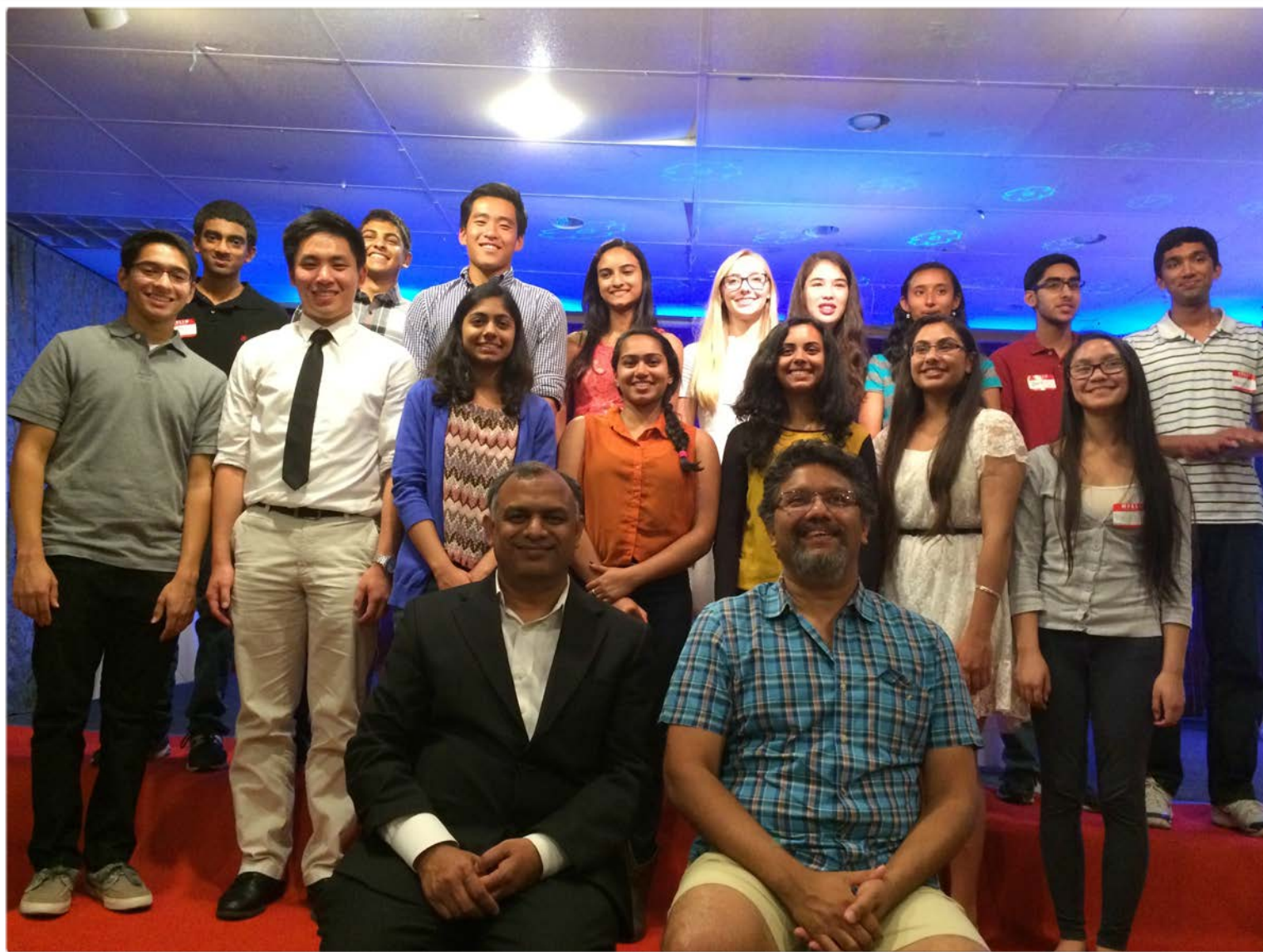


Science Gurus

Empowering NEXTGEN Scientists

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CELL-SCIENCE INTERNSHIP
ANNUAL REPORT
2014

Overview

Science Guru's cell-science internship is an annual, seven week program held in the summer, during which selected applicants are exposed to the world of life sciences. The 2014 curriculum centered around cancer, covering all aspects from mechanisms of the disease to the drug discovery process and prospective treatments. The current educational system, unfortunately, often focuses solely on highly constricted curriculums, thereby restricting students to a generally dull perspective of biosciences. This program enables individuals to discover their interests in science by bridging the gap between academic learning and the bioscience industry in hopes of guiding their future prospects.

