School of Life Sciences

Manipal
INSPIRED BY LIFE

Newsletter

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Science Zone

The Saccade Controller

- Ketki Mulay, BSc Year II & Anant Kakar, MSc Year I

What happens to a small child in a candy store? We have all been there. We remember our eyes feasting on as many candy bars as it possibly can. But have we ever wondered what goes on behind the scenes? What controls the quick, jerky eye movements known as 'saccades', which occur as the eye explores a scene? Our brain, of course. But how?

We already know that the cerebellum is involved in the control of saccades, as well as the control and coordination of other body movements. Our cerebellum is composed primarily of one type of cell, the 'Purkinje' cells, whose activity fluctuates with saccades, proving that these cells play a crucial role in saccadic movement. What we did not know is how they affected this crucial type of eye movement.

It was found that there are broadly two types of Purkinje cells involved in the reflexive saccade : *burst cells*, whose activity temporarily increases during saccades, and *pause cells*, whose activity decreases before saccade begins. Unfortunately, it was found that the activities of the burst cells did not correlate to saccadic movement. Why there was an increment in the burst cell activity during saccades? The solution to this query was elucidated by Dr. Herzfeld and his team in October 2015. They analyzed Purkinje activity during saccadic movement in monkeys, and found that neuronal fibres known as 'climbing fibres' receive information from various sources and are involved in controlling the direction of saccadic movement. These fibres project into the Purkinje cells and send sensory information to two types of Purkinje cells involved in saccadic eye movement -burst cells and pause cells, change their activity (the activity of burst cells increase and that of pause cells decrease). This change in Purkinje cell activity is sent to clusters of neurons collectively known as the cerebellar nuclei. The cerebellar nuclei, normally responsible for most of the cerebellar output, integrate this information collected from the entire population of Purkinje cells and thus regulate saccades. The speed at which this entire process takes place makes one marvel at the complexity and efficiency with which the human body encodes, decodes, and processes information.

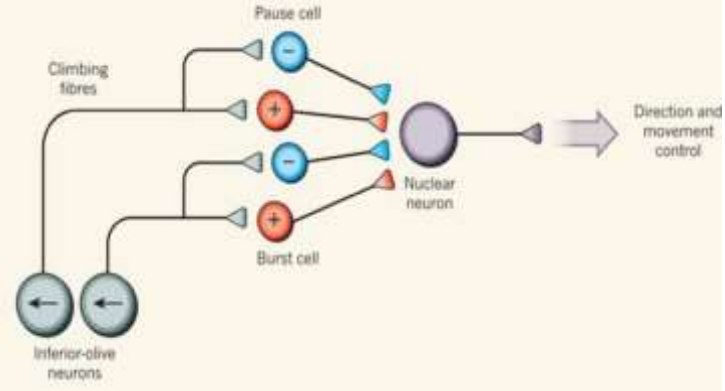


Image: Wiring up Saccades

Photo credit: nature.com/Neuroscience

Reference:

1. Khodakhah K. (2015). 'Neuroscience: decrypting a brain enigma' **Nature** 526, 326-327

Implants to Trap Cancer Cells

- Namita Bhyravbhatla, BSc Year II

Recently US researchers have developed a small implant that has the ability to absorb metastasizing cancer cells. 5mm in size, this sponge-like implant once imbedded into the abdominal fat or under the skin has the ability to suck up cancer cells.

The ongoing research involves mice in which breast cancer is induced. The principle behind these implants lies in the intersection of spreading of cancer cells and the role of the immune system in such events. Normally, the tumors break off and get attracted to other areas of the body by immune cells. Instead, these immune cells can set up a camp of sorts on the implant itself as a natural immune reaction to a foreign antigen and draw the cancer cells in. Through special imaging techniques that can distinguish between normal and cancer cells, the cancer cells can be detected via the use of the implant. Another effect of this implant that is still being researched is its ability to actually reduce the number of cancerous cells. Though the finer details still remain vague, it was noted that the mice with the implant showed a considerable decrease in the number of cancerous cells in comparison with the mice without the implant. During metastasis, the cells generally break away from the tumors and then proceed to spread through the blood stream into various areas of the body. Because of the inability to track the whereabouts of the spreading tumors, identifying where the cancer will spread and thus treating it has proven to be difficult. Researchers hope to use this device as a system to alert doctors of the tumors spread, so that halting the rogue cancer cells can be possible. Through this the death rate of cancer patients could be drastically decreased.

Clinical trials on humans are yet to start but will proceed soon. So far trials have been conducted and proven successful on mice with breast cancer.

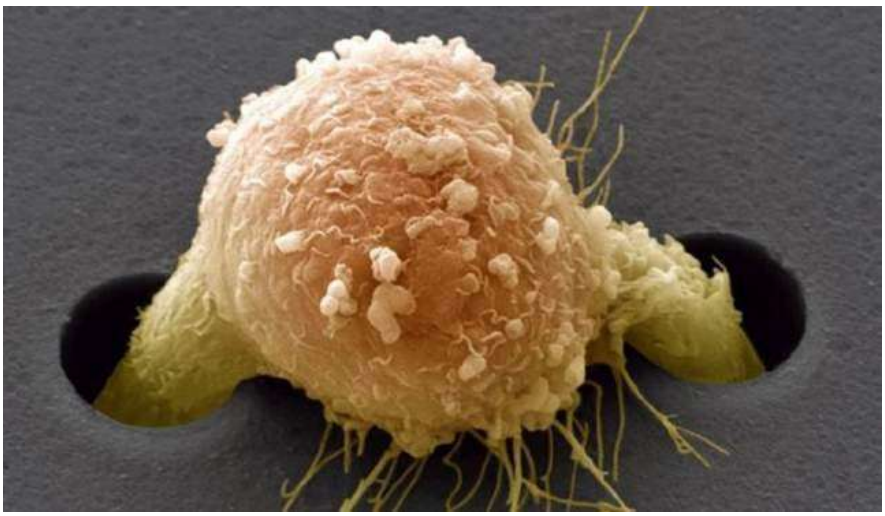


Image: *Metastizing breast Cancer Cell as seen under an Electron Microscope*

Photo credit: Pulse Headlines

References:

1. Azarin S. M. et al (2015). 'In vivo capture and label-free detection of early metastatic cells' **Nature Communications** 6, Article Number: 8094

Nobel Prizes 2015

- Megha Patro, BSc Year III

Nobel Prize for Physiology or Medicine

The Nobel Assembly at Karolinska Institute awarded the 2015 Nobel Prize in Physiology or Medicine jointly to **Satoshi Omura and William C. Campbell** for their discovery concerning a novel therapy against infections caused by roundworm parasites, and the other half to **Youyou Tu** for her discoveries concerning a novel therapy against Malaria.

