

HUMAN PRACTICES

‘Evincing Synthetic biology’

PROBLEM STATEMENT:

Antibiotics are type of antimicrobials used in prevention and treatment of bacterial infection.

Development of a new antibiotic is a long and tedious process which involves various phases of clinical and preclinical trials along with approval and marketing

It nearly takes 11-14 years for a drug to be marketed. Penicillin was the first antibiotic discovered by Alexander Flemming in the year 1928 in England. It was then used to treat infection from 1948. Antibiotic resistance is a serious problem faced by the world. WHO has released a report in April 2014 stating that "this serious threat is no longer a prediction for the future, it is happening right now in every region of the world and has the potential to affect anyone, of any age, in any country". Antibiotic resistance—when bacteria change so antibiotics no longer work in people who need them to treat infections—is now a major threat to public health. "Common types of drug resistant bacteria are: *Staphylococcus aureus* (MRSA), vancomycin resistant *S. aureus* (VRSA) etc. The origins, evolution, and mechanisms of antibiotic resistance have appeared over last 60 years. As an example, Penicillin was discovered in the year 1928 and its resistance was developed in the year 1952. Antibiotic resistance is developed both due to the over use and misuse of antibiotics. These are due to the following reasons.

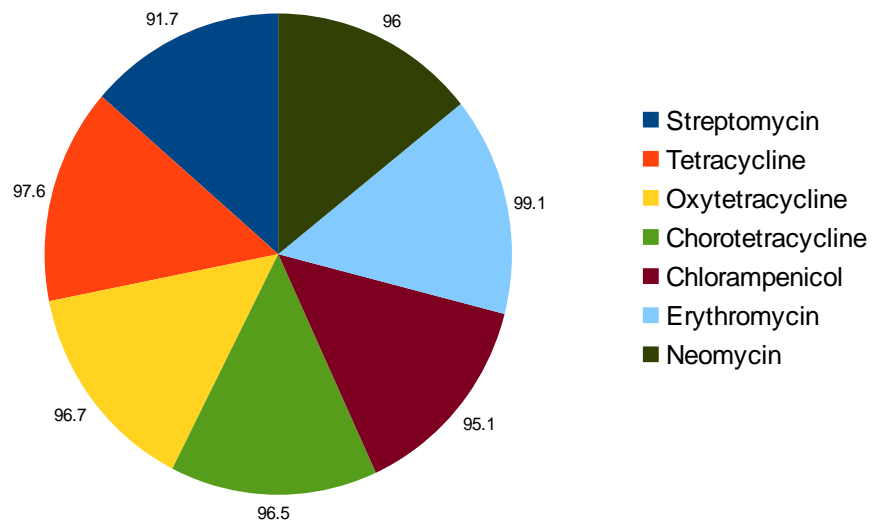
- Poor prescribing practices
- Self medication
- Failure to finish a course of antimicrobial medicines
- Lack of regulations or standards
- Mutation
- Genetic information acquired from other microbes to develop resistance.

The below table shows the mechanism of action of certain antibiotics and its mode of resistance

Antibiotic class	Example	Target	Modes of resistance
β -Lactams	Penicillins,Cephalosporins	Peptidoglycan biosynthesis	Hydrolysis,efflux,altered target
Aminoglycosides	Gentamicin,streptomycin	Translation	Phosphorylation,acetylation,efflux
Glycopeptides	Vancomycin,teicoplanin	Peptidoglycan Biosynthesis	Reprogramming peptidoglycan biosynthesis
Tetracyclins	Minocycline,tigecycline	Translation	Monooxygenation,Altered target
Macrolides	Erythromycin, azithromycin	Translation	Hydrolysis, glycosylation,efflux
Lincosamides	Clindamycin	Translation	Nucleotidylation, efflux
Streptogramins	Synercid	Translation	C-O lysase,acetylation,efflux
Oxazolidinones	Linezolid	Translation	Efflux, altered target
Phenicol s	Chloramphenicol	Translation	Acetylation, efflux
Quinolones	Ciprofloxacin	DNA replication	Acetylation, efflux
Pyrimidines	Trimethoprim	C1 metabolism	Efflux, altered target
Rifamycins	Rifampin	Transcription	ADP-ribosylation, efflux
Lipopeptides	Daptomycin	Cell membrane	Altered target

