Science Gurus

Empowering NEXTGEN Scientists

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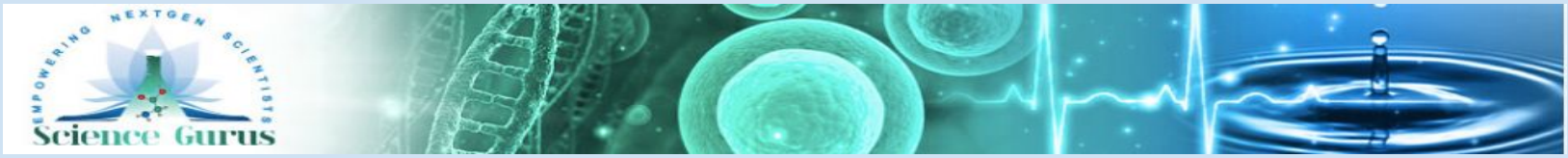
Cell Science Internship

Annual Report

2017

Table of Contents



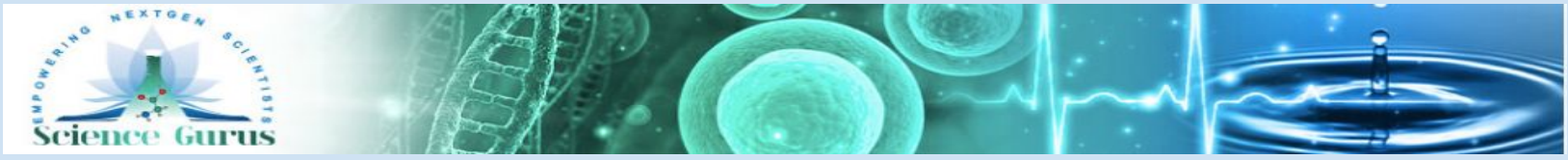
Introduction

The cell-Science Internship is a seven-week summer program organized by the Science Gurus Organization enabling high school students to have the opportunity to learn more about cancer biology, drug discovery, and the process of drug development. The curriculum goes into depth about different types of cancer therapies available, such as small-molecule drugs and immunotherapy.

Interns gain this knowledge as every class a credible guest speaker active in the fields of cancer biology and biotechnology present about advanced research related to a specific type of cancer or a cancer drug. A lot of the speakers work at renowned biotechnology companies such as genentech, which truly allows the interns to get an understanding of careers in the biotechnology field.

Over the course of the two weeks, interns undertake two presentations. The first presentation asks each intern to choose a specific type of cancer, research the cancer in-depth, and share the knowledge they learned to the rest fo the interns. The second presentation, the final presentation, was with a partner and was a study of a specific gene or gene pathway that plays a major role in cancer. Using bioinformatics tools and databases such as Uniprot and cbioportal taught by the computational biologists in the internship, the interns were able to gain a wealth of information about genetics aspects, physiological features, and current treatments.

Finally, the interns write a detailed research paper, in conjunction with their final presentation, and present their findings in front of an audience of interns and parents. The program concludes with an annual celebration consisting of an awards ceremony and a nice dinner for interns, their families, and the entire science gurus organization.



Curriculum Overview

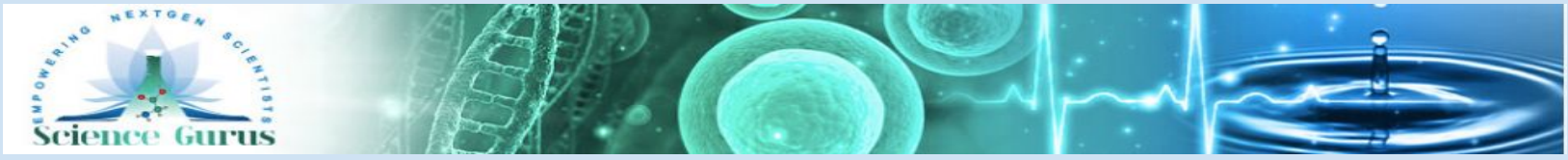
Cell-Science Summer Internship Program

Date and Time: June 15 – July 30, 2017; Tuesday and Thursday, 5.30-8.15pm*
Location: 1531 Industrial Road, San Carlos, CA, 94070.

Day	Date	Instructor	Hours	5.30-6.00pm Class	6.00-7.00pm Class	7.00-7.15pm Break	7.15-8.15pm Class
Thu	6/15/17	Jagath Reddy Junutula	2.5	Meet and Greet; Goals of Internship	Introduction to Cancer Biology & Cancer Basics		Cancer Phenotypes & Signaling
Tue	6/20/17	Akshata Udyavar/Kiran Mukhyala	2.5	Introduction to Bioinformatics	Introduction to Bioinformatics		Bioinformatics tools/applications
Thu	6/22/17	Kiran Mukhyala/Pradeep Fernandes	2.5	Bioinformatics tools/applications	Bioinformatics tools/applications		Cell Signaling/Systems Biology
Tue	6/27/17	Kiran Mukhyala/Chakk Ramesha	2.5	Bioinformatics tools/applications	Drug Discovery & Development - Overview		Drug Discovery & Development - Overview
Wed	6/28/17	Student speakers	2.5	Cancer Presentations	**Group 1 (9)**		**Group 1 (9)**
Thu	6/29/17	Ganesh Koluman/Jagath Reddy Junutula	2.5	Bioinformatics tools/applications	Interplay between Cancer and Inflammation		Antibody Therapeutics
Thu	7/6/17	Kiran/Student speakers	2.5	Bioinformatics tools/applications	**Group2 (7):**		**Group2 (7):**
Sat	**7/8/17**	**Bob Figari (10-2pm)**	**4**	**Workshop: "Effective Content Development & Delivery"**			**Workshop**
Tue	7/11/17	Pablo Garcia/Sanjeev Redkar	2.5	Bioinformatics tools/applications	Small Molecule Drug Discovery: Kinases		Small Molecule Manufacturing & Formulation
Wed	7/12/17	Student speakers	2.5	Cancer Presentations	**Group 3 (9)**		**Group 3 (9)**
Thu	7/13/17	Heather Maecker/Sreedhara Alavattam	2.5	Bioinformatics tools/applications	Cancer Immunotherapy		Large Molecule Manufacturing & Formulation
Tue	7/18/17	Talat Ashraf/Ram Mandalam	2.5	Bioinformatics tools/applications	Clinical Trail Design & Execution		Stem cell Therapeutics
Thu	7/20/17	Alex Szidon/Sekar Seshagiri	2.5	Bioinformatics tools/applications	Business Development		Cancer Diagnostics-NextGen Sequencing
Sun	**7/23/17**	**Aparna Gandhari/Raji Pingali (12noon-2pm)**	**3**	**Workshop: "Preparing Effective College Applications"**			**Workshop**
Tue	7/25/17	Sreedhara Alavattam/Jagath Reddy Junutula	2.5	Bioinformatics tools/applications	Cancer-Nanoparticle Therapeutics		Mentoring/Career Growth
Thu	7/27/17	Khaled Sarsour/John Storella	2.5	Bioinformatics tools/applications	Real World Data & Analytics		Overview to Patents-IP
Sat	7/29/17	Final Project Presentations	6	Final Project Presentations (1pm-6pm)	Final Project Presentations		Final Project Presentations
Sun	7/30/17	Science Gurus Annual Day	3	Certificate presentations (6-9.30pm)	Certificate presentations		Certificate presentations