The daily agenda started with lectures featuring eminent guest speakers from various biotechnology companies and academic institutions throughout the Bay Area, including Genentech, Gilead, and Stanford to discuss their work. The lecturers presented advanced material excerpted from their own research, often years beyond the scope of high school biology curriculums,

regarding the system of cancer and approaches to finding targeted therapies. It was therefore imperative that interns independently familiarized themselves with the selected topics to enhance their educational experience.

Although the lectures provided insight towards the biotechnology industry, the bulk of the program still lay in the participant's own work in the form of two major projects; the first of which is a research report on subsets of cancer. Upon scouring databases for information on their selection, interns created and delivered an oral presentation regarding all facets of their disease ranging from the biomechanics of the ailment to the future treatments. The purpose of the first project, though, is mostly foundational work, providing basic information about cancer. The second and undoubtedly the more intriguing project required interns to run their own experiments on cancerous systems. Facilitated by the Cell Works platform, interns simulated the effects of FDA approved, chemotherapeutic drugs on cancerous cells, focusing their efforts on

monitoring biomarkers indicative of various cancer phenotypes including accelerated cancer apoptosis and inhibited replication. Upon familiarization with the program, interns ran experiments with drug combinations at different concentrations to test for improved efficacy in treating cancer. Interns monitored variables meticulously and repeated experiments several times to ensure the outcomes they obtained with utmost accuracy, thus emphasizing and reinforcing professional experimental practices. Upon finishing their hands-on work, interns created a mock research paper and presented their findings orally in front of all participants and their parents.

The seven week program concluded with dinner and an awards ceremony to commemorate the completion of the program, sending off the interns with their newfound knowledge about life sciences.

Participating Interns

Name	School
Arundhati Suresh	Monta vista High School
Ashin Mehta	Harker High School
Ashish Keshan	Monta vista High School
Ashni Shetty	Cupertino High School
Chetan Gomatam	Fremont High School
Divek Toprani	Monta vista High School
Hemang Jangle	Mission San Jose High School
Kajol Ahuja	Arroyo High School
Lindsay Mendoza	Arroyo High School
Paige Hansen	Palo Alto High School
Pooja Vasudevan	Dougherty Valley High School
Rahil Khasgiwale	Saratoga High School
Rudra Aiyar	Palo Alto High School
Ryan Ta	Arroyo High School
Sonal Pai	Saratoga High School
Tiffany Streitenberger	Palo Alto High School
Xuankang Pan	American High School

Curriculum



Cell-Science Summer Internship Program

Date and Time: June 10 - July 26, 2013 Tuesday and Thursday, 5.30-8pm*
Location: 2000 University Avenue, Suite#602, Palo Alto, CA, 94301.



