programme.

In another piece of work, we have investigated the therapeutic potential of certain sound stimuli, wherein worms infected with pathogenic bacteria could score better survival upon exposure to the sonic stimulation through sound corresponding to 'OM' and 400 Hz

[https://doi.org/10.1101/351924; https://doi.org/10.31219/osf.io/kewps]. Our group also generated the first-ever report [https://doi.org/10.1101/098186] describing effect of sonic stimulation on bacteria at the whole transcriptome level, wherein sonic stimulation was demonstrated to be capable of modulating quorum-regulated pigment production in an opportunistic pathogen *Chromobacterium violaceum*.

We believe that taking the reverse pharmacological approach for identifying effective anti- pathogenic leads from TM can result in development of efficacious anti-pathogenic phytopharmaceuticals. On the other hand, efficacy of sonotherapy remains to be demonstrated in higher organisms.

WASTEWATER TREATMENT AND MANAGEMENT

-Dr. Nasreen Munshi

According to the number of industries in India, Gujarat is ranked second after Maharashtra. Concomitant with industrial development, a huge amount of wastewater is also generated which needs proper handling. Industrial wastewaters have different characteristics as compared to the municipal or sewage wastewater and today, we are facing tremendous pollution problems associated with these types of wastewaters. Generally, the wastewater is being treated in three stages in the treatment plants, amongst which the crucial stage is the secondary stage which is biological in nature. This makes use of microbial catalytic activity for breaking down the organic material leading to their mineralisation and making the wastewater free from organic pollutants. The municipal wastewater is generally being treated satisfactorily by achieving near complete removal of organic and inorganic waste from domestic sewage. But the wastewater effluents released from industries have lots of pollutants which remain in the effluents even after its treatment and few industries do not have their own treatment plants. Hence, Common Effluent Treatment Plants (CETPs) are built up in or around industrial estates which are the centralized facilities for treatment of such pooled industrial wastewater. Gujarat has nearly 34 functional CETPs in different industrial areas.

The task of treatment of effluents produced by a myriad of chemical industries is challenging since the pooled effluents are rich in different types of pollutants. Some types of organic pollutants such as hydrocarbons are not degraded and hence, they still persist in wastewater apart from toxic heavy metals which also are not removed. The performance of most of the CETPs are found to be unsatisfactory. The two basic problems which need to be addressed include detection of the level of hydrocarbon pollutants and development of a process for their removal. We are working on development of a bioprocess for the detection of pollutants. Two bacterial biosensing strains were developed with the tools of genetic engineering in such a way that they emit quantifiable green and blue fluorescent coloured light in presence of mono- and poly-aromatic hydrocarbons. These biosensors have the ability to detect pollutants at minute level (micromole levels). Such strains can be applied for on-line monitoring of pollutants during the wastewater treatment (Figure 1), which may help to modify the treatment steps and increase their efficiency. For example, if the hydrocarbon pollutant levels are higher than the maximum permissible limits prescribed by the pollution control boards, then the stream can be directed for treatment of wastewater by specifically designed systems for removal of hydrocarbons. And if the levels are within the limits after secondary treatment, then the wastewater can reach the tertiary treatment stage without delay. These biosensors have shown their effectiveness in detection of such pollutants from environmental samples also, e.g. canal or river water. Therefore, the developed biosensors can be applied for pollution monitoring of rivers or any other aqueous environments.

To address the second problem, a bioremediation process was developed with a specific type of bacteria which was applied for treatment of wastewater containing high load of aromatic hydrocarbon compounds. As the environment of industrial wastewater is stressful due to the presence of a wide variety of solvents, acids, alkali, cyanide and other toxic compounds, synthetic compounds, etc., very few species of bacteria are able to survive in such wastewater. It is assumed that the bacterial species present in high abundance should be best adapted to that environment. Hence we tried to isolate an abundantly present bacteria from common industrial effluent pools, which also demonstrated to have the capacity to bring about near complete degradation of aromatic hydrocarbon pollutants. It was able to grow in presence of other native bacteria and show the activity. The bacteria were later identified as Pseudomonas citronellolis.

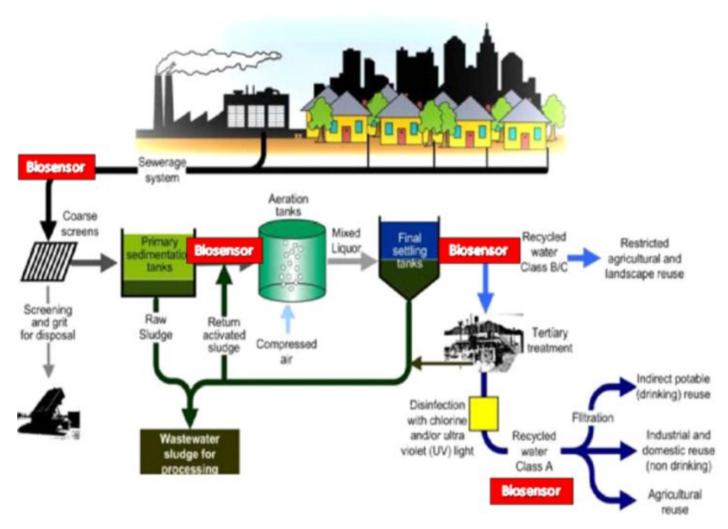


Figure 1: Application of biosensors in wastewater treatment.

For the study, sodium benzoate was selected as a model aromatic hydrocarbon compound and it could be degraded in actual wastewater by Pseudomonas citronellolis in a bioreactor system with as high as 100 litre volume. This bacterium is also able to degrade complex substrates such as poly-aromatic hydrocarbons, naphthalene and anthracene. Since the application of bacterial consortium is more preferred than a single species of bacteria for wastewater treatment, a consortium can be developed using bacteria capable of working in different environmental conditions for application in treatment of different types of industrial wastewaters.

CO-CURRICULAR AND EXTRACURRICULAR ACTIVITIES DURING A STUDENT'S JOURNEY: RELEVANCE OF IMAGINATION AND CREATIVITY

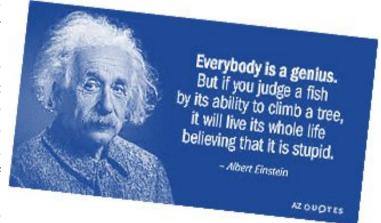
-Dr. Amee Nair

The today's educational system aims at overall holistic development of students. This has eventually led to improvement of teaching – learning methodologies. Yet the major chunk of the assessment is inclined more towards memory-based learning. This involves hours of academic learning on a regular basis for attaining scores that fulfil basic requirements for higher studies desirable or mandatory to obtain lucrative job prospects. Such is the pressure that most students slowly drift away from recreational activities and social events. Eventually they tend to spend their

leisure time more on online platforms like Whatsapp, Facebook, Instagram and Pintrest to name a few for sharing their 'news' which may be liberating but at same time may be a virtual 'happy façade of one's life' having mere semblance of reality. Generally, the mind of a student does not conform to the linear path and nor does imagination. However, the standardized methods of our so called 'evolved' yet conservative educational system however does so. So where does it leave our students? In the event of failure to achieve the requisite scores, the students' lives get plagued by anxiety that gravely affects their social and learning behaviour. Let me quote Albert Einstein – one of the greatest scientists of all time, who said 'The value of college education is not the learning of many facts but the training of the minds to think'. He believed that the true sign of intelligence is not mere knowledge but imagination. Imagination is power that lends wings to soar into the realm of experimentation. It

is said that the worst form of imagination manifests as 'anxiety' while best ultimately fuels creativity. The latter is equally important as literacy in the educational system and should be motivated amongst the students. However, an imaginative mind that cannot translate its ideas does not achieve creativity. It is the curious minds that questions the existing knowledge or wanders on the path of imagination captures novelty. Art in all its forms remains the explicit form of imagination and novelty. It not only refreshes the soul but also inspires the individual to think and shape their abstract imagination into a tangible form of art