Main Topics

- Introduction to Cancer Biology
- Cancer Signaling
- Introduction to Bioinformatics
- Systems Biology
- Drug Discovery and Development
- Interplay between cancer and Inflammation
- Antibody Therapeutics
- Nanoparticle Therapeutics
- Small Molecule Drug Discovery, Manufacturing, and Formulation
- Cancer Immunotherapy
- Large Molecule Manufacturing and Formulation
- Clinical Trial Design
- Stem Cell Therapeutics
- Real World Data And Analytics

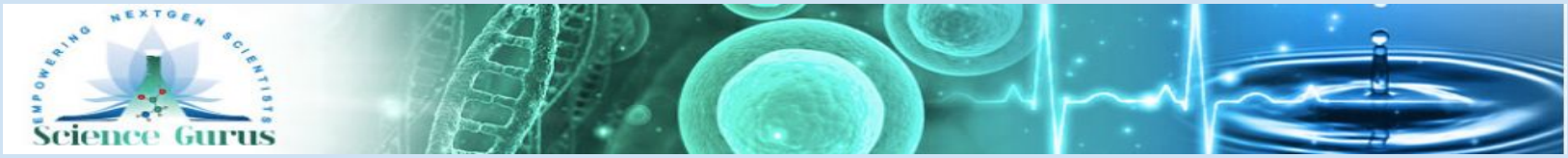


Participating iNterns

1. Aditi Kumar	Irvington High School
2. Aditya Prabhu	Cupertino High school
3. Amrita Sivia	University Preparatory Academy
4. Anjali Bhagat	Mission San Jose High School
5. Catherine Lin	American High school
6. Debarshi Basak	Cupertino High School
7. Manav Shah	Monta Vista High school
8. Mekhla Kapoor	Moreau Catholic High school
9. Naman Patel	Irvington High school
10. Nikita Chigullapally	American High School
11. Nikita Redkar	Dougherty Valley High School
12. Pavithra Pandian	Monta Vista High school
13. Pranav Jammalamadaka	Amador Valley High school
14. Pranav Muthuraman	Los Gatos High School
15. Radhakrishnan Arunkumar	American High School
16. Rajita Pujare	Lynbrook High school
17. Reva Kakaria	Notre Dame High School
18. Rishabh Sanghavi	Monta Vista High school
19. Ruchika Singla	University Preparatory Academy
20. Samyuktha Lokanandi	Dougherty Valley High School
21. Sara Varadharajulu	Menlo High School
22. Sarvesh Nagwekar	Irvington High School
23. Shreya Kochar	Mission San Jose High School
24. Soumya Turumella	Monta Vista High school
25. Sruthi Sakthivel	Crystal Springs Uplands School

HONORARY GUEST LECTURES

1. Akshata Udyavar, Ph.D.	Associate scientist	Genentech, Inc.
2. Alex Szidon, Ph.D.	Executive Director	Merck
3. Aparna Gandhari	Counselor	Arroyo High School
4. Bob Figari, MA	Founder & CEO	INnerTrek
5. Chakk Ramesha, Ph.D.	COO/CTO	Medhus Bio
6. Elisa Brunette, Ph.D.	Director	Cellerant Therapeutics
7. Ganesh Kolumam, Ph.D.	Scientist	Calico Labs
8. Heather Maecker, Ph.D.	Associate Director	Abbvie
9. Jagath Reddy Junutula, Ph.D.	Vice President	Cellerant Therapeutics
10. John Storella, MS, JD	IP Attorney	John Storella, P.C.
11. Khaled Sarsour, Ph.D.	Associate Director	Genentech, Inc.
12. Kiran Mukhyala, MS	Sr. Computational Biologist	Genentech, Inc.
13. Pablo Garcia, Ph.D.	Director	Circle Pharma
14. Pradeep Fernandes, ME	Co-FOunder	CellWorks Group
15. Raji Pingali, Ph.D.	Vice President	Science Gurus
16. Ram MAndalam, Ph.D.	President & CEO	Cellerant Therapeutics
17. Sanjeev Redkar, Ph.D. , MBA	President & CEO	CB Therapeutics
18. Sekar Seshagiri, Ph.D.	Associate Director	Genentech, Inc.
19. Sreedhara Alavattam, Ph.D.	Senior Scientist	Genentech, Inc.
20. Talat AShraf, MD, MS	Executive Director	Astex Pharmaceuticals



Photos from internship

Topic: Introduction To Bioinformatics

Speakers: Akshata Udyavar & Kiran Mukhyala

Topic: Bioinformatics Tools/Applications & Cell Signaling

Speakers: Kiran Mukhyala & Pradeep Fernandes

Topic: Bioinformatics Tools/Applications & Drug Discovery/Development
Speakers: Kiran Mukhyala & Chakk Ramesha

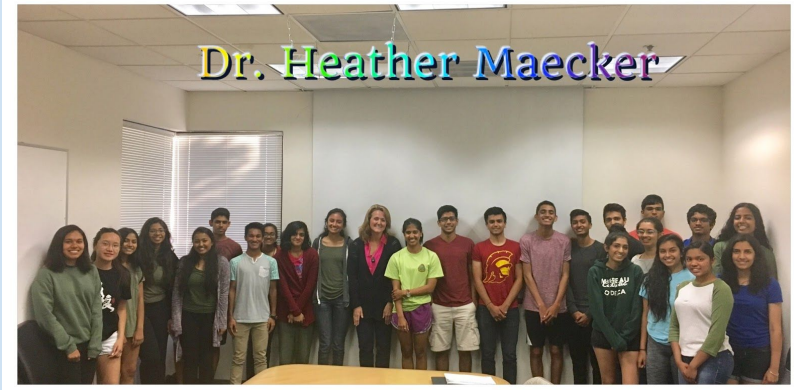
Topic: Interplay Between Cancer and Inflammation & Antibody Therapeutics
Speakers: Ganesh Kolumam & Jagath Reddy Junutula

Topic: Effective Content development & Delivery (Workshop)