Day	Date	Instructor	Hours	Course Title	5.30-6.15pm Assignment	6.15-7.15pm Class	15min Break	7.30-8.00pm Group presentations/Lab work
Tue	6/10/14	Jagath Reddy Junutula	2.5	Introduction to Cell, Cancer Biology	Meet and Greet; Goals of Internship/Assignment Overview	Cell and Building blocks		Cancer Basics and Phenotypes
Thu	6/12/14	Pradeep Fernandes	2.5	Cell Signaling/Modelling/CellWorks	Cell Signaling/Modelling	Review on CellWorks Platform		Lab Work
Tue	6/17/14	Surya Sankuratri	2.5	Drug Development - Overview	Drug Development - Overview	Drug Development - Overview		Lab Work
Thu	6/19/14	Jagath Reddy Junutula	2.5	Antibody Therapeutics	Group1 (3): Breast/Ovarian/Brain	Antibody Therapeutics		Lab Work
Sat	6/21/14	Bob Figari (1pm-4pm)	4	Workshop: " Effective Content Development & Delivery "		Workshop		Workshop
Tue	6/24/14	Pablo Garcia	2.5	Small Molecule- Drug Discovery Kinases	Group 2 (4): Blood Cancers: Lymphoma/Leukemia/Myeloma	Small Molecule- Drug Discovery Kinases		Lab Work
Thu	6/26/14	Sanjeev Redkar	2.5	Small Molecule Manufacturing &Formulation	Lab Work	Small Molecule Manufacturing &Formulation		Lab Work
Tue	7/1/14	Sreedhara Alavattam	2.5	Large Molecule Manufacturing &Formulation	Group 3 (3): Gastric/Colon/Pancreas	Large Molecule Manufacturing &Formulation		Lab Work
Thu	7/3/14	No Class		No Class	No Class	No Class		No Class
Tue	7/8/14	Zora Modrusan	2.5	Cancer Diagnostics-NextGen Sequencing	Group 4 (3): Lung/Prostate/Melanoma	Cancer Diagnostics-NextGen Sequencing		Lab Work
Thu	7/10/14	Anula Jayasuriya/Surbhi Sarna	2.5	Startup-101: Venture Funding	Startup-101: Venture Funding	Startup-101: Venture Funding		Lab Work
Tue	7/15/14	Heather Maecker	2.5	Cancer Immunotherapy	Group 5 (3): Head&Neck/Kidney/Bladder	Cancer Immunotherapy		Lab Work
Thu	7/17/14	Vandana Date/Ganesh Kolumam	2.5	IP & Patents/Cancer and Inflammation	Introduction to Intellectual Property & Patents	Interplay Cancer and Inflammation		Lab Work
Tue	7/22/14	Sukhmani Padda/Kirthik Rajagopal	2.5	Clinical Trails/Nanoparticle Therapeutics	Overview to Clinical Trails	Cancer-Nanoparticle Therapeutics		Lab Work
Thu	7/24/14	Ravi Kiron/Ram Mandalam	2.5	Business Development/Cancer Stem Cells	Business Development 101	Cancer-Stem Cell Therapeutics		Lab Work
Sat	7/26/14	Final Project Presentations	6	Final Project Presentations (10am-3pm)	Final Project Presentations	Final Project Presentations		Final Project Presentations

Intern Presentations

Group1: Brain/Breat/Ovarian

Hemang (GBM/Brain Cancer), Arundhati (Breast Cancer), Ashni (Ovarian Cancer)

Group2: Blood Cancers (Lymphoma/Leukemia/Myeloma)

Kajol (HL/NHL), Sonal (CML/CLL), Rahil (AML/ALL), Lindsay (MM)

Group3: Pancreas/Gastric/Colon

Ryan (Pancreatic Cancer), Rudra (Gastric Cancer), Paige (Colon Cancer)

Group4: Lung/Prostate/Melanoma

Kong (Lung Cancer), Ashish (Prostate Cancer), Chetan (Melanoma)

Group5: Kidney/Bladder/Head&Neck

Divek (Kidney Cancer), Tiffany (Bladder Cancer), Pooja (Head&Neck Cancer)

Group Photos



The interns present their final projects to their peers and family



Relief and satisfaction following the interns' final presentations

Interns with Guest
Speakers Dr. Ram
Mandalam and Dr. Ravi
Kiron



Annual dinner
ceremony at the Vara
Indian Cuisine

Final Reports Abstracts

Pooja and Ashni

CP751871

(Figitumumab)