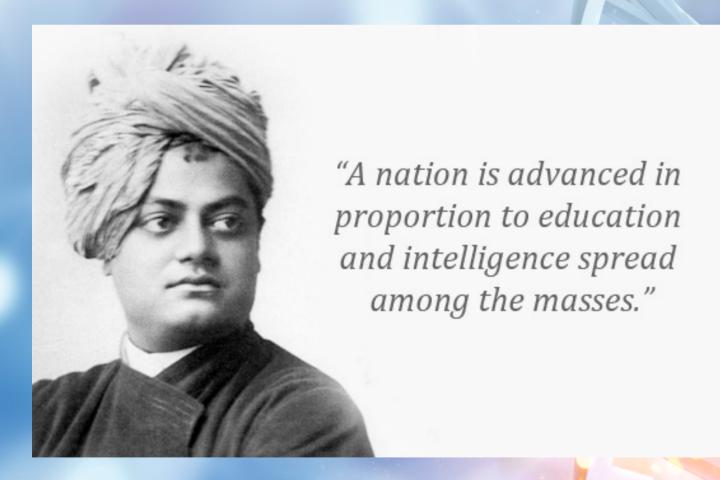




be it literature, dance or fine arts. In a way, it liberates them from the drudgery of the pressures and expectations; helps them to trust their ideas and hone their skills as they improvise. It allows them the freedom to commit mistakes and learn from the same. Let them have some space to express themselves, be it faulty yet original. Be it extracurricular

activities or co-curricular activities whichever they believe will help them to evolve as better and confident individuals. So, what if they mould a career out of their passion and not their professional education. The years spent in attaining the degree is not 'wasted' rather it stems from their individuality by being disciplined if not forming a back-up plan.

Let them take up the opportunity to explore their passion for what we know, not all those who clear the professional degree get the professional roles. Let us not judge a fish for its ability to climb a tree. Let them be creative at their best. This practice will not only be limited to their 'hobbies' but time will see to it that it becomes a part of their character and it will not be very long when they shall commit the same to studies too. Thus, creativity remains the key to success for their future and hence the teachers should help bring out the creativity in students. So even if they spend a few hours outside the classroom to pursue or participate in such activities along with their classmates, it shall not be shunned upon as it would form joyful memories. So down their life, it is these memories that will make them laugh certainly not their marks. These thoughts belong to none other than Dr. A.P.J Abdul Kalam, our former President who was a great scientist and even more remarkable and passionate teacher.







At cellular level we are all 'Ardhnareshwar', which translates to a lord who is half male and half female, as both the parents contribute equally to the genetic content of their offspring. There is a phenomenon in nature where certain genes express or remain silent based on parent of origin, mother or father, this is called 'genomic imprinting' which implies that the genes 'remember' where they have come from and accordingly express or remain shut.

The genes are in pairs, and in case of imprinted genes, either the copy from the mother or the father is epigenetically silenced. Epigenetic silencing is a natural phenomenon in which the expression of genes is regulated through modifications of DNA, RNA, or histone proteins. Silencing usually happens through the addition of methyl groups during ovum or sperm formation.

In diploid genome, even if a copy inherited from one parent is defective, we have a substitute allele from the other parent. However, in the case of imprinting, even though there are two copies of the gene, it is as if we are haploid for this gene because only one copy is expressed.

This phenomenon was first described in 1984 when two laboratories discovered a mark, or "imprint," that differentiates between certain genes for the maternal and paternal origin resulting in the expression of only one copy of those gene pairs in the offspring.

The inheritance of both the maternal and paternal genes is required for normal development to proceed. Uniparental disomy (UPD) occurs when a person receives two copies of a chromosome, or part of a chromosome, from one parent and no copies from the other parent. UPD can occur as a random event during the formation of ovum or sperm cells or may happen during early embryonic development.

In certain cases, UPD is not likely to have effect on health or development if the genes are not imprinted, it doesn't matter if a person inherits both copies from one parent instead of one copy from each parent. In some cases, however, it does make a difference whether a gene is inherited from a person's mother or father. A person with UPD may lack active copies of essential genes that are under the control of genomic imprinting. This loss of gene function is associated with specific manifestations like delayed development, intellectual disability, and other medical conditions.

Prader-Willi and Angelman syndrome are two very different disorders caused by UPD or other errors in imprinting involving genes on the long arm of chromosome 15. Some of the genes in this region are silenced in the ovum, and at least one gene is silenced in the sperm. So someone who inherits a glitch on chromosome 15 can be missing various sets of active genes, depending on whether it is of maternal or paternal origin.

The IGF2 gene (but not the IGF2 receptor gene) is an example of imprinted genes in humans. The IGF2 gene codes for a hormone that stimulates growth during embryonic and fetal development. Methyl tags normally silence the maternal IGF2 gene. But a DNA mutation or an "epimutation" (missing methyl tags) can activate it, resulting in two active copies of the gene.

Activation of the maternal IGF2 gene during ovum formation or very early in development causes Beckwith-Wiedemann Syndrome (BWS). While children with BWS have a variety of symptoms, the most common and obvious

feature is overgrowth. Babies with BWS are born larger than 95% of their peers. They also have an increased risk of renal cancer, especially during childhood.

The parent of origin effect is observed in non-human life forms also. In some species, more than one male can father offspring from the same litter. A house cat, for example, can mate more than once during heat and have a litter of kittens with two or more fathers. If one father's kittens grow larger than the rest, his offspring will be more likely to survive to adulthood and pass on their genes. So it's in the interest of the father's genes to produce larger offspring. The larger kittens will be able to compete for maternal resources at the expense of the other father's kittens.

On the other hand, a better outcome for the mother's genes would be all of her kittens to survive to adulthood and reproduce. The mother alone will provide nutrients and protection for her kittens throughout pregnancy and after birth. She needs to be able to divide her resources among several kittens, without compromising her own needs.

It turns out that many imprinted genes are involved in growth and metabolism. Paternal imprinting favors the production of larger offspring, and maternal imprinting favors smaller offspring. Often maternally and paternally imprinted genes work in the very same growth pathways. This conflict of interest sets up an epigenetic battle between the parents; a sort of parental tug-of-war.

Gregor Mandel was lucky in a way that in his monohybrid and dihybrid cross experiments it did not matter if the traits like smooth versus wrinkled seeds were from pollens or ovum. The results were similar in either case which means that expression of traits in these reciprocal crosses was not sex dependent. We can only imagine now what could have been the scenario if this was not the case. Now there are examples where the parent of origin effect is most clearly demonstrated, which is in case of unusual mating. Lions and tigers don't normally meet in nature. But they can get along very well in captivity, where they sometimes produce hybrid offspring. The offspring look different, depending on who the mother is. A male lion and a female tiger produce a liger, the biggest of the big cats. A male tiger and a female lion produce a tigon, a cat that is about the same size as its parents.

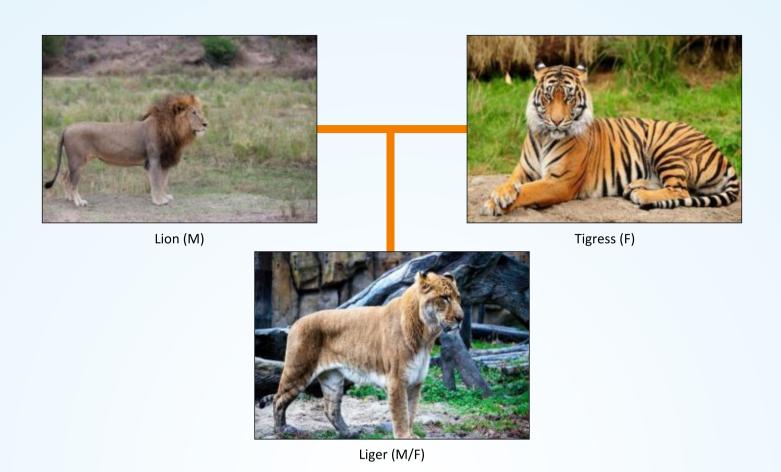
The difference in size and appearance between ligers and tigons is due in part to the parents' differently imprinted genes. Other animals can also hybridize, with similar results. For example, a horse and a donkey can produce a mule or a hinny.