William C. Campbell and Satoshi Omura discovered a new drug, **Avermectin**, for River Blindness and Lymphatic Filariasis, which has an efficacy against a wide range of parasites. Youyou Tu discovered **Artemisinin**; a new class of drug used for its faster action in the initial stages of the disease.

All the three diseases are induced by parasites and have a similar distribution around the world.

After numerous failures in developing a durable medicine against parasitic disease, these scientists succeeded in developing natural (bacterial and plant based) anti-parasite therapies.

Photo credit: nobelprizemedicine.org

After Omura isolated a new strain of Streptomyces, known for its production of various anti-bacterial agents, Campbell acquired those samples for further analysis; isolating and purifying a bioactive agent named Avermectin. The purified product was a chemically modified form of Ivermectin, which acted against human parasites as well.

In the late 1960s, Chloroquine, although a traditional medicine, had limited success. When malaria could not be eradicated, Youyou Tu (in China) consulted ancient literature to uncover clues about herbal medicine and its uses. *Artemisia annua* was selected after a large-scale screening process and after various tests; an active compound was found which was highly effective against both infected animals and humans.

Nobel Prize for Chemistry

The Royal Swedish Academy of Sciences awarded the Nobel Prize in Chemistry for 2015 to **Tomas Lindahl, Paul Modrich**, and **Aziz Sancar.**

The prize was given for providing fundamental knowledge about the functioning of cells, the DNA damage repair mechanism at the molecular level and how genetic information is protected.

DNA is an unstable genetic material - factors like metabolism and radiation cause damage to it. In humans, there are various processes through which such damages/ lesions can be identified and corrected by processes known as DNA damage repair pathways. It is extremely important to map these processes in order to understand the whole cellular system.

Tomas Lindahl mapped the **base excision repair pathway**, which counteracts the collapse of the DNA. Aziz Sancar, demonstrated the mechanisms employed by cells to repair UV damages to DNA via the **nucleotide excision repair pathway.**

Paul Modrich illustrated the **mismatch repair pathway**, which is basically the unique ability of a cell to recognize mismatches formed during DNA replication to reduce the frequency of error.

Nobel Prize for Physics

Nobel Prize in Physics for 2015 was awarded by The Royal Swedish Academy Of Sciences to **Takaaki Kajita** and **Arthur B. McDonald.**

A neutrino is an electrically neutral elementary particle with a half integer spin. They are leptons, and are found in three different flavours – electron neutrinos, muon neutrinos and tau neutrinos. Neutrinos are the only identified candidates for dark matter. Postulated by Pauli way back in 1930, many neutrinos are created in reactions between cosmic radiation and the Earth's atmosphere - some by nuclear reaction inside the Sun, causing millions stream though our bodies every second.

The 2015 Physics Nobel Laureates have been recognized for demonstrating that neutrinos can change identities, hence solving the long standing mystery - where the theoretical calculations could not be summed up with the observations. This showed that metamorphosis requires them to have mass. The discovery has not only changed our view of the universe, but has also explained the innermost workings of matter.

Takaaki Kajita, of Japan, discovered that neutrinos from the atmosphere switch between two identities on their way to the Super-Kamiokande detector.

Arthur B. McDonald, illustrated that the neutrinos from the Sun were captured with a different identity upon arrival to the Sudbury Neutrino Observatory.

Nobel Peace Prize

"The said interest shall be divided into five equal parts, which shall be apportioned as follows: /- - -/ one part to the person who shall have done the most or the best work for fraternity between nations, the abolition or reduction of standing armies and for the holding and promotion of peace congresses."

- (Excerpt from the will of Alfred Nobel)

The Nobel Peace Prize is awarded by a committee of five, chosen by the Norwegian Shorting. The Tunisian National Quartet was awarded the 2015 Nobel Peace Prize by The Norwegian Nobel Committee for establishing a multicultural democracy in Tunisia, in the wake of the Jasmine Revolution of 2011.

The Quartet was formed in the summer of 2013 to protect the collapsing democracy due to political domination and widespread social unrest. Instead a pluralistic democracy was developed, right when Tunisia was on the verge of civil war. This helped build a constitutional system providing equal rights to the entire population.

Four key organizations built the National Dialogue Quartet in Tunisian civil society:

The Tunisian General Labour Union

The Tunisian Confederation of Industry, Trade and Handicrafts

The Tunisian Human Rights League, and

The Tunisian Order of Lawyers

These organizations represent different sectors and values in Tunisian society: working life and welfare, principles of the rule of law and human rights.

Tunisia faces significant political, economic and security challenges. The Norwegian Nobel Committee hopes to inspire everyone who seeks to promote peace and safety by contributing towards the change brought about in Tunisia. The Prize is not only awarded for the hard work of the Quartet but also intends to encourage the Tunisian population and acknowledge the groundwork set up by them despite major challenges.

Nobel Prize for Literature

Nobel Prize in Literature was awarded to **Svetlana Alexievich**, described for "***for her polyphonic writings, a monument to the suffering and courage in our time"***, a Belarusian-Ukrainian writer who crossed all hurdles to beat Japan's Haruki Murakami, Kenya's Ngũgĩ wa Thiong'o and the Norwegian playwright Jon Fosse and win the 2015 Nobel prize for Literature awarded by the Swedish Academy. She was the 14th woman to be awarded the Prize since it started in 1901.

She has written various short stories and essays and has dedicated 30-40 years in mapping the Soviet and the post-Soviet times. Her oral histories have recorded thousands of individual voices to map the implosion of the Soviet Union.

Nobel Prize for Economical Sciences

Angus Deaton was awarded the Sveriges Riksbank Prize in Economical Sciences in Memory of Alfred Nobel 2015 - "*for his analysis of consumption, poverty, and welfare"*.

Angus worked on a similar study as his two competitors, Sir Tony Atkinson and Thomas Piketty, in trying to link the individual choices and aggregate outcomes.

The economics Prize was created by the Swedish Central Bank in Alfred Nobel's memory in 1968. The other five awards were established by Nobel in his will in 1895.

p53 – Guardian of the Genome

- Harsh Ranawat, BSc Year I & Anant Kakar, MSc Year I

An apt name is indeed. We all know what cancer is and how devastating it can be, right? But did you know that it is almost impossible for a normal cell to become cancerous until it is able to inactivate p53? p53, a protein present in all our nucleated cells acts as a tumour suppressor in our body: it tries its level best to ensure we do not get cancer.

