
UC San Diego
Jacobs School of Engineering
BioEngineering
Newsletter
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Fall
2020

Fall 2020

--The Nobel Prize on CRISPR, the voice from industry, and a diverse department.

The People of BEN

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Interviews.....Meenakshi Singhal, Wei Ji Chen,Yichen Xiang

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BEN

If you are interested in joining our staff, please contact us at ucsd.ben@gmail.com!

The BioEngineering Newsletter (BEN) is a student run publication that covers the people, research and events that occur within the U.C. San Diego Bioengineering Department. This WIN21 issue introduces two new sections to our readers for the first time, dedicated to representatives from biotech industry and the Bioengineering Diversity Council.

CONTENTS

DIVERSITY

We Care, We Act:

The Collective Effort to Maintain And Enhance the Diversity of Our Bioengineering Department

By Maria Sckaff & Yichen Xiang | Editors

Dr. Fraley and Her Introduction to The Bioengineering Diversity Council:

"The overall purpose of the Diversity Council is to guide and hold the Bioengineering Department accountable in the integration of diversity, equity, and inclusion into all aspects of the work at UCSD. The UCSD Bioengineering Department, under the leadership of Chairman Dr. Geert Schmid-Schonbein, created the Diversity Council in 2013 with a small group of faculty led by Dr. Karen Christman. In spring of 2020, the department named Dr. Stephanie Fraley as chairwoman of the council with the directive to expand the council to include students and staff and with the goal of having a greater impact on our bioengineering community. In the summer of 2020, the council held the first department-wide town hall on diversity and began engaging with student, staff, and faculty groups to obtain input on important areas of diversity or equity for the bioengineering community. In addition to feedback from specific groups, the council created a survey that will be sent to the entire department within the coming months to determine the top three areas that the department should focus on related to diversity and equity. The areas will form the basis of the purpose and scope of the council. The Diversity Committee will then engage in a strategic planning process between January 2021 and May 2021 to determine how to best achieve the goals set by the department."

More on The Bioengineering Diversity Council Representatives

Faculty: Francisco Contijoch
Staff: Irene Hom & Mariela Saldana
Graduate student: Maya Rowell
Undergraduate student: Luis Gonzalez Barranca

A glance at the tip of the iceberg. More on the next issue!

BE Community Committee

"The BE Community Committee is a staff led committee in the Bioengineering Department. This committee is committed to celebrating diversity and creating more inclusion in the department. Right now, the committee is focused on bringing about these efforts to the staff and narrowing the gap between staff, faculty and students in the Bioengineering Department."

Graduate Student Recruitment Diversity Efforts

"Oversaw the revision of the department graduate student recruitment procedures and raised the enrollment of female graduate students in the first year of my service from a level ~20% to ~50%. The fraction of female bioengineering graduate students in the Department has since been stable at close to 50%."
Contact: Dr. Geert Schmid-Schonbein

NSF CAREER funded outreach

Funds to support STEM outreach programming at Clairemont High School:
"As a part of my NSF CAREER Award, I partnered with the Bioengineering department's graduate student group BEGS to start a new mentorship program at Clairemont High School (CHS). CHS has an enrollment of approximately 2,500 students, of which 45% are underrepresented minorities and 31% are socioeconomically disadvantaged. While 40-50% of seniors are accepted to universities, only 20-30% actually attend. The career and experienced-based learning program I developed with BEGS and teachers at CHS began operation in the summer of 2016 to promote student interest and understanding of science and engineering with the goals of improving performance in these subject areas and increasing motivation and preparedness for enrollment at the undergraduate level."
Contacts: Dr. Stephanie Fraley, BEGS Outreach

From the Editors:

The Bioengineering Newsletter and the Bioengineering Diversity Council are teaming up to produce a diversity feature in every issue of the Newsletter from now on. Our goal is to highlight the diversity, equity, and inclusion efforts from the department and the bioengineering community at UCSD.

We are excited to share with you all this new segment on diversity every quarter. We also invite you to contact us if you would like for us to cover any diversity efforts that you believe deserve some recognition.