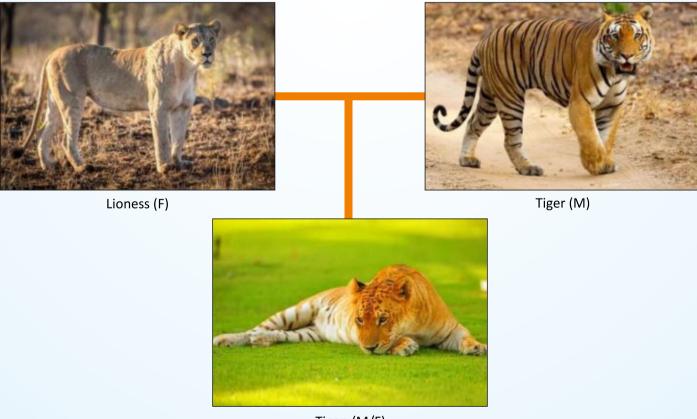
Imprinted genes are especially sensitive to environmental signals. This is because imprinted genes have only a single active copy and no back-up hence any epigenetic changes or "epimutations" will have a greater impact on gene expression.

Environmental signals can also affect the imprinting process itself! Imprinting can occur during ovum and sperm formation when epigenetic tags are added to silence specific genes. Diet, hormones, and toxins can all affect this process in the gametes, impacting the expression of genes in the next generation.

This phenomenon is a lesser-known mode of inheritance, one of the Mendelian Out-Laws! The nature is full of surprises indeed.

My encounter with this curious phenomenon is due to a dissertation project involving a case of genetic disease. This is a girl having 4 copies of the short arm of chromosome 18 instead of a pair which is normal for all autosomes. To correlate her phenotype with this genomic imbalance we not only need to study the genes present on this piece of chromosome and their function, but also the parental origin of extra copies. As elaborated above, it is not only the gene dosage but also the origin which matters when a phenotypic expression is concerned.





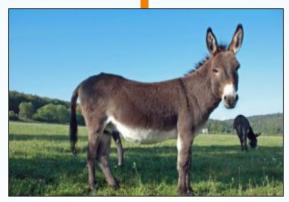
Tigon (M/F)



Donkey (Jack) (M)



Mare (F)



Mule (M/F)



Stallion (M)



Donkey (Jenny) (F)



Hinny (M/F)

ERA OF IMMUNE-BASED THERAPY TO CANCER

-Dr. DabluLal Gupta

Cancer treatment uses different type of therapies, depending on types of cancer, stages of cancer, your general health condition and your preference. The goal of cancer treatment is to achieve a cure for your cancer, allowing you to live a normal life span without cancer. This may or may not be possible, depending on types of cancer, stages of diagnosis of cancer, treatments used, genetic profiles and other factors. If a cure isn't possible, clinicians prefer to use treatments that may shrink your cancer or slow the growth of your cancer or stop metastasis to allow you to live symptom free for as long as possible.



Some people with cancer will have only one kind of treatment. But most people with cancer have a combination of treatments, such as surgery with chemotherapy and/or radiation therapy. Cancer treatments mainly used are nonspecific chemotherapy and radiation therapy since decades and have steer to high rates of relapses. Unlike, chemotherapy and radiotherapy, immune-based therapy is a targeted therapy and attempts to harness the power of an individual patient's immune system to combat cancer.

James Allison and Tasuku Honjo established a ground-breaking research for cancer therapy by activating the immune system and targeting the immune checkpoints, cytotoxic T- lymphocytes-association protein 4 (CTLA-4) and programmed cell death protein 1 (PD-1). They honored with Nobel prize in Physiology or Medicine of year 2018 for breakthrough research, pioneered immunotherapy, which harnesses the body's immune system to fight cancer.

The discovery of targeting immune checkpoints for cancer therapy in the year 2018, leads to burgeoning excitement surrounding development of immune based therapies for the treatment of cancer. Seven drugs targeting CTLA-4 & PD-1 are approved by FDA for the treatment of various types of cancers including metastatic melanoma, lung cancer, breast cancer, head and neck cancer, bladder cancer, cervical cancer etc. Several anti-PD1 antibodies (nivolumab, prembrolizumab etc) and anti CTLA-4 (ipillimumab) showed striking/impressive effects on patients and is also used as an adjuvant to surgery (therapy applied after initial treatment for cancer, especially to suppress secondary tumor formation) for several types of cancer as well.

Although, this therapy has potential to improve the survival of cancer patients who diagnosed at later stages of cancer by enhancing body's natural defence to fight cancer. However, there are many investigations required to understand the mechanism of action, about the combination therapy, dosage and administration section of all five currently approved PD-1/ PD-L1 therapy. The overactivation or constitutive activations of T cells by immune based therapies leads to the exhaustion of T cells and activation induced cell death which may decrease anti-tumor effects and possibly allowing for tumor progression. Therefore, designing a trial rigorously to address the doses of immunotherapy, duration of therapy to reduced the toxicities, and also compromised the activation induced death is a major concern.

By addressing this concern now, not only we may improve patient outcomes, but also gather a deeper understanding of the role and mechanism of the immune system in the control of tumor growth.



The prevalent deadly parasite Entamoeba histolytica (known as pathogenic amoeba) is common among the human population worldwide. This parasite is a single-celled microscopic organism and a major cause of intestinal and extraintestinal amoebiasis. As per the World Health Organization, around 100,000 deaths are annually reported due to amoebiasis, placing it second to malaria in terms of mortality worldwide due to protozoan parasite infections. Interestingly, more than 90% of infections by this parasite are asymptomatic. A recent survey reveals that around 15-20% Indian population is infected by this parasite. The infection and transmission of this parasite not only linked with poor sanitation but also transmitted through heterosexual and homosexual contact with a chronically ill or asymptomatic carrier.

E. histolytica parasite completes the life cycle in two stage cysts and trophozoites. Once amoebic cysts (infective stage of the parasite) enter into the body, it can settle down into the intestine without causing any symptoms and get converted (known as excysts) into the trophozoites (invasive stage of the parasite). The amoebic trophozoites are highly motile and damages the intestinal gut barriers which enable it enters into the bloodstream. Finally, trophozoites migrate to the liver and rare cases brain and causing hepatic abscess and brain abscess, respectively. During the lifecycle, trophozoite becomes converts in to cysts (known as encyst) and passes out from the human body to the environment via stool.

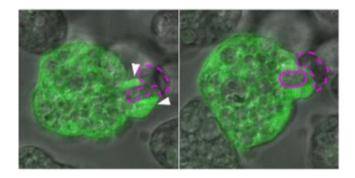


Image: E. histolytica (green) ingesting a bite of Chinese hamster ovary (CHO pink) cell.

The host tissue damage by amoebic trophozoites relies on effective engulfment of human cells and releasing the various substances, which kills the human cells. The host cells engulfment by amoebic trophozoites mediated through classical uptake (pinocytosis/phagocytosis engulfment of whole-cell) and complicated uptake (trogocytosis). Trogocytosis (Greek: nibbling death) means trophozoites recognize specifically LIVE host cells and take a bite which leads in eventually death of the target cell. Now the engulfment gets puzzled that how trophozoite decides that host cells need to be pinocytosis/phagocytosis or trogocytosis. The mechanism of phagocytosis is highly characterized into higher eukaryotes and pathogenic amoeba. The trogocytosis is an evolutionary conserved from amoeba to human cells. The recent research showed that amoebic lysosomes function implicated in trogocytosis of LIVE host cells. Previously, lysosomes were considered for endpoint terminal for degradation of ingested food material. The recent study also delineated the function of lysosome positioning and transport to the plasma membrane are vital and important for the various physiological and pathological situations. The ongoing research in our laboratory aims to understand how amoebic lysosomes sense the signal from LIVE cells and respond to trogocytosis. To know the more details in this pathway, we are specifically looking at the key regulator for lysosomal biogenesis, particularly vacuolar (V)-ATPases. The functional role of V-ATPases in trogocytosis and subsequently in tissue invasion will help in improving our fundamental knowledge on the pathogenesis of during amoebiasis and also contribute to design the amoebic V-ATPases specific drugs or inhibitors against the treatment of invasive amoebiasis.