Speakers: Bob Figari

Topic: Cancer immunotherapy & Large Molecule Manufacturing and Formulation

Speakers:Heather Maecker & Sreedhara Alavattam



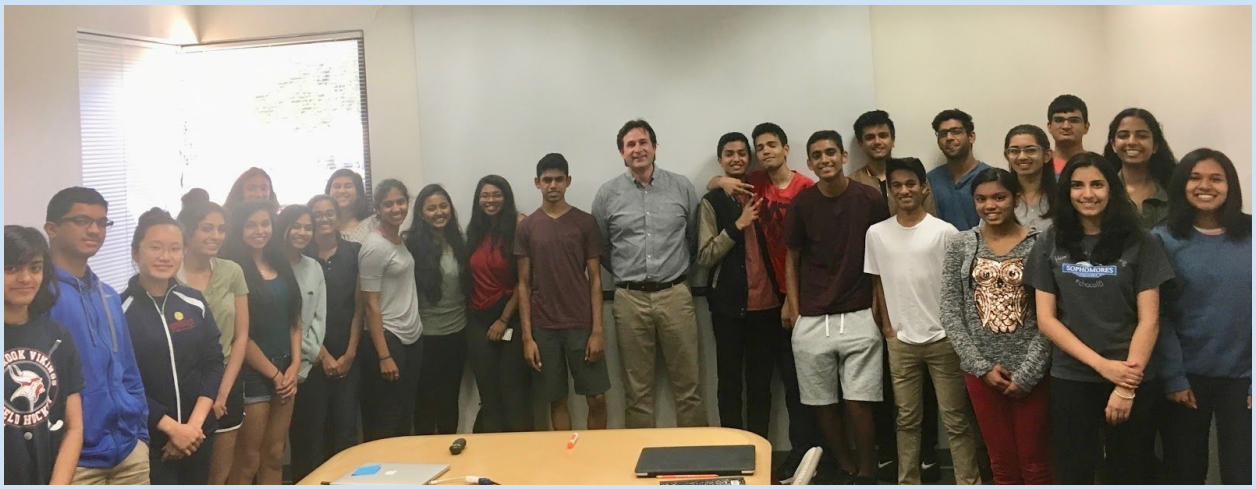
Topic: Clinical trial Design & Stem Cell Therapeutics

Speakers:Talat Ashraf & ram Mandalam

Topic:Cancer Diagnostics- NextGen Sequencing

Speakers: Sekar Seshagiri

Topic:Business Development
Speakers:Alex Szidon



Topic:Preparing Effective College Applications
Speakers:Aparna Gandhari & Raji Pingali

Topic:Real World Data/Analytics & Overview to Patents
Speakers:Khaled Sarsour & John Storella

Genentech Field trip

Final Project Presentations

Annual Celebration

Final Projects By INterns

Hedgehog Pathway

Report of the Hedgehog Signaling Pathway and SMO Structure, Function, and Mutations

Amrita K. Sivia[1,3] and Aditi Kumar[2,3]

[1]University Preparatory Academy, [2]Irvington High School, and [3]Science Gurus: Cell-Science Internship

July 29, 2017

Abstract

Hedgehog (Hh) signaling pathway is crucial in growth and patterning during embryonic development. Recent data have shown an association of its activation with cancer formation and maintenance. A ligand-dependent activation, where Hh components are aberrantly expressed with *PTCH1* being a negative feedback regulator, is a newly identified mechanism for carcinogenesis. SMO is the protein encoded by this gene and it is a G protein-coupled receptor that interacts with the patched protein, a receptor for hedgehog proteins. The encoded protein transduces signals to other proteins after activation by a hedgehog protein/patched protein complex.

HER2 Gene

Structural and Functional Analysis of the HER2 Gene

Anjali Bhagat[1,3] and Catherine Lin[2,3]

[1] Mission San Jose High School, 41717 Palm Ave, Fremont, CA 94539 [2]American High School, 36300 Fremont Blvd, Fremont, CA 94536 [3] Science Gurus- Cell Science Internship, San Carlos, CA

28 July 2017

Abstract

Every year, approximately 250,000 women in the United States alone will be diagnosed with breast cancer and more than 40,000 of them will die. The continuous impact this particular cancer has had on our society has been pinpointed to a particular gene-HER2, the most significant genes linked to breast cancer. HER2, also known as Receptor tyrosine-protein kinase erbB-2, CD340, or Proto-oncogene Neu is a gene located on chromosome 17. As part of the human epidermal growth factor receptors, it's overexpressed in most breast cancer cells (i.e. HER2 positive cancer). Throughout this report, both the structural and the functional analysis of the HER2 gene will be discussed, alongside possible targeted treatments.

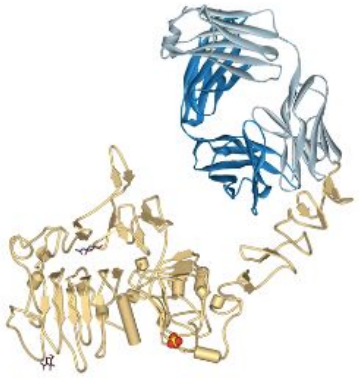


Figure 1 : *Crystal structure of HER2 in humans*

Cancer Analysis of the MAP Kinase Pathway and BRAF

Manav Shah and Aditya Prabhu

Monta Vista High School, Cupertino High School, Cell-Science Internship, 2017 Science Gurus

ABSTRACT

The MAPK (Mitogen Activated Protein Kinase) Pathway involves a chain of proteins that communicates a signal from a receptor on the surface of a cell to the DNA inside the nucleus. Formally known as the Ras-Raf-MEK-ERK Pathway, the process starts with the signalling molecule attaching to a cell-surface receptor and ends when the protein product is formed, which has its own unique function. BRAF, a gene that codes for its corresponding protein B-raf, plays an important role in the MAP Kinase Pathway and can activate the pathway. Since it is an oncogene, mutation in BRAF or amplifications of the gene have the potential to cause cancer. Mutations cause continuous production of B-raf which eventually lead to uncontrollable cell growth and proliferation. This, in turn, affects the MAP Kinase Pathway, which can also play a prominent role in the possible development of a tumor. As a result, it is critical to understand the structure of the genes and proteins involved and their relationship to cancer. This report analyzes these aspects and using this information, addresses therapies that are effective.

Report on PD-L1 Structure, Function, and Mutations

Mekhla Kapoor[1,3] and Nikita Chigullapally[2,3]

[1]Moreau Catholic High School, [2]American High School, and [3]Science Gurus Cell Science Internship
San Carlos, CA
29 July 2017

ABSTRACT

PD-L1, also known as CD274, is a key protein involved in T-cell immune suppression as it induces a co-inhibitory signal in activated T-cells and promotes T-cell apoptosis, anergy and functional exhaustion. It is an immunoglobulin molecule with two domains and a protein structure that allows it to cleave double strand DNA. PD-L1 has 3 isoforms and multiple orthologs and homologs including those of mice and pigs. The most common form of mutation in PD-L1 protein is found to be a missense mutation and the most number of copy number alterations are found in a form of prostate cancer, however it is not shown to be a significantly mutated gene in any specific cancer. Regardless of this, it is still a gene that causes cancer and needs to be targeted. Therefore, scientists are largely leaning towards using immunotherapy to inhibit PD-L1. Some specific targeted therapies that will be focused in this paper are the drugs Atezolizumab, Avelumab, and Nivolumab. Immunotherapy is really the future of drug therapy and crucial in targeting PD-L1 in cancers, therefore attracting the attention of many scientists and researchers.