A recent study conducted at the University of Chicago showed that p53 was the protein that explained Peto's Paradox. Peto's paradox states that the occurrence of cancer in an organism is not directly proportional to the number of cells in that organism. By logical reasoning, one would expect elephants to have a higher incidence of cancer than humans- as they have a much larger amount of cells. P53, however, makes sure that this does not happen. The study proved that there were more number of p53 copies in larger animals. This allows the damaged cells to self- destruct, thus preventing cancer.

The growth of a normal body cell can be compared to the motion of a car. The driver controls how fast (or how slow) the car goes, and in which direction. And this is based on the needs of the driver, as well as the situation. Driving fast in an unfavourable environment such as heavy traffic could have severe consequences. In the same way, cell growth is regulated by the needs of the body as well as the environment the body is in. The normal cell has an accelerator as well as a brake to control the rate of growth and proliferation. So what would be a cancer cell in this analogy? It is a monster truck that has a brick on the accelerator, and a brake that is not working. It will accelerate as fast as it can, mowing down everything in its path. For cells, that brake is the p53 tumour suppressor.

Situations that 'stress' the cell, such as DNA damage, or over-stimulation of growth, could lead to cancer. But they do not ALWAYS lead to cancer. So how can cancer come about? Rather, how is cancer related to p53? p53 is responsible for pressing the brake in a 'stressed' situation such as DNA damage, informing the cell that it needs to stop growing right away. If, for instance, the cell is able to repair its DNA, p53 will lift its foot off the brake and let the cell grow. If not, p53 will signal the cell to kill itself, since a cell with damaged DNA could harm the organism. It is important to understand how this process works: DNA damage will lead to the mutation of a particular set of proteins. And if the proteins involved in cell growth are mutated, their natural tendency is to stimulate increased and uncontrollable growth of the cell. But, luckily for us, the cell recognizes these mutated proteins and relays this information to p53, which then directs the cell to stop growing, and, as a result, 'cancer' is averted. But here is the clincher: what if the DNA damage affects p53 itself? Who can the cell turn to then? The result is chaos, manifested in the form of uncontrolled cell division: what we know to be cancer.

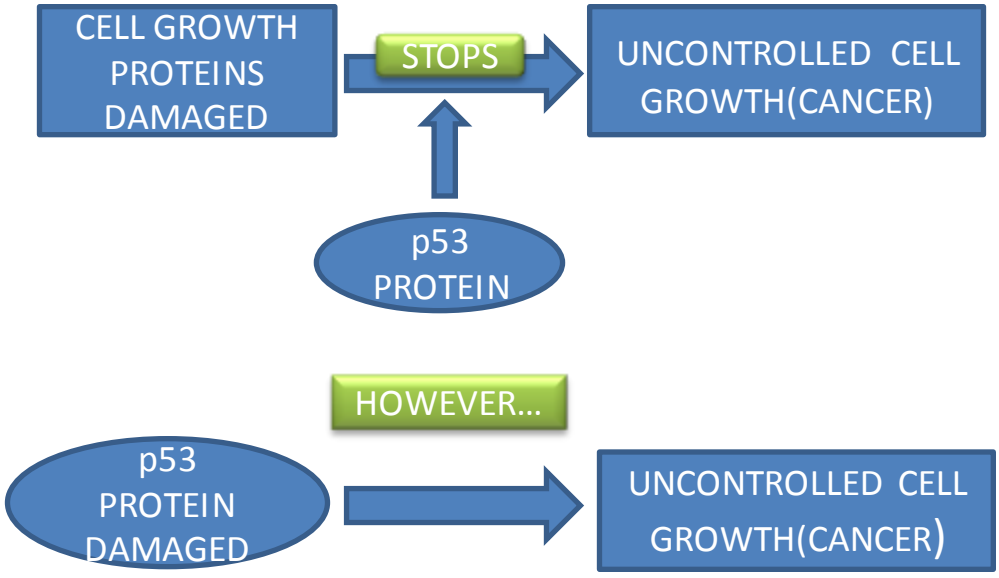


Image: *How p53 helps prevent cancer*

Reference:

1. Bieging K T et al (2014). 'Unravelling mechanisms of p53-mediated tumor suppression' **Nature Reviews Cancer,** 14, 359–370

Malaria and Asthma – an Unforeseen Link

- *Harithaa, BSc Biotechnology year I & Syamala Inumella, BSc Biotechnology year III*

Malaria has been plaguing the world since time immemorial. Peruvians were responsible for the first ever treatment for malaria to be recorded way back in the 1600s. This disease, as we all know, is mosquito-borne, and can be caused by parasites of the *Plasmodium* genus. The protozoa responsible are about 5 species: *P. falciparum, P. vivax, P. malariae, P. ovale and P. knowlesi*. Understanding these parasites is essential to improve the efficiency, with which this disease can be cured.

The School of Life Sciences, Manipal is involved in research related to this tropical disease, in particular malaria caused by *P. falciparum*. The pathogenesis and susceptibility of individuals with respect to asthma are being investigated with respect to Indian population. The role of alleles, genotypes and the associated haplotypes of six *ADRB2* SNPs (Single Nucleotide Polymorphisms) with respect to *P. falciparum* malaria is being looked into.

ADRB2 (Adrenoceptor Beta 2) is an intron less gene located on chromosome 5 which belongs to the G-protein coupled receptor family. The polymorphisms and mutations in this gene have been found to be involved in various forms of asthma, obesity and diabetes. Of the six polymorphisms tested, one locus (rs1801704) showed an increased influence on malaria. The various haplotypes tested also showed some important results, as one was protective against asthma and one was protective against malaria.

An extension of the study could lead to potential identification of reliable markers for malaria and asthma, using malarial resistance or susceptibility as a link to associate with haplotypes. However, it is limited by the homogenous and identical ethnicity of the participants. Thus, using this information, the role that *ADBR2* has in malaria therapy can be improved.

Asthma and Malaria: Could there be a link?

Photo credit: Google Images

Reference:

1. Saadi A V et al (2013). 'Single nucleotide polymorphisms of ADRB2 gene and their association with susceptibility for *Plasmodium falciparum* malaria and asthma in an Indian population' **Infection, Genetics and Evolution**, 20,140-7

SCCmec Elements and their Significance

- Syamala Inumella, BSc Year III

Microbial drug resistance is one of the major problems faced by drug developers and healthcare specialists alike. It is a phenomenon that is becoming increasingly widespread all over the world. Due to this, bacteria, fungi, and even some viruses exhibit resistance to drugs that are aimed at attacking and destroying them.

Our own School of Life Sciences, Manipal has an on-going research project that deals with this pressing matter. The development of foot ulcers is one of the major complications of diabetes. These diabetic foot ulcers are often infected by various pathogenic microorganisms. The diversity of these organisms is affected by many factors, one of them is their resistance to drugs.