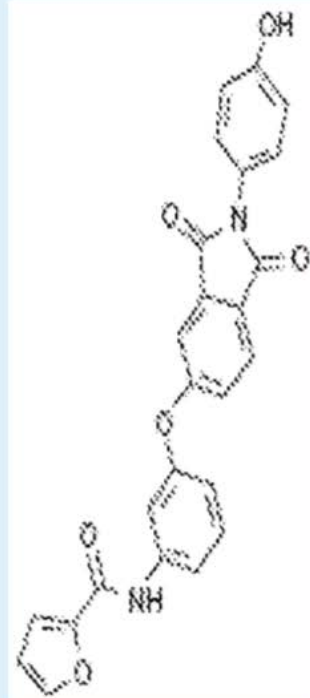
By: Pooja Vasudevan &
Ashni Shetty

Dougherty Valley High
School &
Cupertino High School

Cell Science Internship Program
July 26, 2014

ABSTRACT

This project was executed to further our knowledge of the drug CP751871, also known as Figitumumab. CP751871 is a monoclonal antibody that targets the insulin-like growth factor-1 receptor and is used to treat various types of cancer such as non-small cell lung cancer, and adrenocortical carcinoma. After phase 1 of a clinical trial with CP751871 in combination with Sunitinib for the treatment of certain detrimental tumors, the company Pfizer stopped manufacturing this drug due to surfeit screen failure rates and business purposes. The Cellworks platform is used to run trials and analyze the trends of CP751871 with the biomarkers of the six major phenotypes: apoptosis, proliferation, survival, angiogenesis, metastasis, and kinases. Once the analysis of the drug has been effectuated, one can test the combination of CP751871 with other competent drugs to see if new, efficacious drugs can be fabricated for future treatment of various cancers.



Hemang and Ashin

In-silico Examination of MEK1 Inhibitor AZD6244 (ARRY-142886) and Combination Therapy to Treat Cancer

Authors

Hemang Jangle, Mission San Jose High School

Ashin Mehta, The Harker School

Cell-Science Internship Program

Abstract

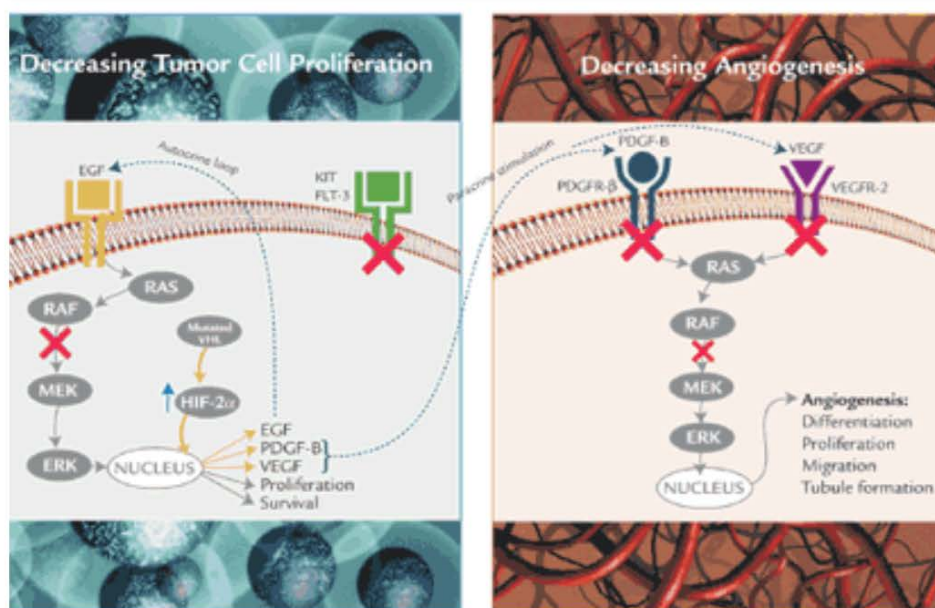
Selumetinib, also known as AZD6244 or ARRY-142886, is a non-ATP competitive inhibitor of MEK1. It was discovered by Array Pharmaceuticals and licensed for development to Astra Zeneca. Selumetinib is currently under various phase II and phase III clinical trials determining its efficacy in KRAS positive non-small cell lung cancer, thyroid cancer, and uveal melanoma. The efficacy of Selumetinib will be assessed by its effect on various biomarkers in simulations run on the Cellworks cell physiology platform. Selumetinib will be assessed on its own and also with three other drugs: Tarceva, XL147, and Nexavar. Findings from this report suggest that Selumetinib has a low optimal concentration. It is also seen that combination therapy with Tarceva and Nexavar do not improve cancer conditions, but combination therapy with XL147 is efficacious.

Efficacy of Nexavar

Xuankang Pan and Chetan Gomatam
American High School and Fremont High
Cell Science Internship

Abstract

In this project, experiments have been run with the cancer drug Nexavar, which is an oral drug used for the treatment of liver, thyroid, and kidney cancer. This drug is an inhibitor of tyrosine protein kinases VEGFR and PDGFR and RAF kinases; thus,



experiments for our drugs have targeted these biomarkers. Through our experiments we have found that the drug Nexavar showed significant improvement on these biomarkers. In addition to the confirmation of Nexavar's efficacy, we have combined the drug Nexavar with a multitude of other drugs and looked for change in the biomarkers for proliferation and angiogenesis. Much of the combinations have not shown promising results, but some of the trials have yielded interesting findings.