Analysis of the TP53 gene, mutations, genomic profile, and the search for targeted therapies

Pranav Jammalamadaka[1,3] and Naman Patel[2,3]

[1]Amador Valley High School [2]Irvington High School [3]Cell-Science Summer Internship, Science Gurus

Abstract

The most widely recognized gene in cancer research and oncology, TP53. This powerful gene is one of the main causes in almost every cancer and it affects the G1 checkpoint o the cell growth and division cycle. This G1 checkpoint during the cell cycle is when the cell decides to whether to go on to divide into two cells or not. This checkpoint ensures that the cell is in an appropriate position in terms of size, duplicated structures, and multiple sets of genomic information to split into two. This stage is commonly associated with nutrition and cell growth. p53, also known as TP53 or tumor protein is a gene that codes for a protein that regulates the cell cycle and hence functions as a tumor suppression. It is very important for cells in multicellular organisms to suppress cancer. P53 has been described as "the guardian of the genome", referring to its role in conserving stability by preventing genome mutation. The name is due to its molecular mass, it is in the 53 kilodalton fraction of cell proteins.

Structural and Functional Analysis of Bcl-2 Gene and Bcl-2 Inhibitors

Pranav Muthuraman[1,3] and Sruthi Sakthivel[2,3]

[1]Los Gatos High School, 20 High School Ct, Los Gatos, CA 95030 [2]Crystal Springs Uplands School, 400 Uplands Dr, Hillsborough, CA 94010 [3]Science Gurus- Cell Science Internship, San Carlos, CA

28 July 2017

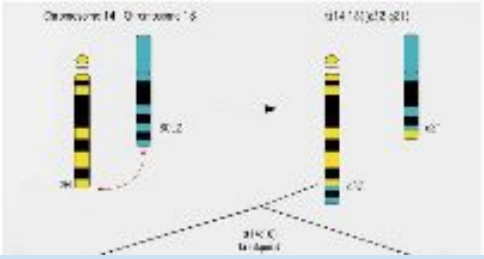
Abstract

BCL-2 also known as B-Cell Lymphoma 2 is a gene that encodes for the BCL-2 protein which regulates the process of apoptosis in cells. The gene is located on chromosome 18 and has other proteins in its range located on chromosome 14 and 18. It is an anti-apoptotic protein which has a clinical significance in lymphoma. The BCL-2 gene has 4 domains and 2 isoforms in humans. Its structure allows it to bind to other proteins in the apoptotic pathway to either induce or inhibit apoptosis from occurring. BCL-2 has orthologs and homologs including mice, rats, and chicks. The most common type of mutation to this gene is a missense mutation and the most copy number alterations are found in diffuse large B-Cell lymphoma and it is significantly higher in other lymphomas as well. It also causes cancers in other organs which are less common and less expressed, therefore it still needs to be targeted throughout the body. Treatments for this include targeted therapies such as Venetoclax and ABT-737. The future of treatments for identifying BCL-2 related cancers is promising with new research and data being discovered continuously.

Introduction

Bcl-2 is a protein encoded by the Bcl-2 gene in the human body. Bcl-2 is the founding member of the Bcl-2 family that regulates programmed cell death, apoptosis. The family consists of both pro-apoptotic and anti-apoptotic proteins that induce and inhibit apoptosis, respectively. Bcl-2, specifically, is an important anti-apoptotic protein playing a major role in the survival of cancer cells.

Bcl-2, also known as B-cell lymphoma 2, derives its name from the major role it plays in the progression of various types of lymphomas, specifically follicular lymphoma. Bcl-2 was the second member in a group of proteins initially described in the chromosomal translocations involving chromosomes 14 and 18 in follicular lymphomas.



EGFR GENE

Analysis on the Structure, Function, and Mutations of the EGFR Gene and Protein

Radhakrishnan Arunkumar[1,3] and Debarshi Basak[2,3]
[1]American High School, [2]Cupertino High School, [3]Cell Science Internship, Science Gurus

ABSTRACT

EGFR(known as Epidermal Growth Factor Receptor) is a gene that encodes the EGFR protein, which regulates the cell growth and division within a cell. The gene is located in chromosome 7(base pairs 55,019,032 to 55,207,338 on homo sapiens). Mutations of the gene leads to formations of cancers such as lung cancer and breast cancer. The EGFR gene has 5 main domains and 4 isoforms. The structure of the protein allows it to be located within the membrane of a cell, and bind to specific ligands that lead to specific signal pathways. EGFR has orthologs as well as homologs, including those within organisms such as mice and chimpanzees. The most common type of mutation within EGFR is deletion. There are many types of treatments for EGFR, some target therapies including Erlotinib (Tarceva), Gefitinib (Iressa), andOsimertinib (Tagrisso). Despite the many treatments, there is constant research being developed to find inhibitors to more types of EGFR mutations.

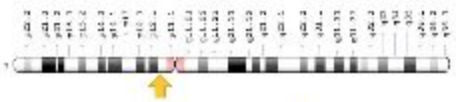


Figure 1: Position of the EGFR gene on chromosome 7, as marked by the arrow.

INTRODUCTION

Basic Information

The epidermal growth factor receptor gene, also known as EGFR, is a gene that transcribes for the transmembrane protein with the same name found in many animal cells and is a receptor for members of the epidermal growth factor family (EGF family) of extracellular protein ligands. It is a member of the ErbB family of receptors, a subfamily of four closely related receptor tyrosine kinases: EGFR (ErbB-1), HER2/neu (ErbB-2), Her 3 (ErbB-3) and Her 4 (ErbB-4). The epidermal growth factor receptor gene promotes cell growth and division in all cells, and in mutated cancer

Analysis of CD30 function, mutations, and role of treatments in CD30+ lymphomas

Samyuktha Lokanandi[1,3] and Soumya Turumella[2,3]

[1]Dougherty Valley High School, 10550 Albion Rd, San Ramon, CA 94582 [2]Monta Vista High School, 21840 McClellan Rd, Cupertino, CA 95014, [3]Science Gurus:Cell-Science Internship, San Carlos, CA

29 July 2017

Abstract

CD30, or known as TNFRSF8, is fundamental in protecting an individual against autoimmunity. While usually activated by T and B cells, it is important as a positive apoptosis regulator with also controlling proliferation of CD8 effector T cells, which kill pathogenic cells immediately. Mutations of CD30 are mainly present in Hodgkin's Lymphoma as well as Systemic Anaplastic Large Cell Lymphoma, a cancer that affects all the organs. Although there are many treatments currently in clinical trials, Brentuximab Vedotin, or Adcetris, has been successful at targeting this antigen on CD30 positive cancer cells in lymphoma patients. Other antibody drugs are also being tested for efficacy on targeting the antigen.

are also many other important genes. Genes similar to CD30 like CD27 which is important in T cell activation. Many of these genes are type II transmembrane proteins on T and B cells which signal to other immune cells about pathogens.