CAMPUS LIFE

Nirma University is not only a great place for academic activities and intellectual development, but it is also a vibrant and lively place for personal and social development. The campus is abuzz with numerous curricular, co-curricular, and extra-curricular activities in the fields of sports, adventure and culture. Several literary activities also take place on the campus. Each institute has a rich calendar of sports, adventure, literary and cultural activities.

In addition, the University organises annual sports and cultural activities for all the institutes at the central level. The University and its constituent institutes ensure that all students have sufficient opportunities for their holistic development.

About the Institute

Established in 2004, Institute of Science although a new entity as compared to other institutes under the University, has grown in leaps & bounds in the last 16 years. Nirma University has established the Master of Science in Biochemistry and Biotechnology, and initiated a Masters Program in Microbiology from 2009-2010, not only in anticipation of this need to provide an alternative to the students who desire a postgraduate degree and whose career objectives goes beyond academic research. The Institute aims to provide students with a broad training and education in Biochemistry, Biotechnology and Microbiology encompassing science, business, legal, social and ethical aspects to enable them to explore wide career opportunities.

The Institute also has an Alumni Association which meets on an Annual Basis and the Alumni are well placed in companies like Reliance Life Science, TCS Life sciences, Ranbaxy Ltd, Quintais, India, Lupin Pharmaceuticals, Pune, Intas Biopharmaceuticals and Zydus Cadila etc and in research Institutions pursuing their Ph.D. like NIPER, Chandigarh, JNCASR, Bangalore, TIFR, Bangalore, CCMB, Hyderabad, IISER, Bhopal, Institute of Science, Hyderabad, Texas A & M University, USA, Griffin University, Australia, Laval University, Quebec, Canada, Drexel University etc.

The Institute has professionally experienced qualified permanent faculties drawn from various areas of Life Sciences. A balanced mix of academicians and professionals, with rich academic and research experience contributes to the Institute's academic excellence. The quality and progress of the Institute is coordinated and ensured by the Institute of Science Advisory Committee (ISAC) and Internal Quality Assurance Cell (IQAC) of the Institute.



Research Activities & Instrumentation

The Institute is actively involved in research projects, with each faculty supervising 8-9 M.Sc. students for their In-House Dissertation and full-time Ph.D. scholars working under them. The Faculties not only work on University Aided Research Projects but have also got extramural research funding from various government funding agencies such as Department of Biotechnology, Department of Science and Technology, Ministry of AYUSH, Government of India, Gujarat State Biotechnology Mission and

Gujarat Council of Science & Technology. This has led to recognition as SIRO by the DSIR. For these research activities, the Institute boasts of a Sophisticated Instrumentation Facility which includes instruments like thermal cycler, gradient PCR, qPCR, HPLC, Fluorimeter, Denaturing gradient gel electrophoresis, BiologTM, Hybridization Oven, ELISA Reader, Gel Documentation system, Ultra sonicator, Bath Sonicator, -80°C and -20°C freezers, CO2 incubator, Biosafety cabinet, liquid nitrogen storage facility; Compound, Inverted, and Dissection microscopes, etc to name a few. We have received FIST grant to equip our lab with a Flow Cytometer, inverted Fluorescence microscope and fermenter. These instruments are used by the IVth semester students for their dissertation work which is conducted In-House. The Human Ethical Committee, Animal Ethical Committee, Biosafety committee, and Research Advisory committee are in place for excellent monitoring of biological research.

The students have communicated their research work in journals of repute like Journal of Biotechnology, Journal of Basic Microbiology, International Journal of Environmental Research, International Journal of Toxicology, Environmental International, Reproductive Toxicology, American Journal of Infectious Diseases, Expert Reviews and Asian Journal of Experimental Sciences to name a few.



LIBRARY THEN, NOW AND FUTURE

Libraries over the centuries have undergone a drastic change in response to change in the learning and research environment, information need of users and application of information technologies from the age of Microfiche to 3D printers. According to Kemp (1976) Information is considered as the fifth need of man ranking after air, water, food and shelter.

If we look back some 2 to 3 centuries ago, the libraries were the store houses of books (usually chained to the shelves) and only accessible to rich and royal families. Kings and monarchs used to keep a vast collection of books in their personal Library as a status symbol which was used for showcasing their culture. The Library was formed in total work of art, combining painting and sculptures. It was believed that knowledge was not considered for everybody. It was for a limited set of people and given based on their caste.

Today, libraries are not only the hub for knowledge but also play a vital role in the generation of new knowledge directly or indirectly. The whole purpose of the library is to serve the right information to the right users at the right time and the same is explained in five laws of Library science provided by Dr. S. R. Ranganathan a father of Library and Information Science in India. The ICT (Information and Communication Technologies) revolution has changed most of the patterns of traditional services, information processing and handling as well as information dissemination to the end-users. The traditional library has transferred to the digital library. Electronic books, e-journals, e - archives are now a part of library collection. Libraries are categories in digital library, hybrid library and virtual library. The library not only functions to support higher education but also serves as gateways to the collection of global libraries and supports informal self-education and learning. In the current scenario, library professionals must have knowledge of information and technologies like HTML, coding, the ability to deal with online resource queries, the ability to transfer resources in digital form and the ability to learn emerging technologies.



- The role of Library is not just to provide access to resources but to support
- · Higher education
- User education
- Recreation place
- Societal and cultural support to communities

Some of the future technologies which incorporate to facilitate users are virtual reality technology, coding, connecting with users through social media, offering experiential learning, educating users for science and technology, role as a data analyst, support in research activities, information literacy and many more. In the near future the library will become solely digital space.

Kemp, D. A. (1976), "Nature of knowledge: and introduction for librarians"; Clive Bingley, London.

"Libraries are community centres. We are very aware of what is happening locally and have research services and books to meet that demand."



STUDENT'S ACTIVITY



























STUDENT'S CORNER

Heart Vs Brain

-Heena Dadlani (19mbc004) -Saloni Raval (19mbc020)

Is it my heart or is it my brain?
That makes me feel happy, anger and pain.
Is it what I know or is it what I feel?
Brain cracks the deal and heart tries to heal.

Heart Always Wants To See The Good, But brain see's the truth. Finally when brain see's the good, But now my heartism is understood.

My brain tells the body how to react, When my heart is under attack. When my heart is not correct, Brain keeps the track.

Heart is not a brain,
And brain is not a heart,
Because heart cannot think,
And Brain cannot feel.

Childhood-to-Sciencehood

-Sunny Kumar, JRF

Ek bachpann ka jamana tha, Jisme khusio ka khajana tha.

Chahat chand ki thi pr space science kisne Jana tha.

Pankh-rang virngi kyu uski is bat se mai anjana tha,

Dil to bus us Titli ka Diwana tha.

Kismat ne kyu mod liya yu, ye tab kaha mai jana tha, admission ke waqt pata chala ki ISNU jo aana tha. Wo bachpann ke the din jaha na lab., na Lecture koi Jana

Ab na kuchh subah ka na sam ka koi thikana hai, Ye dil to bus ab Research ka diwana hai.

tha.

Khidkiyan

-Divya Tailwani, 19mbt040

Khidkiyon se bohot lagaw tha mujhe
wo kya hai na...
Qki Khidkiyan chahe ghar ki ho ya dil ki
ek yahi to khubi hoti hai inme,
ye hume uss jahan se wakif krwati hain jo darwaze kabhi
nahi dikha sakte.....
To bas isi khidki par
Aya karte the parindey inpr
Kuch waqt bitate fr udd jate,

Or esa hi ek parinda shayad tumhre pyaar ka bhi tha
Jo udane ke baad kabhi wapas nahi aya...
Shyad islye apne dil k darwaze to nahi
Par khidkiyan jaroor band kar bethi hu ab...

Womenhood

- Ami Mehta (19mbt022)

I am a woman

A little shy, a little bold

Be in your limits, I've always been told

I am a woman
Who expresses her pain and sorrows
World sees them but still ignores

I am a woman

Flooded with comments like you are ugly,tall,short and too much wise

I would love you if you were of perfect size

I am a woman

Takes all the responsibilities with a smile

Burry me deep but I'll still rise

I am a woman

A mother, a daughter, a sister and a wife

Just to shape all these forms don't take her life

"My EXTRAordinary...."