Gut contains large number of bacteria. The resistant microbes remain in gut without causing any symptoms. They induce health associated infections and undergo cross-transmission to other individuals. This occurs due to horizontal gene transfer among Enterobacteriaceae and other pathogens and the gut flora. Infectious gastroenteritis is one of the most common diseases worldwide killing millions of people. There are enormous number of bacteria causing gastrointestinal infection like *E.coli*, *Salmonella*, *Shigella*, *Campylobacter*, *Clostridium*, *P.aeruginosa*. Most of these infections leads to diarrhea, abdominal cramping, nausea, vomiting, diarrhea is one the most common gastro intestinal infection. Over 211 million cases have been reported to have diarrhea in US every year. *P.aeruginosa* is an opportunistic pathogen. It has become the main cause of infection in immunocompromised patients. Pseudomonal infections are complicated and could also be life threatening. Generally such infections are treated with antibiotics such as beta-lactam (penicillin, cephalosporin) and an aminoglycoside. They develop resistance to antibiotics by chromosomally encoded AmpC cephalosporinase, the outer membrane porin OprD, and the mulrug efflux pumps.

RESISTANCE OF PSEUDOMONAS AUREGINOSA



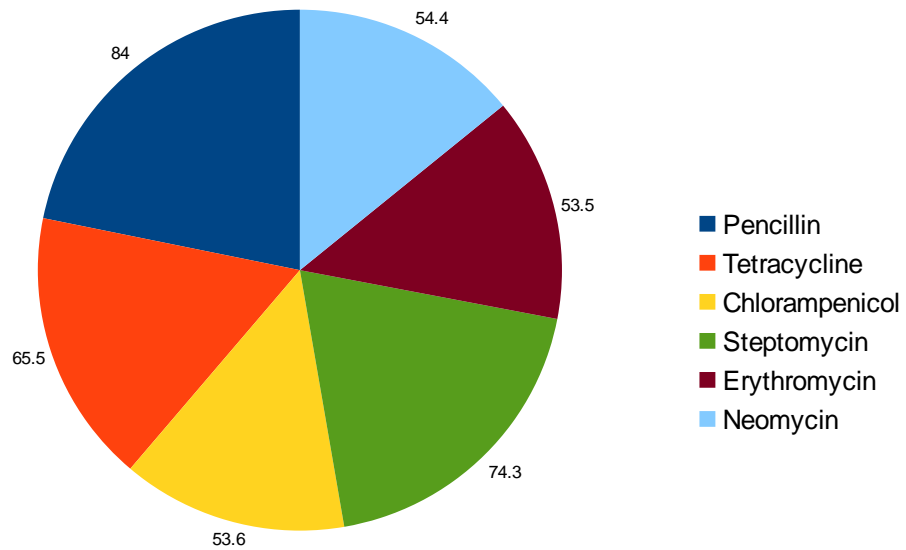
Pseudomonas aeruginosa has become an important cause of infection, especially

in patients with compromised host defence mechanisms. It is the most common pathogen isolated from patients who have been hospitalized longer than 1 week, and it is a frequent cause of nosocomial infections. Pseudomonal infections are complicated and can be life-threatening. The infections are Endocarditis, Pneumonia, and Malignant otitis externa.

The antibiotics such as tobramycin, cephalosporin, ceftazidime are used so far. The antibiotic for the strain was first introduced in 1991. But approximately since 2001 it acquired resistance to antibiotics due to following reasons: production of beta-lactamases, loss of outer membrane proteins, and upregulation of efflux pumps.