An important signaling pathway with CD30 is the NF-κB pathway. Through forming a complex with other TRAF proteins present, CD30 can either activate a canonical or alternative NF-κB pathway in tumor cells. In a normal cell, CD30 stimulation will lead to cell cycle arrest, apoptosis, and the transcription factor NF-κB. T cell and B cell activation usually lead to this pathway activation when signal transduction will occur. These immune cells, depending on where in the body, will have different expression of CD30.

VEGF AND VEGF PATHWAYS

Analysis of VEGF and VEGF pathways, their implication with Angiogenesis and the Growth of Cancer Tumors, and Treatments

Shreya Kochar[1,2] and Nikita Redkar[1,3]

[1]Science Gurus Cell Science Internship; [2]Mission San Jose High School; [3]Dougherty Valley High School

29 July 2017

Abstract

In cancer, vascular endothelial growth factor and its receptors are often found to be mutated. These mutations typically result in an overall increase of angiogenesis. Angiogenesis is the formation of blood vessels. The vasculature provides means for tumor development and strength by providing it with the nutrition it requires to survive. This paper will analyze the importance of VEGF in the body, its role in cancer, and the significance of angiogenesis for a tumor. The focus will be on the roles of VEGF-A and VEGFR-2. VEGF is often targeted in cancer therapies because of its key role in the nutrition supply of a tumor.

Figure 1: The six original hallmarks of cancer, published in 2000

original six, first described as a hallmark in 2000, is angiogenesis. As a tumor in its early stages develops, it is able to acquire sufficient oxygen and nutrients by the blood

CD-20 Gene

SCIENCE GURUS - Cell Science Internship 2017

Structural and Functional Analysis of the CD-20 Gene and the Drug, Rituxan

Pavithra Pandian[1,3] & Rajita Pujare[2,3]

[1] Monta Vista High School, 21840 McClellan Rd, Cupertino, CA 95014 [2] Lynbrook High School, 1280 Johnson Ave, San Jose, CA 95129 [3] Science Gurus - Cell Science Internship, San Carlos, CA 94070

29 July 2017

ABSTRACT

CD20 is a member of the membrane spanning 4A family which is expressed on the surface of B lymphocytes. Located on chromosome 11, this protein acts as a calcium channel and as the target of several monoclonal antibodies. This gives it enormous potential as a pathway for immunotherapy in cancer and autoimmune diseases, specifically in cancers that involve B lymphocytes or tend to have CD20 positive blood cells. Rituxan, also known as rituximab, is the most well known of these antibodies, and functions by binding to CD20 and triggering an apoptotic response in the corresponding cell. Thus, it is a critical drug in treating various autoimmune and cancer diseases.

BCR and ABL

Analysis of Mutations in BCR and ABL, Their Role in Chronic Myeloid Leukemia, and Available Treatments

Reva Kakaria[1, 2] and Ruchika Singla[1, 3]

[1]Cell-Science Summer Internship, Science Gurus, San Carlos, CA; [2]Notre Dame High School, 596 S 2nd St, San Jose, CA 95112; [3]University Preparatory Academy, 2315 Canoas Garden Avenue, San Jose CA 95125

1 Abstract

BCR and ABL, normally two genes found on chromosomes 22 and 9 respectively with no significant roles, form the BCR-ABL fusion gene upon chromosomal translocation, resulting in the creation of a Philadelphia chromosome. The gene product of BCR-ABL is continually active tyrosine kinase, resulting in uncontrolled proliferation and the eventual formation of cancer cells. Upon observation, it has been discovered that such a mutation is most commonly present in 95% of Chronic Myeloid Leukemia (CML) patients, as the presence of the Philadelphia chromosome and thus BCR-ABL fusion gene converts normal cells into tumorous ones. Though treatment of this disease seemed difficult, in 2001, Gleevec was introduced to the market, and it continues to effectively treat CML patients. Other clinical trials for CML therapies are currently in various stages of investigation.

The BCR gene has two known isoforms; more is known about isoform 1 because of its prevalence over isoform 2, which is not as heavily researched. The amino acid sequences of both isoforms are shown side by side below, with isoform 1 on the left (figure 2) and isoform 2 on the right (figure 3). Isoform 2 has a similarity of 96.5% with isoform 1. Comparing isoform 1's sequence to other species using the BLAST tool, which is a resource that compares either protein or nucleotide sequences between species, it is shown that rhesus monkeys (*Macaca mulatta*) share a 95.4% similarity while mice (*Mus musculus*) have a 93.8% similarity (figure 4)[2]. Although the BCR-ABL fusion protein has been extensively studied, the function of the normal BCR gene product is not clear. The protein has serine/threonine kinase activity and is a GTPase-activating protein for p21rac, meaning it promotes the exchange of Rac or CDC42-bound GDP by GTP, thereby activating them[3]. Known domains of the BCR protein include the Dbl homology

CD19 & Targeted Therapies

Sarvesh Nagwekar & Rishabh Sanghavi

Science Gurus Cell Science Internship

Background

Cancer is one of the leading causes of death today in the world and it is a chronic disease which is incredibly hard to combat. Cancer becomes more prevalent in people as they get older and older. This is because of 2 main reasons: One, since they are older, their cells have had more mitosis which gives the cell more time to mutate. Two, their immune system weakens and as a result of this weakening, the immune system cells that were once holding off the tumors and killing them are no longer

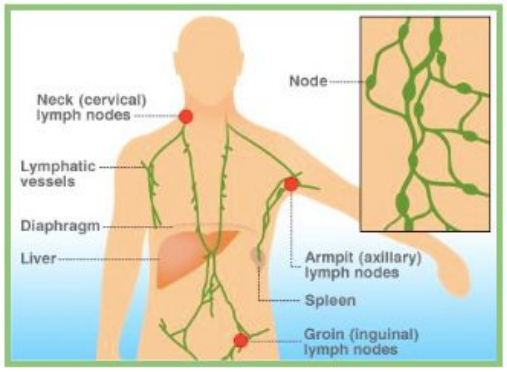


Figure 1: lymphatic system

The Structural and Functional Analysis of the PARP Gene

Sara Varadharajulu[12]
[1] UCLA, Los Angeles, CA 90095
[2] Science Gurus Cell Science Internship, San Carlos, CA

29 July 2017

Abstract

Poly (ADP-Ribose) Polymerase (PARP) encodes for an enzyme known as the Poly (ADP-Ribose) polymerase enzyme. PARP is a multifunctional, structurally intricate protein with numerous isoforms. PARP is necessary to regulate a variety of cellular processes including DNA repair, cell death, chromatin modification, inflammation, transcriptional regulation, and mitosis. Mutations in the PARP gene causes overexpression in a variety of cancers, predominately ovarian and breast cancer. PARP inhibitors are targeted therapies currently being used to use PARP-based cancers.