-Bhavya Nanavati

Oh my God!

It's day to go home

It's time to meet her,

My Little Rose, roselet,

at times tiny and naked,

as though she fitted in my hands,

as though I'll clasp her like this

and carry her to my arms

and carry her to my arms but suddenly my feet touch her feet, her shoulders raised like hills, she has grown, But i can still manage to encircle the thin, moon line of her waist. and when she looks at me with love in her round sparkly eyes And loses herself Like a Pearl in the ocean, which probably can be measured to infinity the sky's most spacious eyes and its the time to lean down in her lap, forgetting all the sorrows and fall asleep, having kiss on forehead once and being blessed forever...

Beauty

-Divya Tailwani, 19mbt040

I lived in my heaven
One day I was told that I was black
Back then for me it was just the opposite to white
And the color of the night
And i couldn't understand Why they used it with beauty
But as young trusting them was my duty
But people, complexion can never the measure for my
beauty

Days turned to years

And soon this thought became one of my fears

This girl turned to eleven,

But the things remained same as she was seven

Now I knew why the color was not of pride

Because it was not something that was white

I cried the day when I got to know

But deep inside i knew people were wrong though
I wanted someone to accept me affectionately

Because people, complexion can never be the measure

for my beauty

By the age sixteen
I wanted someone to hear the keen
For every day I punched my face with creams
The only thing I searched was fairness schemes
Those things were just burning my face
And the outcome brought disgrace
All I asked was- how can I turn fair?
But the answers made me scare
The failure just made my vision blurry
Because people, complexion can never be the measure
of my beauty

And today when I am nineteen
I have gathered the courage to change this scene

Let me today raise my voice

Because it is not something, I have got by my choice

This is the color to which I feel proud

And I want to tell this whole crowd

Today telling them is my duty

Because people,this complexion can never be the

measure for my beauty

BLIND WORLD

-Udita Pal (19mbt028)

Sometimes I wonder....

Is it so difficult for people to ponder?

The world is blind it seems

So, it even doesn't dare to gleam.

When you get to know about this world

You are already hurled.

Lost in the dark
Unable to find an ark

I believed some people
Was it my biggest mistake?

Left me, making me feeble Where I am lost in worldly lake

But now I am strong

And will be thankful to them lifelong

Learned many things about me Learning the worldly cree...

Still more to go

Believing to escape every blow

Be yourself, find yourself

And of all believe yourself.

Do scientific experiments fail?

-Dhara Dhagat

Apparently, it seems a casual question as we face failure almost every day performing various experiments. As we know experiments are conducted to validate or support a hypothesis. And every experiment has an equal probability of success and failure. When we talk about scientific experiments we set a standard for a result, sometimes we obtain the set results and sometimes not. But thinking over the question again I would say that every failed experiment provides a scientist with a better experience and more confidence to improvise on methods. And not just this sometimes it may also occur that unexpected products are more useful than actual results expected. Recently, we saw that Chandrayaan 2 could not successfully land on the moon's orbital but it provided our scientists with better experience and India a pride to be the fourth country to work on this project. Even in the field of medicine, we have an example of a pacemaker that was originally designed to be a huge size television but due to a mistake it revolutionized the field of medicine. When building a heart rhythm recording device, the scientist pulled out the wrong size resistor and plugged it into the circuit. When it was installed he realized it sounded like a human heartbeat. With some work, he miniaturized the device to two cubic inches the result was a pacemaker that is saving the life of many people. Even the synthetic dye that we are using today was expected to be an artificial version of the malarial drug, quinine. Unfortunately, it wasn't useful. It left behind a dark oily sludge which turned silk a striking shade of purple. Thus, a failed experiment produces a product that is useful to color so many fabrics.

Thus, every scientific experiment has something to teach and failure sometimes helps to bring a great revolution in the world.



Autobiography of an Agar-Agar

I kept lying in this discard bag, stuffed, alone in this enormous lab. Departed from my friend 'petri plate'. Waiting for my death. I was so happy before some days. Let me take you a few days back. I was in powder form packed inside a white container. It was all darkness there and one day a girl opened that container. I was in a hope that this time I will be able to see the outer world but that girl looked at me and after smelling my fragrance she said 'ewww' awful smell and closed the container. Again I was in that darkness with some hope. After 1 year in the month of June I heard some students shouting my name, Where is Agar-Agar? Let's search for it immediately, we are running out of time. I heard some footsteps coming towards me and then a girl named Akanksha held the container in which I was and said happily I have found it. They took me towards a weighing machine. Opened my container I was praying to God please, God let them make me see the outer world. They all did not like my fragrance but covered their nose and put a spatula and started putting me inside the machine. I was so so happy to see the outer world I was in a beautiful microbiology lab with so many brilliant students. Then that girl mixed me with some water and I was transformed into liquid form. I was swirling with the water droplets it was so fun. Then she plugged cotton upon it and covered the flask with a newspaper.

I was taken into an Autoclave machine. I heard them saying we need to sterilize the Agar-Agar and then pour it into Petri plates. Once my grandfather told me that he had his life's best experience in the petri plate I was also excited to meet it. The Temperature was rising, water started to evaporate and some molecules that were in my contact remained with me. I noticed changes within me I felt so amazed I was now thicker. Then I was taken out and was in Semisolid form. I felt stronger than before. I was taken towards a petri plate. We were just 5 cm apart from each other and my heartbeat sped up. Then when I became a little cool, Akanksha poured me into the petri plate. I was spread around the whole petri plate. It belonged to me I was the owner now. I felt more stronger I was of solid form now. They inverted me and kept me in the Fridge. There I talked with the petri plate a lot. It shared with me how my father, grandfather and even my great-great-grandfather met him; they all shared their experiences and were wishing to be with him forever.

After 2 days I was removed along with petri plate. We were kept between the burners and lid was opened and a short hi hello was there with Nichrome wire loop. Then I was again kept inside but this time I visited a place named 'Incubator'. I felt heavier something was upon me but I did not know what it was! After 24 hours when I opened my eyes I saw small-small red colored colonies upon me, they were so cute! They were called Serratia marcescens, I was not feeling alone anymore and was so happy but did not know this happiness won't last anymore. In the morning they were looking at me so enthusiastically. It felt like because of me they were able to see those red colonies. They took some pictures of mine, kept me on the top of the shelf I saw so many equipments, people. I peeped outside of the window, saw Trees, birds. Finally, I saw this beautiful world.

The evening I have separated it from the Petri pate and put in a transparent discard bag. Here I am waiting for my death and memorizing all excellent memories.

-Aakansha Shinha, 19mmb027

The Streets Are Empty in the Reign of Crowned Virus

- Shivani Sanjay Kumar - Nidhi Shree

Coronaviruses (CoV) a large family of viruses that causes an illness that ranges from the common cold to severe diseases such as Middle East Respiratory Syndrome (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS-CoV).

Coronavirus disease (COVID-19) is a new strain that was discovered in 2019, has not been previously identified in humans, and became pandemic in 2020. The genome of COVID -19 is enveloped non-segmented positive-sense RNA. Its incubation period is 1–14 days, mostly 3–7 days it is contagious even during the latency period. Coronaviruses are zoonotic, which means they transmit from animals to people. Though there are several known coronaviruses are circulating in animals that have not yet infected humans, this new strain had affected a major population of humans.

Bats are the natural sources of CoVs, including SARS-CoV-like and MERS-CoV-like viruses. When virus genome sequencing was done the COVID-19 genome was analyzed with respect to the genome to Bat CoV RaTG13, it exhibits 96.2% overall genome sequence identity, suggesting that bat CoV and human SARS-CoV-2 might share the same ancestor.

Diagnostic criteria

The clinical diagnosis method of COVID-19 is nucleic acid detection in the nasal and throat swab sampling or other respiratory tract samplings by real-time PCR and further confirmed by next-generation sequencing.