There are microorganisms resistant to multiple drugs - Multi Drug Resistant Organisms (MRDOs) - as well as those that are resistant to specific drugs, such as Methicillin Resistant Coagulase Negative Staphylococcus (MRCONS). SLS deals with a specific single drug resistant microorganism - Methicillin Resistant *Staphylococcus aureus* (MRSA). Detection and characterization of MRSA is crucial in treatment strategies. The strains of *Staphylococcus aureus* resistant to methicillin can be characterized via SCCmec typing. This is done based on the presence of a particular genetic component- the "Staphylococcal Cassette Chromosome mec" (SCCmec). Such elements can be identified by the presence of four constituents – terminal repeats, a "mec" element, a site-specific cassette chromosome recombinase (ccr) and an insertion site within an open reading frame. There are seven types of SCCmec viz., types I through VII. SCCmec types I, II, and III are typically found in the case of nosocomial infections. Types IV, V, VI and VII are usually associated with community acquired infections.

Strains of *Staphylococcus aureus* have developed resistance due to the insertion of these SCCmec elements via the mecA gene. However, the origins of the mecA gene are still vague. It is speculated that the SCCmec complex integrated into the *S. aureus* genome had initially originated from *S. fleuretti*. Improving our knowledge of the genetics behind such drug resistant pathogens is essential for their control and proper treatment. This way, the rampant spread of such resistant pathogens can be well controlled.

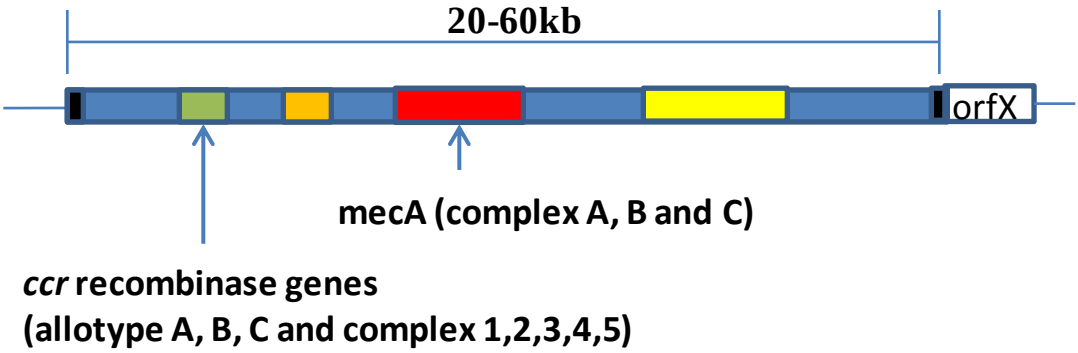


Image: *Positioning of the mecA Gene on the SCCmec Element*

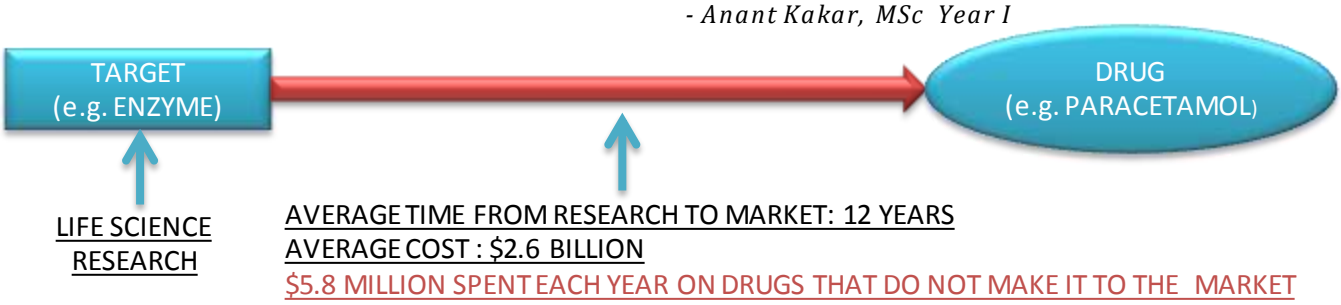
Photo credit: slideshare.net/MRSA seminar

Reference:

1. Murali T S et al (2014) 'Genome Sequences of Four Clinical Staphylococcus aureus Strains with Diverse Drug Resistance Profiles Isolated from Diabetic Foot Ulcers' **Genome Announcements,** 2, e00204-14

Drug Discovery - Why?

- Anant Kakar, MSc Year I



How does one 'discover' a drug? What goes into making that small little tablet that your doctor asks you to take when you fall ill? Years and years of extensive research, truckloads of money, blood, sweat and tears don't even begin to describe the process of 'drug discovery'. I hope that, by the end of this article, you will take some time out to appreciate the history behind that 'small little tablet' that we all take for granted.

So, to cut to the chase, where does the process of drug discovery really begin? The obvious answer would be 'in the lab', however, think again. It truly begins when a particular disease or disorder has been identified, so that scientists can strategize how best one could tackle it. The next step is to develop a 'drug target', a process that involves extensive research on the disease or disorder itself. It is at this point that research such as that carried out at SLS comes to the fore, as it provides a foundation upon which a target based drug can be developed.

So what is a 'drug target'? Say, for example, someone has suffered an injury and is experiencing pain. This indicates that something inside the body has changed ; that change is experienced as pain . So undoing that change, in theory, should relieve the pain as well. This 'something' is what life scientists are looking for: what it is and how it has changed? This altered entity is known as a drug target; as it provides information regarding where and how a molecule could act in the body to have a desired therapeutic effect. A common example of a drug target is an enzyme or receptor whose activity in the body increases/ decreases in an abnormal or diseased condition.

After a target has been definitively identified, the process of developing a suitable molecule to interact with the target in a desired fashion begins. This is an extremely complex process as this molecule has to fulfill a variety of criteria before it can be marketed as a drug:

- The molecule must alter the target effectively; this means that a small concentration of the molecule must be able to alter the target to a degree that would result in the desired therapeutic effect.
- The molecule must interact specifically with its target; any off-target action could lead to a range of side-effects that can sometimes be dangerous.
- The molecule must reach its target in the human body at a sufficient concentration for it to elicit a therapeutic response.
- The molecule must stay in the body for an optimum amount of time; fast elimination (limited therapeutic effect) as well as slow elimination (toxicity) are both undesirable.
- The molecule must be rigorously tested for safety and efficacy in both animals (rodents, dogs, primates) as well as humans to ensure that it elicits the desired therapeutic effect with minimal side effects.
- The molecule must be easy and cost effective to synthesize.