Internship Reflections

Amrita Sivia

The Cell-Science Internship was a very valuable and interesting learning experience for me. I was introduced to a myriad of new topics in the cancer biology and drug discovery fields, much of which I had never even heard about before this program. In every lecture, there was at least one part that I found exciting from Pablo Garcia staying later to answer my questions about the education path to take to be involved in genetics to Heather Maecker making her talk interactive and more meaningful with discussions. The best part I must say though was the field trip to Genentech. I had never been there before and it was my first time going into labs and seeing scientists doing experiments and work in front of me. This visit was the most inspiring part of the program and the best thing I have done in any program in my life. Although I have mainly focused on the scientific aspects of the program, I also really appreciated the delicious food that was brought in for all of us, as well as all the new people I met and got to know better. Meeting new people who could help me and I could depend on was another critical part of this internship that I will always remember; this not only includes my fellow interns but the lecturers and coordinators as well. I can say with certainty that this was an opportunity I will always remember.

Aditi Kumar

This internship was an amazing opportunity to learn about biotechnology, cancer therapies, drug discovery, as well as many additional topics. From the beginning, the interns were able to witness amazing and informative speeches about various different concepts that inspired students to pursue careers in bioinformatics and drug research. For example, one of the first speakers of the internship was Akshata and her presentation really set the standard for the rest of the internship. Listening to her speak about bioinformatics proved to me that I was at the right internship. Her presentation about cancer genomics shed a new light on the topic of DNA sequencing and gene expression. In addition, there were a few workshops throughout the course of the internship that helped students improve their speaking skills. Bob Figari, one of the speakers who discussed public speaking skills, aided each student one by one and helped them work on their flaws. This kind of one-on-one attention was very beneficial and helped the interns improve their speaking skills which were evident in the final presentations. Overall, I learned a lot during this internship particularly about drug therapies and this knowledge has motivated me to continue learning about drug research and stay well-informed about the advancements made in this field.

Catherine Lin

Before this internship, I was not exactly sure what I wanted to do with my future. But, I was intrigued with what the program offered. At every single lecture, I learned something new and this piqued my interest to even deeper into my studies. Each one of the speakers had a lot of knowledge and experience on their topic, showing us the in-depth perspective on new things. Without this program, it would have been hard to choose what major or career path that called to me most. Along with that, I made many new connections that helped me along the way.

I would also like to thank Dr. Jagath Reddy Junutula for founding this internship program and for sharing his extensive knowledge with us high school students. We thoroughly appreciate the time you both took out of your busy schedule to answer our questions and help us with the problems we had when we didn't understand a certain concept. Thank you so much for teaching us about bioinformatics and informing us about the various resources and tools that we can use to further our knowledge on cancer research. Your talks really inspired and helped us look at different aspects of the biomedical field.

Debarshi Basak

When I came into the internship program, I was just a regular high school student who knew nothing more than just the information given within the Biology textbook. However, the past 6 weeks at Science Gurus have been a phenomenal experience for my learning through a specific part of Biology, the research of cancer. Through the various guest speaker seminars, I was able to learn the various fields within the research of cancer, such as the entrepreneur part, the legal part, the research part, and the drug making part. These seminars were an amazing outlook into how each of these fields combines together to form the development of treatments for cancer. Additionally, the workshops were a great part of increasing my knowledge outside of Biology, as I was able to improve my public speaking much more as well as gain more insight into the college application process.

Apart from the seminars and workshops, I was able to gain a new view of how the scientific community works together, through the online databases of millions of genes, proteins, or DNA/RNA sequences. With access to these online resources, I was able to do my research on the topics of CML Leukemia as well as the EGFR gene and its therapeutics. These projects led to the increase of my knowledge within the field of bioinformatics, as I was able to explore through various websites to find different gene sequences, protein structures, or functions of drugs.

Overall, my experience as a Science Gurus Cell-Science intern was one not to forget, as through the span of 6 weeks I was able to walk out with so much more information and experience within the field of Bioinformatics than I had ever imagined.

Manav Shah

The Cell-Science Internship was an amazing, rewarding experience that really changed how I view biology and medicine as a whole. Listening and interacting with numerous guest speakers who described their real-life journey and taught us about current advancements and opportunities in their respective fields was invaluable. Because of these speakers, over the 7 weeks of the internship, I have learned so much about biological topics such as cancer, genomics, and medicine in addition to other interesting areas of focus including the drug discovery process, patent development, and public speaking. I now have a much stronger understanding of how biological companies and research work in the real world, which has definitely influenced my career choices. Outside of guest speakers, the cancer readings and presentations both helped increase my knowledge in an area that is so meaningful to all of us and is the cornerstone of medicine and targeted therapies. The 7-week bioinformatics project and final presentation was an eye-opener for me. I never knew that so many databases and programs existed online and could be used to conduct an in-depth analysis of genes and proteins related to cancer. Given a topic, I was able to collect data and reach significant conclusions through bioinformatics. Through this internship, I grew as a scientist and a presenter, I made important connections with speakers and other interns and learned about myself. I plan on majoring in chemical engineering with an emphasis in biology and hope to join the drug development process or design devices and therapies for future treatments. I would like to thank Mr. Jagath and the entire Science Gurus organization for providing me with this incredible opportunity. I hope to come back and serve as a guest speaker for this internship in the future!

Nikita Chigullapally

The Summer Cell Science Internship was an educating and enlightening experience. Throughout the seven weeks, I heard 20 amazing guest lectures that gave me further insight into cancer research and drug development. This experience further solidified my interest in pursuing a career as a doctor, specifically an oncologist. The whole program works together to give the interns an in-depth and detailed understanding of all the aspects of cancer research. It is a well-developed program of mentorship, including a fun and hands-on field trip to Genentech that allows us, interns, to see the topics we were lectured about being applied in real life. It gave us a real-life perspective of the bioinformatics career path and showed us the various possibilities waiting out there for us. I specifically enjoyed that they got in speakers from disciplines other than just science, such as accountants and lawyers. This diversity helped us to understand the different career paths and opportunities available in the biological field and exemplified the importance of a biology degree. Also, this experience allowed me to discover new friends and peers of my own age with similar educational interests as me. The assignments we are given force us to learn how to be resourceful and do our own research with room for creativity and originality. This is an unforgettable experience that definitely convinced me biology is the field for me.