The next strain which cause havoc is *Staphylococcus aureus* strain. Methicillin-resistant *Staphylococcus aureus* is a bacterium responsible for several difficult-to-treat infections in humans. It is a serious health concern for past 4 years. It is hospital acquired infection. The medical treatment for *S. aureus* has been evolved in 1940 with the discovery of penicillin. But within 10 years that is by 1950 it acquired resistance to penicillin. Then methicillin was introduced to treat *S. aureus* but to this also it acquired resistance by 1961. From then on it is called Methicillin Resistance *Staphylococcus aureus*. MRSA is actually resistant to an entire class of penicillin-like antibiotics called beta-lactams. This class of antibiotics includes penicillin, amoxicillin, oxacillin, methicillin, and others. The disease caused by *S. aureus* are Cellulitis, staph infection, sty, boils sepsis, impetigo etc. The treatment with the antibiotics become negligible because of acquired resistance to antibiotics by these strains. MRSA strains worldwide are multi drug resistance. They develop antibiotic resistance due to horizontal gene transfer. The other mechanism are drug inactivation or modification, alteration of target site, alteration of metabolic pathway and reduced drug accumulation. These make the strain more and more resistance to antibiotics which in turn make the treatment difficult.

RESISTANCE OF *STAPHYLOCOCCUS AUREUS*



SPARK:

During those days, our parents used to take different antibiotics for various types of infections, such as, common cold, fever, stomach ache, etc. Do we still use the same?

The answer is a big "NO". The major reason is the antibiotic resistance developed by some micro-organisms. Antibiotic resistance evolves naturally via natural selection through random mutation. This is clearly understood from the data given by few experienced Doctors and knowledgeable Professors who have a wide exposure to the field of Antibiotic Resistance.

Dr. KANNAN

MD in General Medicine

Saveetha Medical College and hospital

There is a switch-over to new antibiotics as it is target specific, has less side effects and also is given as a single dose.



Fig: Dr. Kannan, Saveetha Medical College

Dr.SULOCHANA SOMASUNDARAM

HOD, Department of Biotechnology,

SVCE

"Drug resistance Bacteria has become the major global concern due to misuse of drugs, overusage of drugs and non-compliance of drugs with the patients. Earlier there were only multi-drug resistance (MDR) strains. Resistance to drugs is increasing day by day to extremely drug resistance (XDR) strains and totally drug resistance (TDR) strains."



***Fig: Dr. Sulochana Somasundaram, HOD,
Department of Biotechnology, SVCE***

Dr.KALYANI

**HOD, Department of Microbiology,
Saveetha Medical College and hospital**

"Gastro intestinal diseases are both infectious and non-infectious. *Shigella*, *Vibrio cholerae*, *Salmonella typhi* are the most common micro-organisms. Primary measures to be taken are personal hygiene, improving sanitary conditions and consuming homemade foods. Antibiotics should be given only when necessary. "



Fig: Dr.Kalyani, Saveetha Medical College

Dr.JAYALAKSHMI

HOD, Saveetha Medical College and Hospital

"Infection increases day by day. Diarrhea, dysentery, *Helicobacter pylori* infections are major gastro intestinal infections caused by microorganisms. All these nosocomial infections can be prevented by following proper sanitary practices as suggested by WHO and CDC. Oflaxacin and Perflaxacin are higher class of antibiotics given."



Fig: Dr. Jayalakshmi, HOD,

Saveetha Medical College

Dr.MUTHULAKSHMI

MD in Pathology,

Meenakshi medical college

"The major gastro-intestinal tractinfection causing organism is *Shigella* and for food poisoning is *Staphylococcus*, *Clostridium* and *Bacillus*.A new class of

antibiotics is required due to mismanagement of drugs as the clinicians initially give high dosage. Also, people don't take drugs in a regular basis."



Fig: Dr. Muthulakshmi, Meenakshi Medical College

Through this knowledge and survey taken from doctors, professors and WHO Statistics we formulated our idea of producing bacteriocins using minicells and utilize it for different applications.

SPREAD OF KNOWLEDGE

“Learning gives creativity, Creativity leads to thinking, Thinking provides Knowledge, Knowledge makes you great.”

- A.P.J. Abdul Kalam

In this aspect, we have shared our thoughts among few school and college students.

SCHOOL

SBOA SCHOOL AND JUNIOR COLLEGE

The students were excited about the program and the competition. We reached out to the 11th and 12th gradestudents of biotechnology. A presentation was done to make the students understand the basics of Biotechnology, rDNA technology and applications of synthetic biology in modern world. This presentation triggered the young minds to come up with new ideas.