From the Council:

The BE department should feel encouraged to reach out to any of our representatives. To join us on Slack, search for "bioengineerin-va33033" or use the link (expires Feb. 18)
https://join.slack.com/t/bioengineerin-va33033/shared_invite/zt-lbv5rdut-0ej4yj5myGwplyhaPExtFO

IDEA Center

The IDEA center has the mission "to foster an inclusive and welcoming community, increase retention and graduation rates, and promote a sustainable culture of academic excellence among all engineering students at UC San Diego"
Contact: Dr. Pedro Cabrales, Dr. Bruce Wheeler
Web: http://jacobsschool.ucsd.edu/idea/index.shtml

Society of Women Engineers

" UC San Diego Society of Women Engineers is a diverse group of passionate young engineers excited about women in STEM. Through outreach to K-12 students, socials with other female engineers, networking workshops with industry, and technical teams, UCSD SWE provides women engineers with a welcoming environment to grow professionally and academically."
Web: https://swe-ucsd.netlify.app/

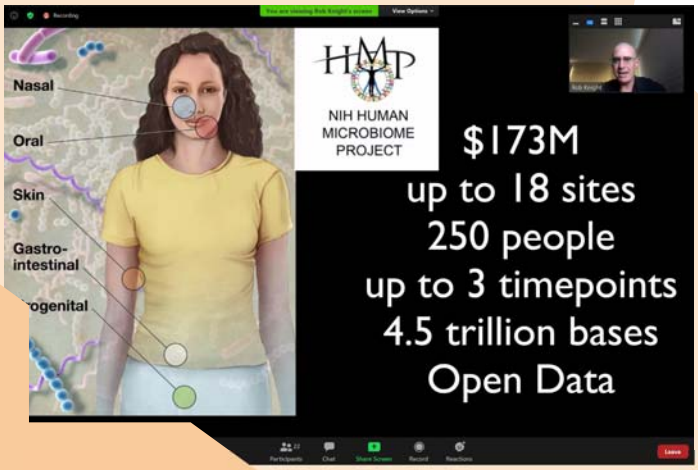
FEATURES

Staircase in PFBH.

Trust Your Gut:

UBIC Chalk Talk with Rob Knight

Joyce Zou| Student Org Representative (UBIC))

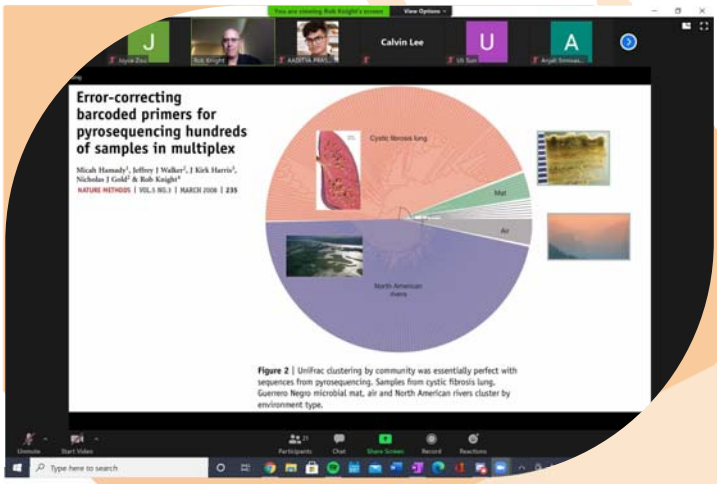


Dr. Knight introducing his research on the human microbiome at UBIC's Chalk Talk

Chalk Talk is a biweekly event that UBIC has been putting on for a few years now. During a Chalk Talk, professors from various departments talk about their bioinformatics-related research related, engaging with students in a quaint classroom setting. This year was no different; except that the event was hosted through the hottest video communication software of the year, Zoom.

Despite the loss of the intimate classroom charm, professors pulled through with their shared screens with informative lectures and a fun Q and A session at the end. Every professor's presentation on their research was a delight in their own way. Professors introduced students to new topics and exposed them to real world applications of bioinformatics. This quarter Chalk Talk showcased various research topics, ranging from immunology and genomics to the gut microbiome - a personal favorite.