The extent of the work that goes into both target identification as well as molecule design are beyond the scope of this article; however, this process remains to be one of the most fascinating processes in research and development today.

Reference:

1. Benjamin Blass (2015) 'Basic principles of Drug Discovery'

Interviews

Interview with the Vice-Chancellor, Manipal University

The Vice-Chancellor of Manipal University, Dr. H Vinod Bhat, graciously accepted our request for an interview for the SLS e-newsletter recently and spoke on a range of topics. Here are the excerpts:

Students Council (SC): As students of SLS, we are indebted to the wealth of knowledge imparted by the dedicated professors, exposure afforded by the overseas exchange programs and the excellent, world class research facilities; the overall experience has been immensely rewarding and enriching. Given its tremendous potential, what is your vision for SLS over the next couple of years? Also, as a leader and a mentor, how would you suggest we apply this knowledge in a practical context in a country like ours where the masses urgently need improved healthcare solutions?

Dr. Vinod Bhat(VB): We have done the homework right, when we set down the priorities for establishing the School of Life Sciences. I see no reason to change those priorities. It is now only a matter of scaling up, in terms of doing more of what needs to be done. My firm belief is this: if there is a good thing to be done, and then it ought to be done. If you do it well, why not do more of it? So you are talking about both quality and quantity. We have done the right things here, in terms of producing a world-class institution. It is time that we scale up to more students, more projects, more doctoral candidates, more international collaborations, more exchange possibilities.

SC: Sir, how do you think more awareness about the importance of research could be created, especially in terms of the extent and applications of biotechnology in the real world?

VB: It is happening to an extent – although not with the speed that impatient people like you and I want it to happen with (*smiles*). If you look at India's own contribution in the world of science in the last 5 years, there has been a significant increase in publications. There was, however, a period of lull, where many people were happy with the programmes but not with the research; or happy with the research but not the publications; or happy with the publications but not with the patents. These kinds of things are now going away, and you can find India resurgent with an increased research output. In the next 5 years, you will see more of this happening. In a way, the country has done right by promoting science. But you need to put money on the table. High quality research requires money. This is something that the government should support, in terms of backing up laboratories, making more money available for research so that more people can compete. For example, the best projects can be funded; anything to make sure that the best kind of focus comes on good research. That is something that is lacking. So correction of this will, perhaps, aid us in further research.

SC: How would the general population be more aware of how the research being done will help them?

VB: We are missing a point here. The common man will not be able to understand the complex work being done in the lab. What will matter to them ultimately are the applications.

So, that should be the focus here. It might be asking for too much if you want your kind of work to be understood by everyone. But make sure that the kind of work you do is at least understood by the people who matter – like those in governments, industries, healthcare, and diagnostics. Make sure the necessary stakeholders understand. We don't need an overly general, 'carpet-bombing' kind of awareness campaign.

SC: Do you feel that right now, there is a communication gap between scientists and doctors? Doctors may not exactly understand the science behind a particular drug, for example. Do you feel this combination of both clinical and scientific knowledge is recommended, or do you feel society as a whole would benefit more from the interaction of more specialized doctors and scientists?

VB: There has to be a constant engagement between clinicians and scientists. What you do here has to be directly applicable there. Clinicians are unfortunately, extremely busy. It's in their DNA (*smiles*), so if you ask them to view and understand your research they simply will not have the time to do so. But we, as scientists, need their input. So programmes such as symposia or workshops can be organised to bridge the gap between science and clinical medicine.

But what would really help is if there were a generation of interdisciplinary people, who have enough experience with both clinical sciences as well as medicine.

SC: In today's generation, a lot of people start out with MBBS and then continue on to do a PhD. Is that what you mean?

VB: Yes. Such learning would make doctors understand the genetics and the molecular basis behind a disease. This would create people who are able to look at all the possibilities and applications as well. I think a future generation such as this would greatly benefit the science community with a fresh outlook.

SC: You have brought about revolutionary changes in the field of Community Medicine dealing with pregnancy & childbirth. Thanks to you, the infant mortality rate has gone down considerably. What else would you like to be involved in?

VB: Community medicine was my core. The focus 20-25 years ago was mother and child care. When 40% of our population is made up of mothers and children, this was necessary. But now fresh problems must be addressed, such as cancers, communicable diseases, diabetes, etc. These are all something we cannot afford to have as a country. Typically, India has been historically associated with many communicable diseases. We have overcome some of these. I feel this should be our priority – along with many other social issues, not just healthcare.

SC: Manipal University today is a leading frontier in both high quality education and research. What is your vision for the future to catapult it to the next level?

VB: Well I don't see Manipal here growing any further – physically, I mean. It is already rather large and imposing on the environment, in terms of water, power, supplies, etc. I feel we should cap Manipal at 25,000 students. If you're capping growth at Manipal, however, we are growing in other parts of the world. There is no limit there. There could be spectacular growth happening in some projects that we take up in the near future. For example, this year alone, we have started 60 new sectors in Manipal University.

SC: What, according to you, is the tactical advantage that today's generations of scientists have that was missing a couple of years/decades ago in the field of Life Science research?

VB: Collaborations today are easier. In the 1980s if I wanted to work with a scientist in the U.S, I had to write a letter, wait 6-8 weeks before I got a reply. That isn't the case now. Also, funds are better and this leads to much better equipment. Scientific inventions and innovations are fastracked. Scientists then used to be a little more focused. They used to be very protective of their work, perhaps even overprotective.

SC: What is tougher, being a doctor or an administrator?

VB: (*laughs*) Well, I haven't been a doctor in a long while. But I would have to say that being a doctor is harder.

SC: Your way of unwinding after a long day of work would be?

VB: To sit down and read a good book.

SC: What do you love the most about Manipal the township?

VB: I like the diversity, the youth… it makes me feel so much younger and energetic. It is very quiet and peaceful.

SC: How do you balance your professional and personal life?

VB: It is actually easy if you learn how to compartmentalise. You don't bring your professional life home; you don't bring your personal life to work.

Image: *The Editorial Committee Interviewing Dr. Vinod Bhat*

Interview with Dr. PN Rangarajan

P. N. Rangarajan, Senior Professor at the Department of Biochemistry, Indian Institute of Science, Bengaluru visited the School of Life Sciences on 10th October, 2015, on official duty. Despite his busy schedule, he took a few minutes to give us a peek of his life as a researcher.

Dr. Rangarajan did his PhD at the Indian Institute of Science, Bengaluru, under the guidance of eminent scientist and administrator, Dr. G Padmanabhan, who eventually became the Director of the reputed institution. His PhD was in the Cytochrome p450 family of enzymes, specifically determining how the drug phenobarbital (used in epilepsy treatment) was metabolized. Through his experiments, Dr. Rangarajan noticed that whenever the drug was administered, a high level of an isozyme of cytochrome p450 was recorded. Thus, he found out that phenobarbitone activates a particular gene, which leads to the formation of p450.