Fig: Presentation at SBOA school

COLLEGES

A presentation was done to all the U.G and P.G students of Biotechnology department at few engineering colleges in and around our place. A questionnaire regarding the basics of Biotechnology, synthetic biology and our project was given before the presentation and the same was given at the end of the presentation too and was evaluated. Increase in the knowledge of the students after the presentation was observed.

This gave us a great opportunity to interact with the professors from various disciplines of Biotechnology. Their opinions and ideas encouraged us to take our project to the next level.

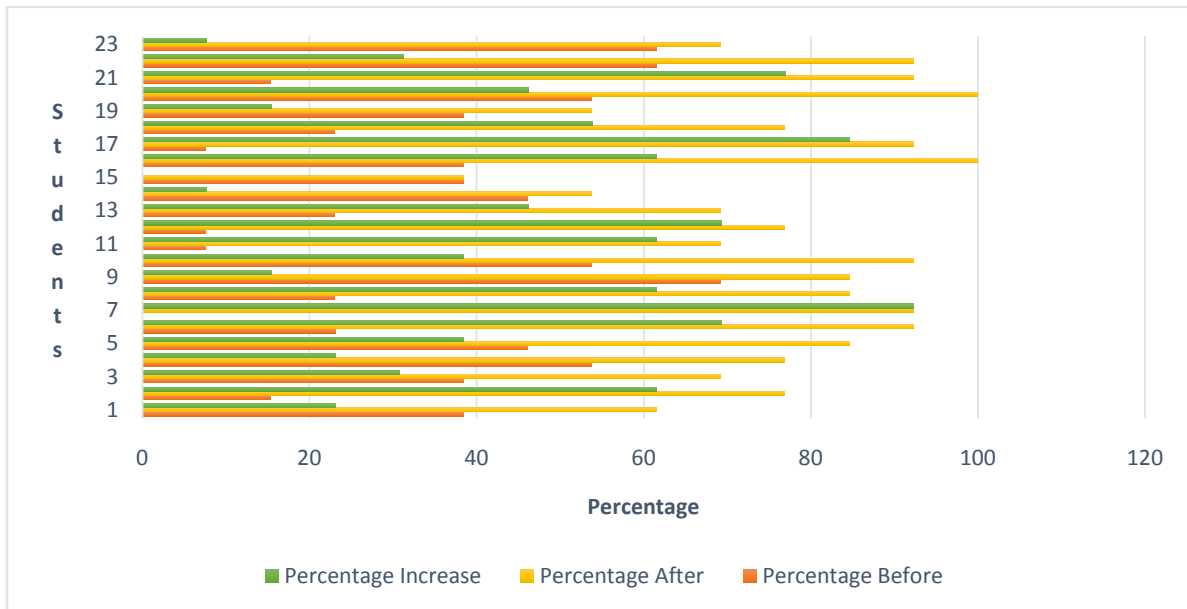
We also took an initiative to start up an intercollege Biotech Forum and a Journal club. There was a good response from all the colleges and the young minds were inspired by the prospects of the competition and willingly wanted to join the Biotech Forum.