Lindsey and Ryan

Lindsay Mendoza, Ryan Ta

Arroyo High School

CellScience Summer Internship 2014

CellWorks Platform Trials with IPI-926

Abstract

IPI-926 is an experimental cancer drug that seeks to inhibit the SMO gene, a ~~proto-oncogene~~. By inhibiting this gene, which is a part of the Hedgehog signaling pathway, IPI-926 aims to reduce proliferation of cancer cells. In this experiment, cancer was induced in the CellWorks cell model platform, and the effects of IPI-926 were studied. In addition, IPI-926 was combined with other cancer drugs in three separate trials: one with ~~Tarceva~~, one with ~~Nexavar~~, and one with ~~Perifosine~~ and XL147. The results indicated that IPI-926 had little to no effect on cancer phenotypes, such as apoptosis and proliferation, showing that IPI-926 has an extremely low potency. However, when the combination trials were run, there was a significant increase in apoptosis, and significant decreases in proliferation, angiogenesis, and metastasis.

Tarceva (Erlotinib)



Rahil Khasgiwale & Sonal Pai
Saratoga High School
Cell-Science Internship Program

Abstract

Tarceva (Erlotinib) is an oral anti-cancer drug. It is designed to inhibit the tyrosine kinase activity of the HER1 (EGFR) signaling pathway inside the cell, which may block tumor cell growth. This drug is used to help cure non-small cell lung cancer and pancreatic cancer, both in metastatic forms. In our experiment, using X2go client, we tried many different Loop Configuration (simulations with different drug different combinations, we were able to add Control times, Diseases). After finishing single drug analysis, we began trying to create a novel drug combination, to improve our index result. The drug worked better for some indexes than others. Each biomarker also went the way that we expected; however, some biomarkers were less affected by the drug than others. The drug used in our trial were Perifosine, XL147, and Nexavar. In the real world, perhaps a Nexavar and Tarceva combo in concentrations (0,1,2) would produce the

best results in a cancer patient, and would be the best assortment of drugs to try. The only other competing drug for Tarceva is Gefitinib, but Tarceva is usually more common for the cancer it primarily treats. In conclusion, we found our combination drug analysis to be more successful than the single drug use, but were immersed in the knowledge of the drug and the cancer itself.

Paige and Tiffany

Halting Cancer In Its Tracks With XL147 July 2014

AUTHORS

Paige Hansen, Palo Alto High School
Tiffany Streitenberger, Palo Alto High School

ABSTRACT

Our project focused around the drug XL147. Our attention was on how effective this drug is on cells and how to make it the most successful and efficient it could be. Using *Cell Works'* X2GO platform we were able to perform experiments and access information of a cell with our drug. We looked into how our drug, alone, affects cells on the molecular pathway level within different situations. Afterwards, we looked into how this drug works when paired with other drugs. At the end of our data collecting we found that our drug is, in fact, very effective. It decreases proliferation in the cell, increases apoptosis, and decreases cell survival. Therefore, we determined that the drug alone was sufficient enough. However, if combined with a drug like CP751871, AZD6244, or Nexavar would have an even greater effect because of their similarity in characteristics.

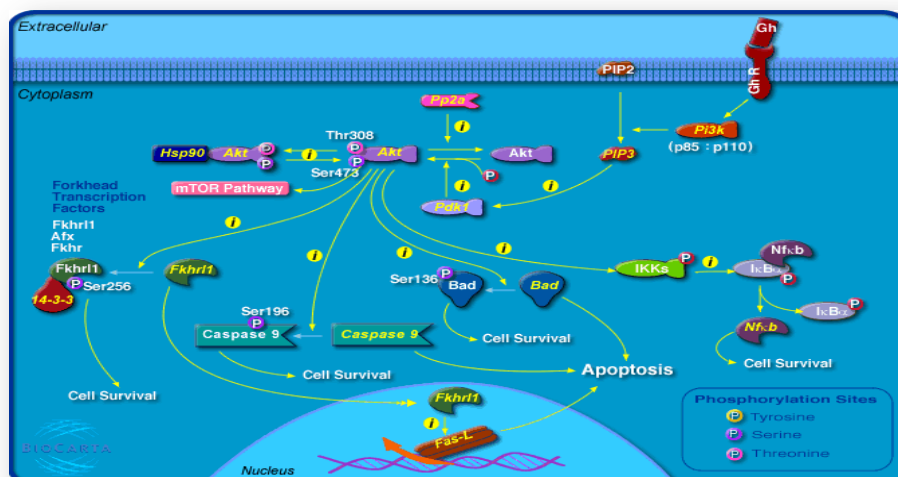
Efficacy of SP600125 as a Single-Agent and in Combination with Multiple Drugs in Affecting Cancer Phenotypes