Common signs of infection include respiratory symptoms, fever, cough, shortness of breath, and breathing difficulties. In more severe cases, the infection can lead to pneumonia, severe acute respiratory syndrome, kidney failure, and even death. Some preventive majors to arrest infection spread includes regular hand washing, covering mouth and nose when coughing and sneezing, proper cooking of meat and eggs. Avoiding close contact with anyone showing symptoms of respiratory illness such as coughing and sneezing can fend you from getting in contact with this virus.

As prevention is very important to fight against this disease because of lack of vaccines and proper treatment, many myths have been raised in the name of preventions such as,

The COVID-19 CANNOT be transmitted through mosquito bites.

Till this date, there has been no evidence that proposes that mosquitoes could be vectors for this virus.

COVID-19 virus can be transmitted in areas with hot and humid climates.

From the evidence so far, the fact is that the COVID-19 virus can be transmitted in ALL AREAS, irrelevant of hot and humid weather.

Cold weather and snow CANNOT kill the new coronavirus.

There is no reason to believe that cold weather can kill new coronavirus or other diseases. As the human body has homeothermy, body temperature remains around 36.5°C to 37°C, regardless of the external temperature or weather.

Taking a hot bath does not prevent the new coronavirus disease.

Taking a hot bath will not fend you from catching COVID-19. Your normal body temperature falls around 36.5°C to 37°C, regardless of the temperature of your bath or shower.

So far, there is neither vaccines nor specific cure is available to this disease.

The best possible thing that we can do is not to panic behind rumors myths and to follow the preventive measures listed up by WHO.

Reference

https://www.who.int/emergencies/diseases/novel-coronavirus-2019



My journey at Nirma

-Nidhi Jodhwani (16MMB006)

The two golden years spent at Nirma hold an important place in my heart. As a student, I felt that a lot of importance was given to practical aspects rather than going only for books. The syllabus is designed so adequately that not only it gets us ready for the practical world but also covers a large part of NET syllabus. I feel fortunate to have such great teachers sharing enormous knowledge. The way we performed practicals in the lab developed the trouble shooting skill in our self. We were provided with laboratory facilities with high end equipment. During the dissertation phase our guide and other faculty members always kept us motivated and pushed us during difficult times. It actually gave us the foretaste of how pursuing a Ph.D. would look like. These two years' experience had a great impact on my career as a teaching assistant.

My journey at Nirma

-Aishwarya Iyer

I had read somewhere that an individual's intellectual and social stimulation gets ignited from college. Today, when I sit back and ponder over the statement, after 3 years from passing out from the Institute of Science, Nirma University (2017 batch), I think it is cent percent true. College life is an important phase in a student's academic journey after the continuous formative years of schooling. While undergoing graduation at Bangalore university, I cherished the feeling of studying at an institute, which focused on career enhancement along with overall practical, application-based skill development, a blend of soft and hard skills for research and I was blessed to experience the same at ISNU.

From walking in as a naïve fresher with no direction and walking out as a confident, intelligent, hard-working girl is probably the best transformation of myself. Two years of mine spent in an environment under the guidance of the right Guru. The professors at ISNU are dedicated in their respective fields and are talented researchers. They not only nurtured our foundation in science but also cared for us as a family.

Experiences at ISNU are priceless and the academic course contributed a lot to my professional growth and skill, playing a significant role in my profession of teaching. The peer group at ISNU involving my friends to seniors and Ph.D. seniors to other institutes colleagues were intellectually stimulating and with some, I have made friends for life.

I would always be grateful to ISNU for giving me multidimensional learning and experience.

Researcher's rant!

- Dr. Rahul Jog

Current affiliation: Postdoc fellow, Environmental Molecular Biology Lab, Hokkaido University, Sapporo (Japan)

PhD student at ISNU (2009-2014) at Professor Shalini Rajkumar's lab.

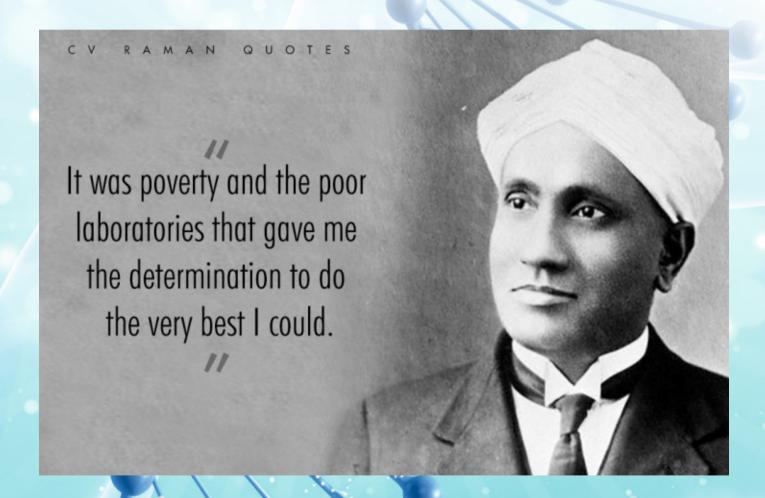
So, you read a paper in Nature and were awestruck by the research. Your next step was to scan for the location: US/Europe or the other usual suspects! A quick glance at author names, you were not surprised to see at least a couple of Indians. Brain-drain you exclaim! If only we had similar sophisticated facilities in labs across India (not just IISc or CCMB or TIFR), we too would have been amongst the top contributors in high-impact journals. Appealing and convenient. Having spent the last 5 years in a par-excellence Japanese lab, I do think it is a bit overrated concept. Of course, high-end facilities are delightful but they are more like chocolate shavings or any other of your favorite cake toppings. Beautiful, eye-catching but certainly not the cake by itself. The foundation of the cake, or in our case fundamental research, is absolutely the same everywhere in the world. The same lab, same equipment, same reagents yet different results probably due to proper organization, planning, and management. So, what makes a near-perfect microbiology or biochem or biotech laboratory (Please stop discriminating between the three)?

It starts with the ratio of fundamental instruments per student. While I have seen a lot of labs in India devote too much funds for buying high-end expensive instruments without building a strong core of workhorses (your clean benches, centrifuges, autoclaves, refrigerators, etc); good labs abroad tend to have a high capacity basic infrastructure first for each lab with a centralized sophisticated instrumentation facility. As the lab grows, it tends to specialize and eventually establish superior expensive equipment as their second step. The next important point in lab setup is your chemicals and their catalog. Each and every chemical that enters the lab has to be registered under a common shared software (we have barcodes here) with its name, pack size, and other relevant information displayed online along with its exact lab location. This way it is very convenient not only to maintain stock but also to locate anything needed in under a minute. Likewise, when a chemical bottle is exhausted, it is removed from the system too. Solvents and inflammable/hazardous chemicals are stored in a locked fire-proof cabinet to avoid accidental fire. The next most important part is waste management. Japanese waste segregation is exemplary and research labs are no different. Apart from separate bins for burnable, plastic, and paper waste; biohazard waste is collected separately and autoclaved before disposing off. Organic solvents, Ethidium Bromide, dyes are all collected in separate containers with detailed cataloging of each item and disposed of through a central waste-collection system. Laboratory cleanliness is a group responsibility and there are no dedicated cleaning staff, instead everyone in lab responsibly clean their workbench and other personal items. Common or shared spaces are cleaned once a week with everyone doing their bit. The other important part in preventing lab contamination is to not bring outside dirt in lab. That's where your lab coats, safety gears and most importantly a dedicated lab footwear comes handy. This is only possible because the labs are isolated from the external environment and temperature is maintained between 22-25oC.

The next thing I want to talk about is the actual research. A systematic, clean and up-to-date record book with images/receipts/printouts pasted (where available) is essential in any research lab. A common folder (hard and soft copy) of the frequently used media, solutions, and techniques is highly recommended so that knowledge is easily shared. Lab members should have good communication between them and should pass their experience and technical know-how to their juniors. While planning experiments, everyone should be considerate of space and resources needed for individuals and should avoid consuming too much at one time ensuring equal distribution. Researchers here are expected to compile their data and present it once a couple of months in a common lab seminar where others

can give their suggestions, comments, and constructive criticism to improve the research work. Apart from how the research is conducted, what is planned is equally important. So, many well-known labs that I have visited/worked generally tend to take a vertical approach wherein you dig deeper to solve a particular problem instead of a horizontal approach where you initiate many projects but only on the surface. The vertical approach may not give immediate high-impact publications but earns you rich dividends in the long-term planning.