ARULMIGU MEENAKSHI AMMAN COLLEGE OF ENGINEERING



Fig: Presentation at Arulmigu Meenakshi Amman College

IMPROVEMENT STATISTICS

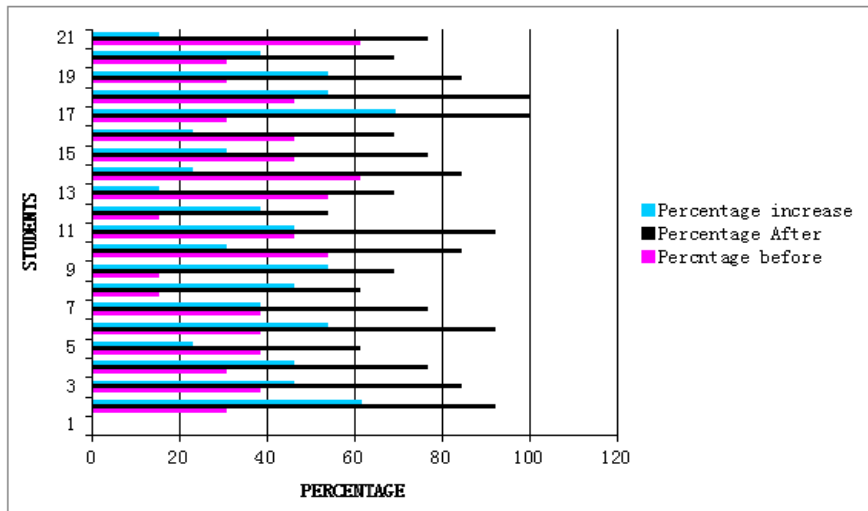


RAJALAKSHMI ENGINEERING COLLEGE



Fig: Presentation at Rajalakshmi Engineering College

IMPROVEMENT STATISTICS



PRATHYUSHA COLLEGE OF ENGINEERING AND TECHNOLOGY



FIG: Presentation at Prathyusha College

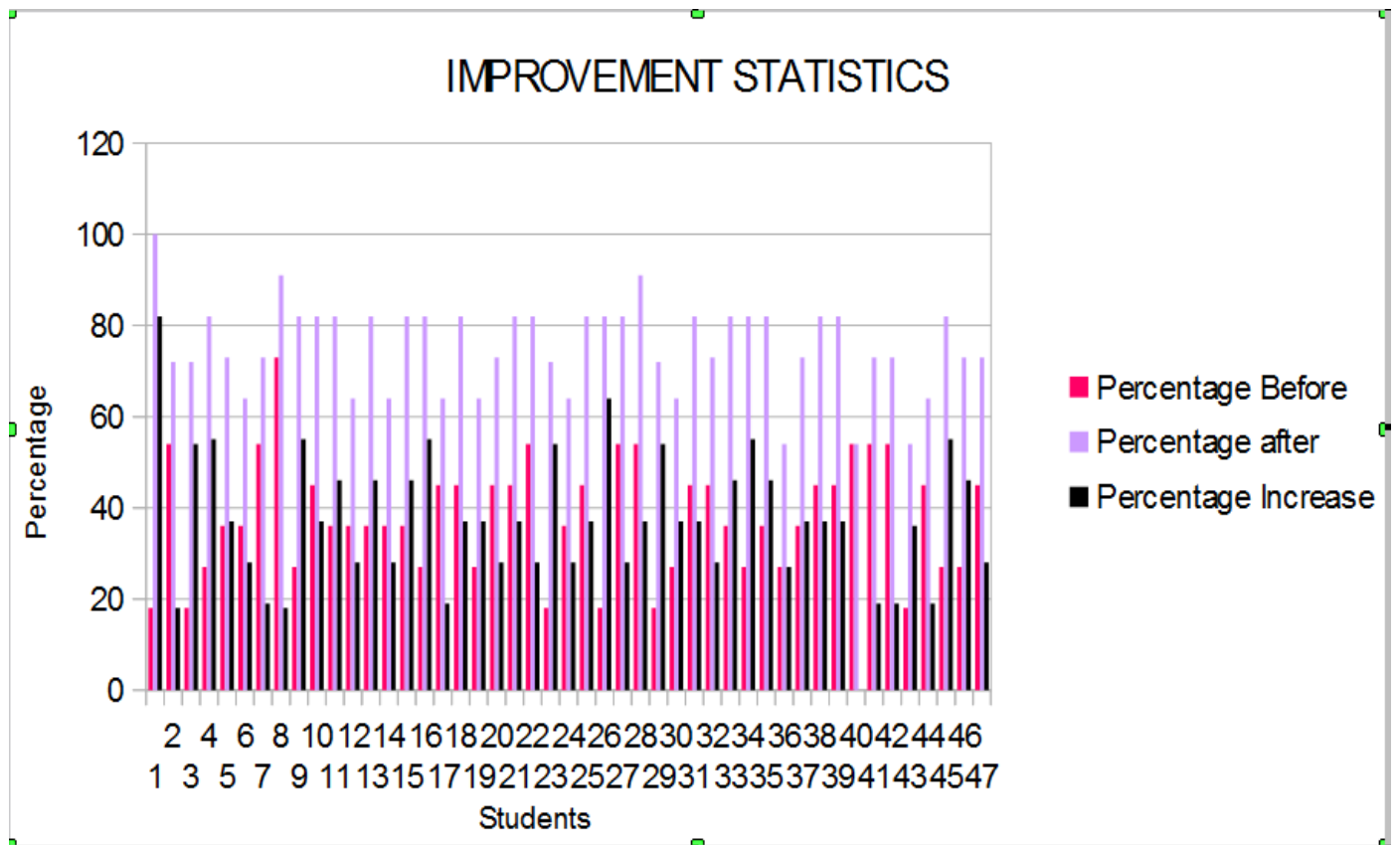
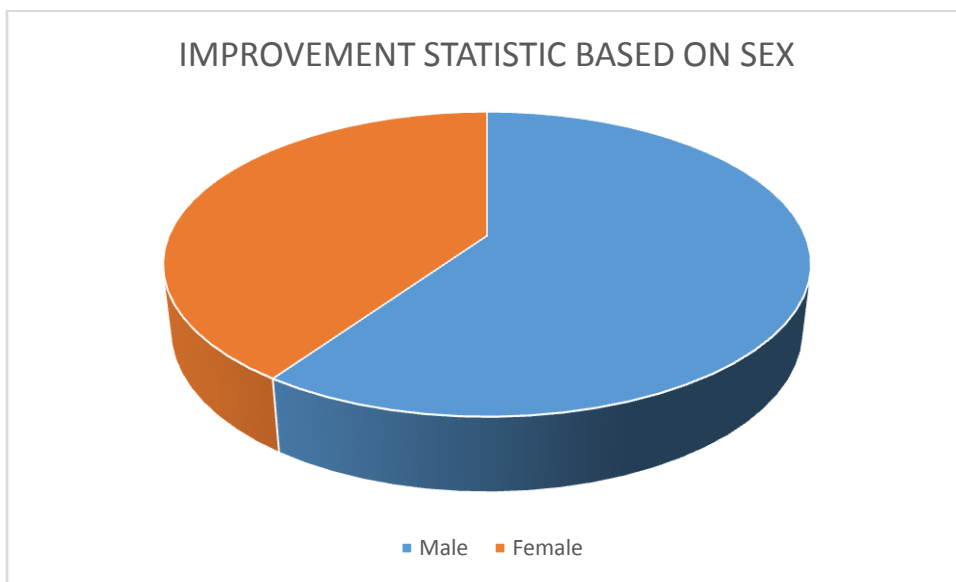