Nikita Redkar

The Cell Science Internship was a wonderful opportunity for me to learn about cancer, its causes, and current and future treatments. Going into the class, I was unsure how it would be, and I was scared to be the one grade younger than the rest of the interns. However, I realized that this group was like a family - we shared many laughs, learned new things together, and had many amazing experiences.

I made many new friends from different schools whom I plan to keep in touch with after this. Even if I did not talk much to some people, I still feel a bond with them that will stick. Mr. Jagath helped create an environment of learning but caring, and we all profited from that.

The homework may seem like a lot of work, but it was so helpful and I would not change how Mr. Jagath ran the internship. Looking back, I realize how much I have learned. The most surprising thing to me was that cancer is not treated by location/type of cancer, but by what genes are affected. If Her-2 is the mutated gene, then even breast cancer and or another cancer can both be treated with the same drug. The guest speakers provided interesting information to learn about and discuss. Each talked about a different subject, so there was little overlap and we were able to learn something new each time.

From this, my perspective about drug discovery has changed. Going in, I knew I wanted to work in molecular biology, but the pharmaceutical industry never piqued my interest. After this, I have a strong desire to work in cancer drug discovery. The internship changed my interests dramatically and I hope that others after me can have the same transformative experience I did.

Pavithra Pandian

I thoroughly enjoyed every aspect of the Cell Science Internship. While some lectures and activities were more favorable than others, I looked forward to coming to Cellerant every Tuesday and Thursday. A few of my favorite guest speakers were Heather and Bob Figari. At the beginning of Heather's lecture, she conducted a simulation to demonstrate how approximately 50% of the population will be affected by cancer. She also proved that all careers will be affected by cancer, whether you're a researcher trying to find a cure for cancer or if you're a lawyer and you/someone you know has cancer. The introduction to her lecture inspired me to look beyond the realm of how many individuals are affected by this illness, and how everyone is connected to it. This also showed me that cancer is significant - it plays an important role in everyone's lives. Although Bob Figari's session was optional, it was definitely one of my favorite sessions during the internship. He not only incorporated interactive activities, like the one minute talk about a random topic but gave us tips to improve our public speaking skill set. Bob Figari's lecture can be applied most to outside life and some common tools that a successful individual needs. Overall, this internship was one of the highlights of my summer, and I am so glad and thankful that I had the opportunity to experience this. Hopefully, I will continue to do something like this in the future!

Pranav Jammalamadaka

This internship taught me the importance and value of oncology research. Each one of the lecturers was very interesting and it was also something that I had never had a chance to experience before. I really enjoyed learning about the structure of the human genome pertaining specifically to cancer, which out of all other maladies, plays a very important role in the problems that occur in the human body. Learning how to combat this disease through research about the treatment methods and therapies that could potentially or can target this disease that affects a very large portion of the human population worldwide helped me understand that this is key to solving one of the world's major problems and also one of the world's leading causes of death. I also learned what drug discovery and clinical development are and I became very interested to know how to make a therapy and to get a drug into the market.

This internship also helped me further understand the true value of research in a way that I have never really understood before I joined this internship. One way in which I think the internship could be improved is the opportunity to do more interactive or hands-on work with a lab portion for the internship to better understand how research is conducted and enriched learning in the lab. Another way to improve the internship is to line up the relevant speakers with the topic on the same day instead of giving another topic on the same day that should have corresponded with another speaker from another day. The most important thing that I learned from this internship would definitely be how to give back to the society with the knowledge that we acquired with our lives. I have seen how Dr. Junutula, all the speakers, and the volunteers in the program have seen all these people come together to help students by giving them the opportunity to learn information about drug discovery and development in depth. I may want to work in a lab or participate in research that is directly or tangentially related to oncological therapies.

Pranav Muthuraman

Having the opportunity to participate in this amazing program has given me so many positive experiences over the summer. Being able to do these projects in cancer research and bioinformatics has been so helpful to me in learning what kind of applications the biology I learn in school can be used for in the future. The guest speakers were all very interesting to listen to, but several that stood out to me were Mr. Alavattam, Ms. Maecker, and Mr. Storella's presentations. They introduced me to some real-world applications of the science I've been learning throughout all of high school in captivating presentations which reached out to me and connected to me very well. Overall, the experience inspired me to hopefully follow some of their teachings and take their place as I will so go off to college to figure out what I want to pursue in my life as a scientist or researcher.

Radhakrishnan Arunkumar

The in-depth cancer research in both the cancer project and the final project really gave me a sense of what scientists do in the field, and as a result, helped me open my eyes to what I wanted to do. This taste of real-world research and development after all the guest lectures was very interesting for me and developed my passion for biology. I really appreciate all of the new career pathways and characteristics I had learned from you and all of the guest speakers. There were many different aspects of biology careers that I had not known before, and as that area of science was what interested me more than any other, this information would greatly benefit my future. Finally, Bob Figari's workshop really opened up new methods of compiling information for presentations for me. What I need most is just to practice and more opportunities to speak publicly. I am really thankful for both your and his efforts in teaching and helping us develop these skills. I sincerely thank Dr. Junutula and all of the other guest lecturers and volunteers for their help throughout this internship.

Rajita Pujare

Reflecting on the Cell Science Internship this past summer, I really learned a lot and gained a lot of important skills that will help me in my future, whether in school or in my career. I expanded my interest in biochemistry and drug discovery and gained a detailed and complex understanding of cancer and cancer therapies. The speakers helped give me an insight into the industry and how it worked, and the concluding Genentech visit visualized that information and gave me another first-hand experience with the drug development process. Additionally, other speakers helped me diversify my view of the field; for example, I learned how patents are written in the drug development industry and how critical business solutions and strategies are. They gave me an insight into many fields and industries, such as law, business, and others. Furthermore, I familiarized myself with important bioinformatic tools and information, and the project I worked on allowed me to focus on a specific pathway/aspect of cancer, and its implications and potential therapies. On the final day, I listened to all of my peers' presentations as well, which gave me important, all rounded knowledge on the myriad of pathways implicated in cancer. All in all, I would like to thank Dr. Jagath Reddy Junutula and the rest of the speakers and mentors in this internship for such a memorable learning experience.

Reva Kakaria

I very much enjoyed the Cell Science Internship in 2017. There was a lot of work involved, but the content was all extremely interesting and it was exciting to be able to learn about the most cutting-edge and recent developments in the field of cancer treatments as well as to learn about the history of cancer and therapies in the first assignment. It was a little hard for me to keep up with assignments because during most of the internship, I was also working on the weekdays from eight AM to 3 PM so I did not have a lot of time to complete work. The Genentech tour was highly enjoyable, and it was one of my favorite parts. I also really liked the last speaker, John Storella, who talked about patents. One change I would suggest is with the organization of the final celebration - it was a bit long and it was also very difficult to hear any of the speakers as we were seated in the back, especially while everybody was getting food. Many of the regular sessions also ran a little late, especially when the second group of people was presenting on their cancer topics, leading me to rush through my presentation as I was going last. Also, with the final presentation, there were conflicting constructions coming from Kiran and you, which made setting up the order and content of the presentation slightly confusing. Overall, however, the experience was excellent and I am sure I will carry the lessons learned about mentorship and about science principles throughout my life.