The most important thing to remember above everything else is to enjoy your research. Develop curiosity, ask questions and try to solve problems. And remember when things are not going your way, as they sometimes won't, rest if you must but don't you quit (Plagiarism alert! Google Don't Quit poem). Finally, for Master's and Doctoral students, please start looking for different fellowship/scholarship options in India and abroad when you enter your last year. I wish everyone the very best for their future endeavors. I am sure I will come up with more things to share in the future. Until then, goodbye and good luck. Stay away from jealousy, petty fights, and groups. Together we rise!



Discovery about how Cancer Cell Hide from Immune System Could Improve Treatment

-Archana Pandit & Mansi Gajjar

Uncontrolled immune response to pathogen/mutated or overexpressed antigen can cause inflammatory tissue damage and autoimmune diseases. Therefore, maintaining immune homeostasis is crucial for survival. Costimulatory and anti-inflammatory signal regulation helps maintain this immune homeostasis. And these signals are collectively called immune checkpoints. These checkpoints are important for self-tolerance, which prevents the immune system from attacking self cells.

Recently cell culture studies carried by Banks-Kohn and team at the University of Freiburg and the Leibniz University Hannover throws light on the mechanism through which cancer cell evade through the immune system

There are many mechanisms of tumor immune escape including immunosuppression and the phenomenon by which it grows and metastasizes avoiding the immune system. This has become a hot topic in recent years. Tumor-induced immunosuppression operates in two main ways. First, by inducing immunosuppressive cells to accumulate around the tumor and secrete immunosuppressive factors. Second, induced expression of immunosuppressive molecules on their receptors which are known as immune checkpoints.

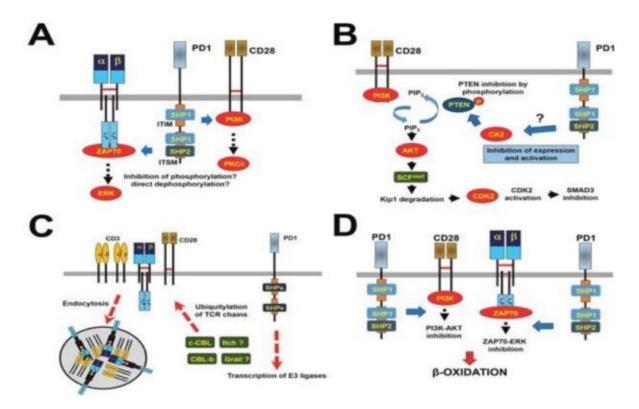
Activated T cells are primary mediators of immune effector function. They express multiple costimulatory receptors such as LAG-3, PD-1(Programmed cell death protein-1, and CTLA-4 (Cytotoxic T lymphocyte-associated protein-4). PD-1 when binds its ligand PD-L1, keeps T cell from killing tumor cells. CTLA-4 binds B7-1/ B7-2 which are present on MHC, and keep T cell in the inactive state.

About PD-1

Programmed death ligand-1 predominantly regulates effector T cell activity within tissue and tumors. It is primarily expressed on mature T cells in peripheral tissues and tumor microenvironment. And are also present on non-T cell subsets, such as B cells, professional APCs, and NK cells. Tumor cells could exploit PDL-1as a molecular shield to attenuate cell-mediated cytotoxicity to evade immune surveillance.

PD-1 binds to PDL-1 (also known as B7-H1 & CD274) and PDL-2 (also known as B7-DC & CD273). When this binding occurs, dephosphorylation and inactivation of T cell Kinase ZAP70 take place. Which then recruits SHP2 signaling protein. SHP2 then dephosphorylates PI3K further inhibiting downstream activation of Akt pathway. This eventually led to decreased production of inflammatory cytokines and cell survival proteins such as Bcl-xl.

- (A) Direct inhibitory mechanisms over the TCR signalosome are shown. The figure represents PD1-dependent proximal inhibitory mechanisms, which depend on the recruitment of SHP1 and SHP2 phosphatases as shown. These phosphatases inhibit ZAP70 and PI3K activities (blue arrows). Downstream intracellular pathways are also terminated, as exemplified in the figure with ERK and PKCO.
- (B) Indirect inhibitory mechanisms over TCR signaling and T cell proliferation are shown through regulation of CK2 expression and activities. On the left, the PI3K-dependent signaling pathway activating CDK2 and inhibiting SMAD3 is shown. Briefly, PIP3 activates AKT leading to production of the ubiquitin ligase SCF that degrades the CDK2 inhibitor Kip1. Activated CDK2 triggers cell cycle progression and inactivates SMAD3 by phosphorylation. These pathways are



negatively regulated by the PTEN phosphatase that degrades PIP3. During TCR activation CK2 phosphorylates PTEN with a concomitant decrease in its activities. When PD1 is engaged CK2 expression and activities decrease resulting in active PTEN that eliminates PIP3 shutting off AKT activation.

- (C) Regulation of TCR surface expression by PD1. PD1 engagement promotes expression of E3 ubiquitin ligases of the CBL family, as shown. As indicated, other ligases may be up-regulated as well. These ubiquitin ligases ubiquitylate TCR chains and PI3K, leading to the removal of TCRs from the T cell surface, possibly by endocytosis. Thus, T cells cannot respond to antigenic stimulation.
- (D) Metabolic control by PD1. Engaged PD1 alters T cell metabolism from glycolysis to β -oxidation by inhibition of ERK and PI3K-AKT activities. PD1-stimulated T cells would then metabolically resemble long-lived memory T cells

Current treatment: Ab to PD-1 and checkpoint inhibitors.

Future expectations: Drug binding SHP2 & PD1 could be used.

DE NOVO 2020-21

INSTITUTE OF SCIENCE, NIRMA UNIVERSITY



COMPETITIVE EXAMS IN BIOLOGICAL SCIENCE

How to prepare for CSIR-NET and GSET

-Nidhi Jodhwani (16MMB006)

The very first thing that comes in our mind after M.Sc. is to clear competitive exams like **CSIR-NET**, **GSET**, etc. Especially if you are planning to go into research or academics. The key to getting success revolves around these four D's-**D**esire, **D**edication, **D**etermination, and **D**iscipline. Implementing these four key steps will differ between those who only dream and those who actually achieve them. Another important factor is to keep a positive mindset and to learn from failures. Apart from these, I would like to share some of the points which can help you out during the preparation of the exam:

- · Get the complete idea of the exam.
- Check the syllabus thoroughly and choose the topics to be covered and material to be referred to wisely.
- Notes should be prepared in your own words to organize important things in one place.
- Solve at least 3 to 4 Questions from each topic.
- Go for online mock tests as time management is a very crucial point. You might be well prepared for the exam but cannot attempt the whole paper due to lack of time.
- Always be positive. All the above things will direct you towards success only if you maintain a positive attitude through all ups and downs. Just remember there is no alternative for hard work.

Some important topics to be covered for NET and GSET:

- Part-A: Number sequence, Series based problems, Days and date problem, probability, Mensuration, Commercial mathematics, statistical methods.
- Part B & C: Mendelian and non-mendelian genetics, cell cycle and regulation, cytoskeleton, photosynthesis, cancer biology, developmental biology (limb development, early embryology axis formation and segmentation in drosophila), gene regulation, protein biology, lipid metabolism, stress physiology, and carbohydrate metabolism, amino acids metabolism, plant physiology(plant hormones, sensory photobiology, reproduction and life cycles of plant system), microbial genetics, gene arrangements, and antibody diversity, pedigree analysis, ecology, evolution, animal behavior, Apoptosis, and cell senescence, hormones and endocrine system, circulatory system, B & T cell biology, Immunological techniques, bioanalytical techniques, excretion, and osmoregulation.

Hope this will help you out.