His research and results led him to his post-doctoral work at the prestigious Salk Institute, California, to work with Prof. Ronald M Evans, the renowned researcher to first clone the gene that coded for the glucocorticoid receptors. There, Dr. Rangarajan also tracked the hormone response pathway related to these receptors. Further investigations revealed that it was not just one, but the presence of a huge family of steroid hormone receptors, thereby opening up entirely a new chapter of research.

In 1994, Dr. Rangarajan rejoined IISc, to be presented with a new challenge typical during the late 90's – the need to produce local vaccines. At that time, most of the vaccines available in India were imported, and therefore, very expensive. A local pharmaceutical company approached him with this issue. He took it up as a challenge, and started working on a recombinant Hepatitis B vaccine. He cloned the gene, that coded for this in one particular methylotrophic yeast, called *Pichia pastoris*, which was known to express proteins at high concentrations. The expressed protein, which was an antigen, was purified and further the technology was transferred to two companies which later worked on the antigen and produced a low-cost vaccine.

His next project was to develop a cheaper DNA vaccine for rabies. Typically, the treatment for rabies involves a minimum of 3-5 injections, each of which cost around 500-800 rupees. This is something that the common man cannot afford. The affordability of the vaccine was a problem, especially considering the fact that it is a contagious virus. He took the gene in question, cloned it in yeast cells, purified the proteins extracted them. He then used yeast promoter and incorporated it into a mammalian cell. This was advantageous as it ensured a high biomass, and also eliminated the need of two different organisms.

Dr. Rangarajan says, "The current challenge in the global market for vaccines is not to make it; the challenge is to make it low-priced. With efforts such as this, the country is now on its way to achieve this goal. India is now one of the largest exporters of "childhood" vaccines - a far cry from the days when it used to be one amongst the largest importers.

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Events

Introducing...

Student Council 2015

The new Student Council for the academic year 2015 was elected by the students of School of Life Sciences on September 14, 2015

Photo Credit: ***Kapil Joshi***

- President – Aditya Sethi
- Vice President – Meetali Morjaria
- General Secretary – Atrishi Badu
- Treasurer – Anirudh Gupta
- Joint Secretary I – Ramya Gupta
- Joint Secretary II – Harsh Ranawat

Committee Heads 2015

Photo Credit: ***Mahesh Nair***

Cultural Committee

Mukunth S

Namita Bhyravbhatla

Sports Committee

Akheel Anees

Sahil Cadiri

Editorial Committee

Anant Kakar

Syamala Inumella

Financial Committee

Thyagarajan

Sumukha Hegde

Confocal Microscopy Workshop at SLS

- Ramya Gupta, BSc Year II

On April 14, 2015, the School of Life Sciences acquired a confocal microscope as an addition to the various technological facilities available at the college. The facility was inaugurated by Dr H.S. Ballal, Pro-Chancellor of Manipal University.

Recently, a workshop on 'Next Generation Sequencing (NGS) for Genomic Applications and Confocal Microscopy for High Resolution Imaging for Cell Biology Applications' was jointly organized by the college and Leica Microsystems to provide hands-on training in operating the microscope from August 26 to 28, 2015.

The three-day advanced technology workshop was inaugurated by Prof. MS Valiathan (National Research Professor and former Vice-Chancellor of Manipal University, Manipal). Prof. Valiathan appreciated Manipal University for not just acquiring such an advanced facility, but for also being involved in actively disseminating the knowledge of its use to the public and the scientific community. However, he also warned against relying upon such high-tech equipment over scientific principles and hypotheses. Giving the example of Dr C.V. Raman and his spectroscope, he stressed that the development of such technologies within the country rather than their import should be supported.

The workshop was attended by researchers and academicians from around the country. It included talks on advanced bioinformatics analysis for genomic landmarks and targeted re-sequencing of the gene panel. The participants gained knowledge on the complete workflow of the facility, including image acquisition, processing and quantification for advanced imaging needs. The confocal microscope is a huge step-up from conventional microscopy such as wide field fluorescence microscopy because it enhances the optical resolution of the micrograph and thus, allows us to convert the imagination of three dimensional subcellular structures into reality. It is used widely in surface profiling and time-lapse imaging.

Image: *The Confocal Microscope at SLS Manipal*
Photo credits: Mr. Vasudeep

PhD Viva Presentations 2015

-Syamala Inumella, BSc year III

During the month of October, 3 Research Scholars from the School of Life Sciences were awarded the prestigious PhD degree from Manipal University for their respective novel contributions to the field of Life Sciences. They were kind enough to give us small excerpts on the research they did and its potential benefits to society:

Dr. Kamalesh D. Mumbrekar:

The aim of our study titled '**Cellular and molecular analysis of normal tissue toxicity induced by radiotherapy in breast cancer patients**' was to identify groups of patients who would develop adverse tissue reactions after undergoing cancer radiotherapy. The identification of these sensitive individuals by performing cellular/ DNA based assays will help to reduce treatment related toxicity by altering their treatment strategy and determining the effective radiation dose in patients who have been identified as 'resilient' to radiotherapy induced toxicity, thus resulting in an overall improvement in the quality of life of cancer patients. A study of this kind helps to a) provide an insight into the role of genetic factors in increasing an individual's susceptibility to radiation induced tissue toxicity, b) develop specific genetic signatures that can be developed into a clinical test to predict the onset of adverse tissue reactions before the start of radiotherapy. This will ultimately help to 'personalize' the radiation treatment in an individual.

Dr. Himanshu Gupta:

During our study titled '**Influence of host genetic factors on erythrocyte phase of malarial infection caused by *Plasmodium falciparum*"** we developed ultrasensitive diagnostic methods for malaria. These novel methods are more sensitive than the existing method in the detection of *Plasmodium falciparum* and *Plasmodium vivax*, the malaria causing parasites, in human plasma. We also identified various factors that confer susceptibility/resistance to malaria, with the help of individual specific genetic and epigenetic signatures. These signatures have immense potential to be utilized in personalized medicine. The objective of our study for developing personalized medicine is to enable anticipation and prevention, early diagnosis, as well as the development of individualized therapeutic approaches to speed up recovery and improve the quality of life of the patient. These technologies are cost effective, rapid and have potential of translation to the bedside, applications in the evaluation of individuals with low parasite levels for epidemiological studies, malaria treatment, blood donation purposes as well as anti-malarial vaccine monitoring. This study may also lead to new strategies for therapeutic invention based variations in genetic make-up of the host.