Ashish Keshan, Arundhati Suresh
Cell-Science Internship, Monta Vista High school

SP600125 is a drug developed by Celgene aimed to inhibit JNK, a c-Hun N-terminal kinase. This drug works to reduce proliferation, rapid multiplication of the cancer cells as well as increases apoptosis, natural cell-death. To determine how well this drug works, a program, iCPHYS Model Development Tool was used to simulate the drugs effect on the disease, in this case, cancer. The program presents graphs that plot the effect of the drug on the different cancer phenotypes. SP600125 was proven as an effective drug due to its ability to reduce proliferation and increase apoptotic occurrences in the cancer cells when tested in combination. Overall the three combinations that were tested showed efficacy in affecting three phenotypes of cancer: proliferation, survival, and apoptosis.

Perifosine(AKT)

Rudra Aiyar & Kajol Ahuja
Palo Alto High School & Arroyo High School



KINASE B INHIBITOR/ ALKYLPHOSPHOLIPID

ABSTRACT

Perifosine is a membrane-targeted alkylphospholipid developed to inhibit the PI3K/Akt pathway and has been suggested as a favorable candidate for combined use with radiotherapy. In this study, we investigated the effect of the combined treatment of changing the concentration of perifosine and radiation (CTPR) on prostate cancer cells *in vitro* and on prostate cancer xenografts *in vivo*. Human prostate cancer cell line, CWR22RV1, was treated with perifosine, radiation, or CTPR. Clonogenic survival assays, sulforhodamine B cytotoxicity assays, and cell density assays were used to assess

the effectiveness of each therapy *in vitro*. Measurements of apoptosis, cell cycle analysis by flow cytometry, measurements in different parameters, and Western blots, used analytical technique used to detect specific proteins in a sample, were used to evaluate mechanisms of action *in vitro*. Tumor growth delay assays were used to evaluate radiation induced tumor responses *in vivo*. *In vitro*, CTPR had greater inhibitory effects on prostate cancer cell viability and clonogenic survival than either perifosine or radiation treatment alone. A marked increase in prostate cancer cell apoptosis was noted in

Internship Reflections

Hemang Jangle



My Cell-Science Internship was truly a rewarding and eye-opening experience. The fundamental reason why it was so enriching is that I was constantly learning new information about everything from the drug development process to the various technologies used to treat cancer today. The program drove my excitement by uniting a morally strong research cause, a direct application-based research opportunity, and a chance to learn from the elite of the industry. The mentors and guest speakers gave us a broad understanding of the tools we would need to properly analyze and understand the significance of our research findings. I found that instrumental. We started by studying the phenotypes of cancer to build a solid foundation for understanding the more complex targeted therapies. This allowed us to contextualize the impact of what we were learning. Moreover, doing and presenting a research project autonomously gave us the opportunity to get a hands-on taste of the scientific process. This too was very valuable. Beyond the stellar educational aspect, the program was run very smoothly and the mentors and guest speakers were very helpful. All in all, I'm glad I had the opportunity to be a part of the Cell Science Internship Program.

Sonal Pai



My experience at The Cell Science Summer Internship Program was fantastic. I could not praise it anymore than I do. The speakers were so enriching and enthusiastic. I felt honored to have these bright minds share their knowledge and insights with our group. I learned so much about biotechnology, the drug industry, and cancer. The methods used to teach our group all of the different aspects of the industry made it easy to learn, comprehend, and work with. Working alongside peers that are also interested in the industry allowed me to form valuable connections which I will have the rest of not only my career but also my life. Because the community within the program's leaders, interns, and speakers was so bonded it made it easy to learn and work with people. To me this internship helped answer many of my former questions about the industry and decide that I am certainly angling my career towards biotechnology. The program is perfect for any student who is interested in this field of science who also wants to know more about the processes that occur within it. Overall I feel the program was extremely beneficial. I attend it again in a heartbeat.