GATE exam tips

The Graduate Aptitude Test in Engineering is one of the most important national-level competitive exams for M.tech and Ph.D. admissions at various national and international institutions. It is very much advisable to 'stick to the syllabus' provided online and prepare strategically. One can decide the sections to attempt and prepare accordingly. GATE life sciences exam is relatively easier as compared to the CSIR UGC NET exam, but it requires directed preparation. The information on sections and marks distribution is provided below:

- Section General aptitude (Compulsory) Carrying a total of 15 marks.
- Section P Chemistry (Compulsory) This section contains 15 questions carrying a total of 25 marks: 5 questions carrying one mark each and 10 questions carrying 2 marks each. Some questions may be of numerical type. Mainly numerical-type questions are basic formula-based questions asked from the physical chemistry part.
- Any two of XL sections Q to U The choice of sections can be made during the paper after viewing the questions. But it is advisable to prepare and choose sections before the examination and prepare accordingly. Each of the optional sections of the XL paper contains 20 questions carrying a total of 30 marks: 10 questions carrying 1 mark each and 10 questions carrying 2 marks each.

You should solve full-length mock test papers available online. It will help you manage exam time and the software interface easily. Give special time to the compulsory aptitude section and chemistry.

Protip – Try to memorize constants e.g. avg molecular weight of Amino acids/nucleic acids. These will help you solve numerical easily and quickly.

-Hrimkar Buch (18mbc002)

My name is Priyamvada Rathaur and I cleared the CSIR-UGC NET exam for JRF in Life Sciences in June 2019 with an All India Rank of 69. Although I did not formally prepare for this exam, I have always been very attentive in my classes and consistent with studying what we have been taught. The syllabus has been designed in a manner that allows us to cover a vast range of important topics that are asked in this exam. I know from my peers that attempting practice questions and studying from books designed to crack these exams can make a huge difference in not only the exam, but also, gaining clarity and a strong foundation for these subjects. We are lucky to be provided with resources like this in our Institute's library. I think one of the most important things that I did was manage my time wisely while attempting this exam and allocate enough time for Section C. I also made sure to attempt questions that could be reasoned out or the ones I knew the answers to. Section A focuses on logical and analytical skills and with practice, this section can also be awarding if its attempted prudently. It is important not to get flustered and get caught up in guessing the right answer because negative marking can make a huge impact on the final score. And lastly, I cleared this exam on my second attempt. The inability to clear this exam shouldn't dishearten students because there is always scope for improvement. As we advance further to gain deeper insight into these subjects, we become better equipped to crack these exams.

-Priyamvada Rathaur

The Science Career Maze

-Pinkal Shah (18MBT029) -Ishani Morabia (18MBT018)

Advancement in Science is at its pinnacle and that's what attracts young and talented minds towards a career in it. Some may think of it as a way to satisfy curiosity, while for others it may seem as a source of making good money. Well, whatever may be the criteria, Science satisfies all of them.

Most of us opt for pursuing Science stream at 10+2 level with an aim of becoming a doctor or an engineer, but many of us due to a variety of reasons fail to procure admissions in this highly competitive era. It may feel as painful as a nervous breakdown and many a times students also face depression-like conditions. One of the main reasons behind this can be the inability to foresee an enormous bunch of bright opportunities that lie out there other than medical and engineering courses.

We have reached at such a stage that from dawn to dusk, we are inevitably aided by Science & Technology. Where it has already solved uncountable issues, a lot many new problems arise day by day. And to solve these, research in Science becomes eminent. Thus, research becomes the greatest career opportunity for individuals who are passionate about Science. Lack of awareness and guidance can be a major factor behind individuals not considering research to be a potent career option.

We normally have a tendency to consider a 'Bachelor of Science' degree after 10+2 to be not as worthy as a degree in medical/engineering. That's the greatest myth one can nurture and it can be quite delusive. A BSc course confronts an individual to a primary glimpse of research and lays the basic foundation for it. Thereafter, a MSc degree further develops an instinct and inclination towards research, following which there's are endless instances to be addressed.

As in any other course of study, it is utmost important to know about various institutes across the country and the programs that they offer for higher studies. Students often fail to avail advantages of studying in national level institutes and other renowned ones, where improved insight and knowledge of research can be gained. Guidance and awareness regarding each and every aspect of higher studies and research can help in shaping best careers.

QUEST CORNER (questcorner1918@gmail.com) is one such startup where students are guided and made aware about all the opportunities regarding higher studies from Bachelor level itself and also coaching is provided for valuable national and state level entrance exams.

To all the Science passionates out there, Good luck!

SELECTED BREAKTHROUGH IN BIOLOGY

2013	CRISPR-Cas9 is used in human genome editing (Jennifer Doudna, Emmanuelle Charpentier and Feng Zhang) https://www.sciencenews.org/article/crispr-gene-editor-first-human-clinical-trials
2010	First bacterial cell to contain a completely synthetic genome (Craig Venter) https://www.newscientist.com/article/dn18942-immaculate-creation-birth-of-the-first-synthetic-cell/
2005	Next generation sequencing https://www.nature.com/articles/nrg.2016.49
2000	Genome sequencing of humans, <i>Homo sapiens</i> https://www.genome.gov/human-genome-project
1995	Genome sequencing of a prokaryote, <i>Haemophilus influenzae</i> https://www.sanger.ac.uk/resources/downloads/bacteria/haemophilus.html
1990	Cryo-Electron Microscopy (Jacques Dubochet, Joachim Frank and Richard Henderson) http://www.nature.com/news/cryo-electron-microscopy-wins-chemistry-nobel-1.22738
1985	In vitro amplification of DNA by the Polymerase Chain Reaction method (Kary Banks Mullis) https://www.nobelprize.org/prizes/chemistry/1993/mullis/facts/
1982	Insulin first genetically engineered product using recombinant DNA technology (Eli Lilly & Co's Humulin) https://www.fda.gov/media/110447/download
1975	Development of DNA sequencing procedures (Frederick Sanger) https://www.nature.com/scitable/definition/dna-sequencing-205/
1975	Monoclonal antibodies production (Georges Köhler and César Milstein) https://www.immunology.org/kohler-and-milsteins-hybridoma-technology-1975
1972	Construction of Recombinant DNA (Paul Berg, Stanley Cohen and Herbert Boyer) https://www.genome.gov/25520302/online-education-kit-1972-first-recombinant-dna

1970	Immunoglobulin structure (Gerald M. Edelman and Rodney R. Porter) https://www.nobelprize.org/uploads/2018/06/edelman-lecture.pdf
1966	Unravelling of the universal genetic code for all lifeforms (Marshall Nirenberg, Heinrich Matthaei, Har Gobind Khorana and Robert Holley) https://www.acs.org/content/acs/en/education/whatischemistry/landmarks/geneticcode.html
1963	Ramachandran Plot distribution of torsion angles in a protein structure (G N, Ramachandran) https://proteinstructures.com/Structure/Structure/Ramachandran-plot.html
1962	Discovery of development of the green fluorescent protein (Osamu Shimomura) https://www.ncbi.nlm.nih.gov/pubmed/19579247
1953	Postulation of a complementary double-helical structure for DNA (James Watson and Francis Crick) http://www.nature.com/scitable/topicpage/discovery-of-dna-structure-and-function-watson-397
1952	Miller and Urey's classic experiment on the Origin of Life (Stanley L. Muller and Harold C. Urey) https://ntrs.nasa.gov/archive/nasa/casi.ntrs.nasa.gov/20050139759.pdf
1952	DNA proves to be the genetic molecule (Alfred Hershey and Martha Chase) http://www.nature.com/scitable/topicpage/discovery-of-dna-as-the-hereditary-material-340
1938	Electron microscopy used for biological samples (Max Knoll and Ernst Ruska) https://www.leo-em.co.uk/history-of-electron-microscope.html
1901	Human blood group discovery (Karl Landsteiner) https://www.nobelprize.org/prizes/medicine/1930/landsteiner/facts/
1860	Mendel's laws of inheritance (Gregor Mendel) https://www.nature.com/scitable/topicpage/gregor-mendel-and-the-principles-of-inheritance-593/

Dr. Kuldeep Verma







Congratulations to GSET Qualifiers!



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