Dr. Vishwanatha U:

I joined the Department of Ageing Research, School of Life Sciences, Manipal in 2007 where I started my work under the project titled "**Evaluation of Amalaki rasayana on DNA repair and Immune Profile in Human Subjects**". As we all know, Ayurveda incorporates a holistic and healthy approach to living, and was developed by ancient Indians to be able to live a long and healthy life. Rasayana therapy is one of the important branches of Ayurveda, which include various types of rejuvenation therapies. In our study, Amalaki rasayana (also known as amla/ Indian gooseberry rasayana) was administered to healthy aged subjects to understand it's role on DNA damage repair capacity and immunological parameters (to help define infection progression and therapy response). This is the first time the effect of amalaki rasayana on human beings has been scientifically documented. The overall result of our study is very encouraging as it clearly showed that Amalaki rasanaya had beneficial effects on DNA repair capacity and immunological parameters of aged subjects.

High Voltage

- Atrishi Badu, BSc year III

The students of School of Life Sciences (SLS) organized one of the biggest and most exclusive events in the history of the college - High Voltage, on October 6, 2015. The nightly event, organized at the Amphitheatre premises, was a musical jam night and intended to provide a stage for bands from within and outside Manipal. Of the 15 bands on show, there were 3 headlining bands from among the student body of various constituent colleges - *Scintillations* from KMC and *The Undecided* and *Cloudburst* from MIT.

Photo credit: Mahesh Nair

The event started in the evening and went till 10:00 p.m. with intermittent rain, but it barely dampened the spirits of the musical crowd, as they were treated to a musical treat by the ensemble. The performances given by the bands included covers of popular songs by iconic bands such as Black Sabbath, Iron Maiden, Metallica, The Doors and many more. The show catered to all types of music lovers, with songs ranging from genres like hard rock to pop, English to Hindi. This went on to show the versatility of the different bands and the sheer talent that thrives in Manipal. The headliners put up the most entertaining performances including singers morphing into their alter egos and interacting with the crowd. Making faces, dancing, jumping around on stage, where some of the maniacal exhibits of enthusiasm exhibited by the band members that added to the vibrancy of High Voltage altogether.

The event, in addition to being a fun-filled night for the music revellers, had a much greater cause as ticket sales through this event directly contributed to "A Meal for A Smile" program of the Volunteer Services Organization (VSO) of Manipal University. The program focuses on providing food for underprivileged children. A total of 800 people were present which was the highest turnout for any musical event ever in Manipal. After the success of High Voltage, many of the colleges have shown support for such an event and there are already talks of making it an official SLS event in the near yet promising future.

Image: *The High Voltage Stage, held at the Amphitheatre*

Photo credit: MTTN

Sharada Pooja

The faculty, staff, researchers and students of the School of Life Sciences celebrated Sharada Pooja on October 13, 2015, with fervor. Floral decorations and a rangoli adorned the site.

Rangoli Competition

Mrs. Veena Bhat and Dr. Vidhu Sankar Babu of School of Life Sciences participated in the Rangoli Competition conducted by the Manipal University during Aug-Sep 2015. Their works (L: Dr. Vidhu, R: Mrs. Veena) were appreciated.

Rangoli Designs by- ***Dr. Vidhu Sankar Babu & Ms. Veena Bhat***

Current affairs

Yettinahole Dam Project

- Varun Ram, KMC year III, and Anant Kakar, MSc year I

Every year, the areas in the region of the Western Ghats (Sakaleshpur, Aluvalli, Kadumane, etc.) receive a whopping 4000-6000mm of rainfall. This is in stark contrast to the less fortunate and highly drought prone areas of central and eastern Karnataka, which receive a meager 400mm. Karnataka is actually the second most drought-ridden state nationwide, after Rajasthan. In a bid to rectify this, as of May 2014, Krishna Neeravari Nigam Ltd. (KNNL) has begun work on the Yettinahole Integrated Drinking Water Project. This project will attempt to solve the ever growing drinking water crisis in these areas by diverting over 24 tmcft (thousand million cubic feet) of water from certain tributaries of the Nethravathi River, namely Yettinahole, Kadumanehole and Kerihole to the Kolar, Chikkaballapur, Bengaluru rural and Tumakuru Districts. The 12000+ crore project entails the laying of 130km of pipeline between the catchment area and the reservoirs downstream, of which over 70km has already been laid.

Much like many of its predecessors, the project has, of course, seen its share of problems. The assurances of the state government that no more than 20 hectares of forested land would be needed have not satisfied many environmentalists, who feel that the project could adversely affect the Western Ghats ecosystem. In addition, more recent estimations have shown that the quoted figure of 24 tmcft of water may have been overly optimistic, and that the actual number is closer to 9.5 tmcft. It is argued that this quantity of water would be insufficient to benefit those downstream, and that the project would actually affect the livelihood of people who are dependent on the catchment upstream.

Perhaps in light of these issues, the project has recently been put on hold. Whether or not it will be brought forth to completion remains to be seen.

Image: *River Nethravathi,*

Photo credit: Parineethi Dandekar, SANDRP.wordpress

Amaravati- Andhra Pradesh's New Capital

- *Anant Kakar, MSc year II*

Following the bifurcation of Andhra Pradesh into Andhra Pradesh and Telangana, Hyderabad was declared as the new capital of Telangana state in 2014 (as per the Andhra Pradesh Reorganization Act). However, Hyderabad would remain the joint capital of both states for a period of time not exceeding 10 years until the development of a new capital city of Andhra Pradesh is complete.

Amaravati is the planned riverfront capital city of Andhra Pradesh, named after the historic Amaravati (which means 'abode of the immortal') village famous for its 'Amarāvatī mahācetiya' (ancient Buddhist monument) as well as its Sri Amaralingeswara Swamy temple, making it a holy town for the Hindus. The foundation stone for the new capital was laid in 2015 around 23 kms from the Amaravati village, on the southern banks of the River Krishna in the Guntur and Krishna districts.

The Andhra Pradesh Chief Minister N Chandrababu Naidu's land pooling scheme was welcomed for successfully acquiring 33,000 acres for the new capital from the farmers without much protest. Mr. Naidu has stated that he would make Amaravati one of the best cities in the world, his aim being to replicate Amaravati as 21st century Singapore, a commercial island city-state on the Krishna riverfront.

By using the name Amaravati, Mr. Naidu managed to strike an emotional chord with countries like Singapore and Japan, where Buddhism prevails. The government of Singapore has presented three master plans for Amaravati and is ready to partner in its development. The government of Japan is also willing to step forward and contribute towards its development with its experience and technological expertise.