Kong Pan



The Cell Science summer internship has provided me with valuable insight towards the multifaceted pharmaceutical industry. The exposure to the process of drug development and the innovative treatment options for cancer has definitely influenced my future career choice. The eminent guest speakers were my favorite aspect of the internship, as they allowed me to experience a “flavor” of the ever progressive and innovative field of drug development. Additionally, the final project was the first time I had ever conducted research of that magnitude; the lessons learned conducting experiments with proper variables on such an advanced system will undoubtedly aid me in my future scientific endeavors. I am sincerely grateful for this invaluable internship, as very few high school students receive the opportunity to talk to senior scientists and conduct formal experiments.

Ashni Shetty



The Cell Science Internship was one of the most fulfilling experiences I have ever had. Before starting this internship, I had very limited knowledge on the factors behind cancer growth and the role various molecules played in the cell signaling process. Starting this internship off with the cancer presentations gave me a good basis on the different types of cancer; however, the several guest speakers that came in afterwards and our research project really expanded my knowledge- not only on the disease, but on biotechnology as a whole. This includes the process of drug discovery, the manufacturing of drug products, the roots and evolution of cancer, and so much more! This program gave me the opportunity to run drug tests virtually as well. Even though it happened to be a tedious process, it was amazing to see how running different drugs impacted the growth or reduction of specific molecules in a tumor cell. Overall, seven weeks of this program really instigated my interest in biotechnology. It was great to see how many advancements this industry is making today; the discovery of new drugs is faster than ever. I realized that this may be something that I would want to pursue in the future. I wouldn't have had this realization without this internship. Thank you so much!

Chetan Gomatam



I found out about this program through my friend Divek Toprani, who had participated in it the year before. I wanted to take part in this internship because it would give me exposure into areas that I am interested in. Over the course of the program, I was able to gain a lot of insight into the biotechnology industry through the guest speakers and the software we ran experiments on. The experiments themselves helped me to better understand what goes on in the industry. I learned about the many different facets of biotech. This was cool because I did not really know how far reaching the industry was, that it encompasses so many job opportunities and lines of work. I feel that this internship gave me a chance to explore the industry and narrow down my choices on what I want to do in this field. The public speaking class and the presentations we did were also good for me because they allowed me to work on my public speaking skills and learn how to give a scientific presentation more effectively. Overall, this program was very helpful for me.

Paige Hansen

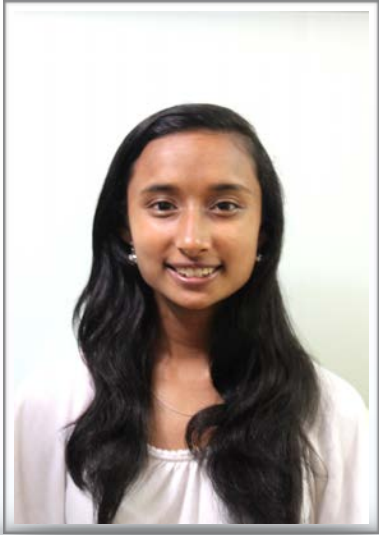


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Tiffany Streitenberger



My Cell Science experience was something I had never experienced before. It truly reminded me how much love I have for science and the ability it has to change the world. There were so many resources available during my experience that it was an honor to be able to participate. Before the internship, I did not really understand what cancer really was. However, I believe now I am confident in voicing what I have learned during the internship, and applying what I have learned whenever and wherever it is needed. I got to meet lots of wonderful people and create bonds with many members in the internship. At the end of the internship, I gained so much knowledge and skills that I can apply as I pursue my career in the future. I am so grateful for the experience and I would certainly recommend it to others interested in science and biotechnology.



When I first came into the program, I expected to study certain parts of cells on a very basic level. However, on the very first day on the program, I was astounded at the material we were going to learn. Several types of cancers I have never heard of were being presented in front of me, after each individual presentation by fellow peers, I could guarantee my time was being well spent. From presentations to guest speakers, this program presented a huge variety of problems and solutions that were taking place in real time. It was a truly insightful experience to learn about the drug development process and even visit a company that has produced many effective drugs. Despite the stress the last presentation brought upon us interns, it was one of my favorite activities during the internship. During that one project, I had learned so much on our given drug, Perifosine. Unfortunately, just when I started getting creative with the CellWorks platform (running a quadruple loop configuration with four different drugs at an interval of .2 in concentration), the program was coming to an end. Overall, it was a pleasure participating in this program because it had opened my eyes to different career paths, gave me advice for my own running business, and intrigued me with a different kind of science that one doesn't read about in a high school textbook.