Ruchika Singla

The Cell-Science Internship was a wonderful experience in which we were not only taught about the technology, logistics, and treatments involved in cancer but also involved in the research and development processes which we used ourselves to delve deeper into specific cancer-causing genes. While we learned about cancer and genetic databases, we simultaneously used those same databases to perform our own research, which helped us remember how to apply the information. This hands-on approach was extremely effective. Next, this internship featured the presence of several highly-qualified individuals who shared information regarding their own inspiring stories and careers. I did not even know so many careers in cancer biology existed! We met with and discussed cancer therapy with doctors, engineers, and even lawyers, all of whom came together to represent the diversity and opportunity related to this growing field. Overall, I am extremely grateful to the Cell-science Internship for the exposure they gave me to the initially daunting but now intriguing and exciting field of cancer biology and treatment. The method of teaching used helped me be confident that I will remember what I learned.

Shreya Kochar

The cell-science internship was truly an extraordinary experience for me. As neither of my parents has jobs in the biological or chemical fields of science, this internship was something radically different from what I have seen/learned about in prior years. However, getting the chance to listen to renown scientists, attending weekend workshops that were both fun and resourceful, and learning about the cancer drug discovery process as a whole was absolutely amazing. Visiting Genentech was one of the highlights; this field trip changed the way that I interpreted the manufacturing process, as we were taught about each step within the confines of the factory. Overall, this was perhaps the best way I could've spent my summer because not only did I learn a significant amount about cancer as a whole, I was able to practice my presentation skills, write more than one report, and watch videos that I would not have been exposed to otherwise. Additionally, I was taught how to use tools such as cBioPortal and UniProt, which are extremely useful in terms of comparing protein structures. I could not have gotten such a vivid experience anywhere else. The amount I learned this summer was exponentially more than I have in any other break, and it was one of the best experiences of my life. I will treasure it forever.

Sara Varadharajulu

The Cell-Science Internship was one of the highlights of my summer. It opened my eyes to the plethora of career opportunities available to those interested in life sciences---now, I am particularly interested in being involved in the business side of drug development. I very much appreciated the diversity of the speakers because it allowed me to process various types of information from different angles. I also liked how much emphasis was placed on bioinformatics---in a regular classroom setting, it is very rare that students are exposed to databases other than PubMed. My favorite part of the course were the two big projects: one on a type of cancer and the other on a particular gene involved in cancer. These assignments not only allowed me to explore some very fascinating material but also gave me the opportunity to improve my study and presentation skills. I have never written a report that large or delivered a presentation that dense in any of my science classes, so having this experience was truly a gift. Overall, I really enjoyed the time I dedicated to the Cell Science Internship. The course was extremely well constructed and the guest speakers, teachers, and my fellow interns were absolutely wonderful.

Sruthi Sakthivel

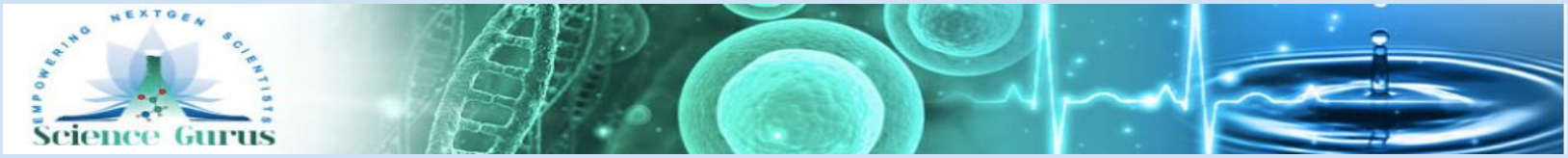
First and foremost, I would like to thank Mr. Jagath and all of the people behind Science Gurus for this amazing opportunities. I decided to dedicate this summer to figure out where I belong. I liked the idea of getting to know more about the biomedical, drug discovery, and biotech company aspects related to majoring in a field of science that the internship offered. I can strongly say that the internship didn't let me down on my expectations. Not only did my doubts about going through with the research path become clearer, but I was introduced to jobs that I could have that I didn't even realize I had the choice to. The guest lecturers, in addition to the student presentations, allowed me to get a broader of view of the scientific community and a career in research. My fear of the research path was instability, but through this internship, I learned that it isn't necessarily a bad thing. For many guest speakers, it was this uncertainty that forced them to discover themselves more and ultimately, helped them end at a position they were truly happy working in. All the information we learned through our homework assignments and guest lectures was perfectly tied together after our trip to Genentech where we got to see the concepts we learned applied in the real world. Not only were the guest lecture sessions very helpful, but the additional sessions with Bob Figari for public speaking and the session for college prep with Raji aunty were also very useful. The internship helped us learn many things outside of the scientific community through these sessions and that's what made this internship very unique. Ultimately, I would just like to thank Mr. Jagath for providing us high schoolers with such valuable experiences and taking time out of your busy schedule to make sure we get as much out of the seven weeks as we can.

Soumya Turumella

The Cell-Science Internship has taught me a lot about bioinformatics and especially drug discovery in cancer research. Before this internship, I knew that I wanted to major in biology, but this internship exposed me to a different field that I never thought about before. There were many different speakers who talked about the newest development in targeted therapies as well as the immense process for a drug to be approved. We learned that scientists, as well as other professions(like a lawyer and marketing), were needed in order to have an approved drug on the market. Through the different lecturers who not only educated us on cancer but the impact their developments had in the field of science, I realized the importance of scientists' contributions no matter their impact towards a cure. This internship helped me understand how important genetics and how it is much more difficult to cure than the public assumes. The information that I learned expanded beyond what I learned at school about cancer which further allowed me to understand how important this research is. I would like to thank all the lecturers and Mr. Jagath for this great opportunity to learn about cancer and targeted therapies much more in-depth.

Acknowledgements

We would like to sincerely thank Dr. Jagath Reddy Junutula for his immense effort, time, and patience through the program. We would like to thank all the wonderful, enthusiastic, and passionate speakers who took time out of their schedules to help high schoolers get a better understanding of their field and work in the specific fields. We would especially like to thank Kiran for working closely with each and every one of us on our final bioinformatics project, providing us with all the necessary and useful resources. We would like to thank Khyati,Vidya, and Anay for grading our homework and keeping us on track. We would like to thank the Science Gurus Organization for facilitating this incredible opportunity. The invaluable knowledge and insight we gained over the 7 weeks will, in no doubt, be incredibly useful to evaluate our future prospects. Finally, we would like to thank our parents for the support through the internship.



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