According to the Amaravati master plan for the Seed Capital Area (SCA) presented by the government of Singapore, the core city will be spread over 16.9 sq. km. Amaravati will comprise of nine cities – knowledge city, financial city, health city, tourism city, government city, sports city, electronics city, justice city and education city. The capital city has been planned for about 300,000 residents, and its first phase is expected to be completed by 2018. Special emphasis has been laid on the development of extensive walkways interlinked with open, green spaces to promote a 'walk-to-work' environment as well as non-motorized transport.

It should be noted, however, that the total estimated cost of building Amaravati is upwards of Rs.1.5 lakh crores; State officials expect the Centre to release at least Rs. 1,000 crores annually for the next three years, but a big funding gap will still remain. Andhra Pradesh will have to either borrow from banks by issuing bonds or approach global funding agencies such as the World Bank. The Andhra Pradesh government has also started a 'crowd funding' initiative, which encourages people across the globe to make an online contribution towards building Amaravati by purchasing a symbolic "e-brick" for Rs. 10 each. So far (as of October 19, 2015), over 25,100 donors have pitched in to make a total contribution of roughly 1.59 crores.

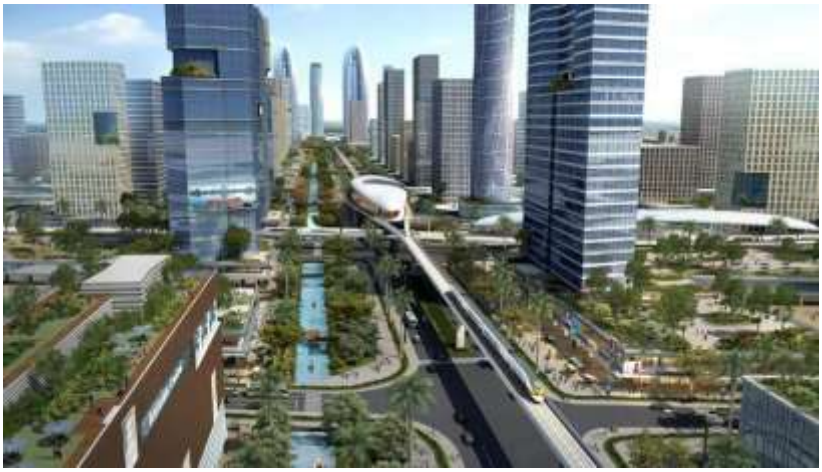


Image: An Artist's Perception of the Proposed Capital City of Amaravati

Photo credit: indianexpress.com/NewAndhraCapital

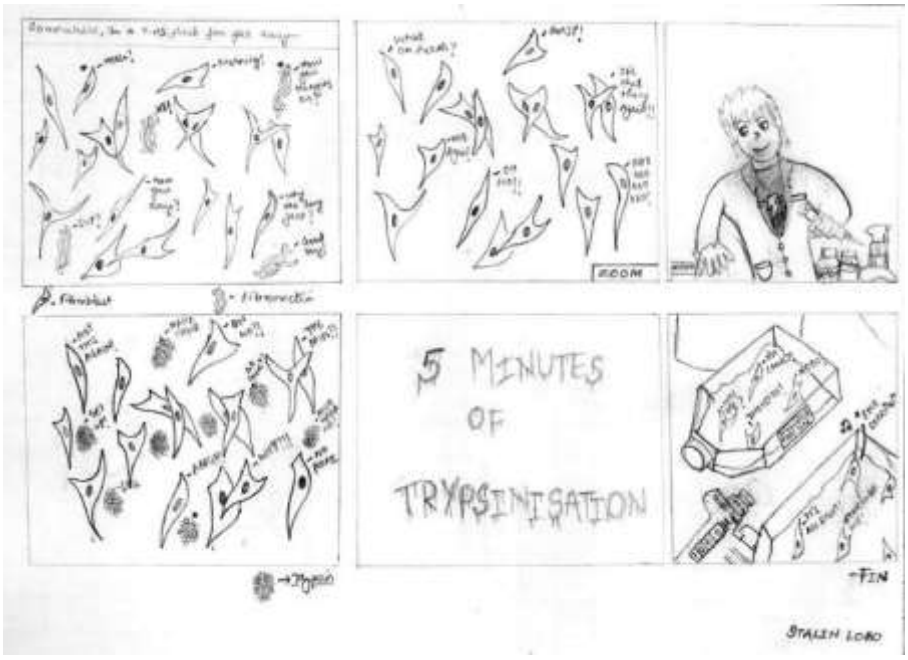
Out of Focus

Love Thyself

Why is it on this day green,
you sit here hidden, cowering, unseen?
Take yourself out, my dear,
for the day is nice and the sky is clear.
Into the gushing sea you should go,
and take me along if you like it so.
And may you admire the beautiful earth,
but never forget your invaluable worth.
Despite this you find sadness, perchance,
upon the golden orb you should glance,
or the silver one if you wish,
I'm not really bothered which.
And think of all the beauty you see,
as the godsend meant to set you free.

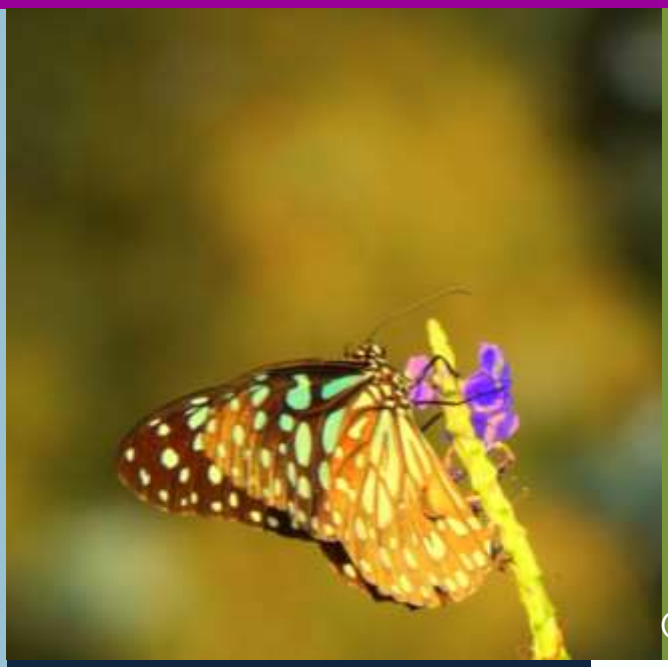
- Anirudh Gupta, BSc Year II

5 minutes of Trypsinisation



- Stalin Lobo, BSc Year III

GALLERY



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Getting Creative with Bacteria

The College Puppy

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All the students who contributed to the newsletter.

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