Rahil Khasgiwale



At Cell-Science Internship, I learned the complex nature of cancer and worked with scientists on "Rational Cancer Drug Discovery and Development." I used innovative computational approach of Cellworks by creating patients' avatar and experimenting with lung cancer drugs in combination with Tarceva. My experiments showed increased efficacy of combination therapies for personalized cancer treatments. I learned about immunotherapy, another innovative approach that harnesses the immune system to fight cancer. I realized that early detection, finding better targets to attack cancer cells, and using novel strategies to reduce risks will go long way in effective treatment of cancer. This internship has sparked my interest in research and I wish to work on personalized medicine research which focuses on the right patient, with the right medicine, and at the right dose to achieve better cancer survival. Seven weeks internship gave me an overview of entire biotech industry from design, development and even startups etc.

Ryan Ta



Overall, I found the Cell-Science Summer Internship to be highly rewarding. Over the course of seven weeks, I was exposed to a wide array of interesting topics, from immunology to stem cell therapy, with the key themes being cancer biology and drug development. Our guest speakers' various occupations reflected the true diversity of the biotechnology industry; from mechanical engineers to venture capitalists, I learned that there truly is a place for almost anyone in this field. From the first week, we were assigned certain cancers to study - my topic was pancreatic cancer, and I thoroughly enjoyed preparing my presentation on the different types of pancreatic cancer. Furthermore, my presentation provided not only information on diagnosis and treatment methods for pancreatic cancer, but also a glimpse into the future of these methods (such as a new method which utilizes carbon nanotubes, which was proposed by the now-seventeen-year-old Jack Andraka). One of the most interesting experiences during this internship was the tour of the Genentech facilities in San Francisco; while it is one thing to study biotechnology from websites and PowerPoints, it is a completely different - and fascinating - experience to see the science in practice. Our final project involved a research project on an assigned drug - my partner's and my drug was the experimental IPI-926. By using the cell model platform developed by the CellWorks group, we monitored the effects of IPI-926 on certain biomarkers and also ran combination drug trials with our cancer drugs, such as Tarceva. Undoubtedly, this internship provided me with a unique exposure to the biotechnology industry.

Honorary Guest Speakers and Presenters

Speakers

Jagath Reddy Junutula, Ph.D.
Pradeep Fernandes, ME
Heather Maecker, Ph.D.
Ganesh Kolumam, Ph.D.
Sanjeev Redkar, Ph.D., MBA
Sreedhara Alavattam, Ph.D.
Karthik Rajagopal, Ph.D.
Anula Jayasuriya, MD, Ph.D., MBA
Surbhi Sarna
Surya Sankuratri, Ph.D.
Ravi Kiron, Ph.D., MBA
Ram Mandalam, Ph.D.
Zora Modrusan, Ph.D.
Pablo Garica, Ph.D.
Sukhmani Kaur Padda, MD

Title

Vice President
President & Co-founder
Senior Scientist
Scientific Manager
Sr Vice President
Senor Scientist
Scientist
Managing Director
Founder, CEO
Drirector
Entrepreneur in Residence
President & CEO
Senor Scientist
Research Director
Clinical Fellow

Affiliation

Cellerant Therapeutics
CellWorks Group
Gilead
Genentech, Inc.
Astex Pharmaceuticals
Genentech, Inc.
Genentech, Inc.
India Life Science Fund
nVision
Roche
SRI International
Cellerant Therapeutics
Genentech, Inc.
Novartis
Stanford University

Acknowledgements

We interns would like to give our sincere thanks to Dr. Jagath Reddy Junutula and Mr. Pradeep Fernandes for organizing this fantastic internship, Bob Figari for honing our presentational skills, the Cell Works group for providing their program, Artiman Ventures for their sponsorship, and the Science Gurus team for their support.

Editor

Kong Pan

Assistant Editors

Hemang Jangle

Sonal Pai