Fig: Presentation at Madha Engineering College



CONFERENCE:

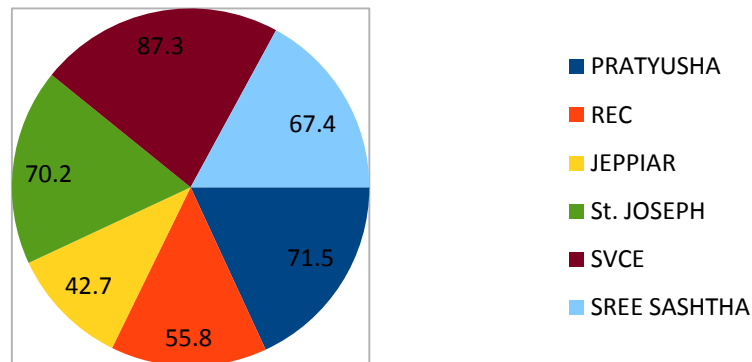
Our team conducted a presentation in anational level technical symposium held at Sri Venkateswara College Of Engineering called “**OMICS**”. More than 200 students from various colleges participated in the symposium. The presentation lasted for an hour and we had a registration desk along with the banner in front of the department and few of our team members were explaining about the project to the students from other colleges. Inspired by their speech, 94 students from others colleges eagerly enrolled themselves for the Biotech forum. They gave a positive feedback about our project and also were happy to know about iGEM. Most of

them were interested in participating in iGEM next year. They were encouraged by this competition that gives a great base for advanced biotechnology.



Fig: OMICS Presentation

PERFORMANCE STATISTICS OF VARIOUS COLLEGES



As a part of encouraging Biotechnology and the ideas of biotechnology we wanted to evolve new interests in students. So, we conducted a conference for the fresher's and their parents in our college. There were nearly 50-60 students along with their parents. The 1st year students were much excited about synthetic biology and curious about the competition. They anxiously wanted to nominate themselves for the biotech forum. Their parents were astonished. They encouraged their ward to participate in the upcoming years. They wanted their children to also develop their ideas and work hard towards it. They were really happy to see students from India improvise the GMOs for health benefit. They wished best of luck for the success of our project.



Fig: Freshers Day

BIOTECH FORUM:

We have taken an initiative to form an inter college biotech association to help the students regarding the processing of their project to the next level in a better way. The Association focuses on issues faced by biotechnologists now a days which includes maintaining the strains, increase in job opportunities, etc.

Nearly 430 students have enrolled themselves enthusiastically from different colleges. The Biotech Association will also help the students to discuss about emerging trends in biotechnology and encouraging new ideas. Students were eager to join in the forum as they have got a more easy way to get into the next year's iGEM team.



PUBLIC INTERACTION

A few members from our team interacted with the public about antibiotic resistance developed by bacteria, the effect of antibiotics used earlier and now and also about Minicins as an alternative to antibiotics in near future. Most of their views had one thing in common as they would take this alternative blindly, if prescribed by their physician.

This survey was conducted among two sections of people- college students and general public of various ages. College students gave their views as GMOs would be accepted if it is promising enough not to cause any side effects. General public included children, middle-aged mothers and elderly people had different views regarding this, which have been depicted in the form of charts.

GENERAL PUBLIC VIEW:



Fig: Elderly opinion

Elderly People from the age of 65-85 years had different opinion about synthetic biology and Minicins. They felt the immune system of our body has changed a lot. They never used to take antibiotics since childhood but it is not the same for their children nor their grandchild. Giving antibiotics to children is a risk from their point of view. Their opinion was also that the resistance power is decreasing vigorously for the present generation. They said that they give the same antibiotics but an upgraded version of them. Even though at this age, they are prone to antibiotics, they don't consume it as it may lead to stomach irritation and throat infection. Nearly 85% people from this age group felt that antibiotics should be avoided unless and until required. They think that herbal medicines and old age herbs essence should be bought back as the side effects may also be reduced.



Fig: Budding minds

Kids are the first to be taught about this antibiotic resistance and also the alternatives in use till date, as they form the tomorrow's community. They were very anxious in knowing the basic biology. After a few minutes of explanation about antibiotics and its resistance, they were asked to name a few antibiotics familiar to them. Their answers made a thing clear that they were keen to know more about biotechnology.



Fig: Public survey

Mid aged people also had a different view on sythetic biology and minicins. They stated that antibiotic resistance is indeed increasing. They did understand and support the idea of minicins but they felt that the product can be consumed only if prscribed by the physicians. They also stressed on the side effects of the new medicine.

COLLEGE STUDENTS' VIEW:

A survey was conducted among the different college students and staffs on Antibiotic resistance. They were asked a very few basic questions about Genetically Modified Organisms (GMOs), Genetic engineering and Biotechnology.



Fig: Students survey

In general, students had a good opinion about GMOs, except a few. They were happy to be utilizing the already existing GMO products and also to use anything new. When we asked them if they were ready to consume a bacteria, knowing that it would be healthy with no side effects, almost about 95% of the students were ready to consume the bacteria if they really are promising enough to cure the ailments.



Fig: Professor survey

The professor, who were interviewed about GMOs had a similar opinion as that of students. Some staffs stated that, GMOs could be used as they are very much promising to cure infections. Also they provided more information on how GMOs effectively substitute antibiotics so that we can overcome resistance. They insisted on certain aspects of genetic engineering which could be efficiently used for producing GMOs.