The Chalk Talk came to an end on week eight of the 2020 fall quarter with a strong finale by Dr. Rob Knight. The UCSD professor and Director of the Center for Microbiome Innovation engages in research which has linked microbes to various health conditions including obesity and inflammatory bowel disease. I was personally fascinated by his research, as Professor Knight explained that the microbiome was an ecosystem that exists within us. Dr. Knight mentioned in his talk that gut microbiomes vary greatly, depending on each individual's diet. For example, he mentioned that a person who lived on a more traditional diet (consisting of less processed foods) would have a completely different gut microbiome from a person who eats mainly processed foods. Consequently, the health of each individual could be inferred through the collected data from their microbiome. Through this close examination of a person's health in relation to their gut microbiome, Professor Knight's research develops tools for analyzing pathological microbiota, pushing forward further discovery on how pathological microbiota behave and how they can be treated.



A slide from Dr. Knight's presentation on his microbiome research

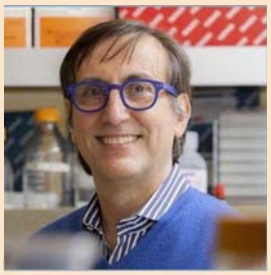
Having done thorough research in the microbiome field, Professor Rob Knight is also in charge of UCSD's on-campus waste water testing for SARS CoV-2. This has been an effective way to detect and contain the virus on campus, thanks to his pathologic microbiome research.

Although Dr. Rob Knight's talk was my favorite, each Chalk Talk has been unique in its own way, appealing to many students with different interests. The goal of the UBIC Chalk Talk is to expose students to a plethora of bioinformatics research conducted in a fun and convenient way.

Professors seem much more approachable in an intimate setting such as a small classroom or a 20-person Zoom call rather than in a large lecture hall. The setting is made to facilitate interaction and encourage students to ask questions about research, ask about the process of joining a lab, or even engage in thoughtful discussions with the professor. Through Chalk Talks, students are able to keep up with all the new types of research in the world of bioinformatics, and they leave each talk with newly learned information of the rapidly developing realm of biology research.

With bioinformatics being a niche field, Chalk Talks also help show students the variety of research to which bioinformatics can apply. UBIC aims to help our students in their future careers and believes Chalk Talks are one of the many doors and insights to their futures. As the fall quarter ended, UBIC began preparing for the winter quarter's batch of Chalk Talks to provide students with the latest scoop on bioinformatics research. We hope to see more new faces at these Chalk Talks!

UBIC give thanks to all Fall Chalk Talk Guests:



Dr. Alessandro Sette
Chalk Talk #1

Dr. Elizabeth Winzeler
Chalk Talk #2

Dr. Bjoern Peters
Chalk Talk #3

Dr. Rob Knight
Chalk Talk #4

More Resources On UCSD's Wastewater Detection of Coronavirus:

From Campus Notice: Office Of The Chancellor on Sept 5, 2020
https://returntolearn.ucsd.edu/news-and-updates/wastewater-detection-sept-5.html

From This Week @ UC San Diego by Erika Johnson
https://ucsdnews.ucsd.edu/feature/qa-wastewater-monitoring-with-professor-rob-knight

INTERVIEWS With Professors

Construction of the Warren Mall outdoor classrooms.

Dr. Trey Ideker

Genomic Data, Computer Science, and the Modeling of Biosystems

By Meenakshi Singhal | Interview Writer

Introduction: *Dr. Trey Ideker is a Professor of Medicine, Bioengineering, and Computer Science at UCSD. He received his B.S and M.S. in Computer Science and Electrical Engineering from MIT, and later his PhD in Biology at UWash with Dr. Leroy Hood. It was during his doctoral work that Dr. Ideker helped lay the foundation for the field of systems biology as we know it today, through the creation of Cytoscape. By applying quantitative approaches to solve complex biological problems, Dr. Ideker now leads a team that aims to advance our understanding of gene regulatory networks in the domains of cancer, CRISPR-Cas9 screens, and more recently, the mechanisms behind COVID-19 infection.*

Q: You are considered one of the pioneers of the field of systems biology. How do you believe the discipline has changed or expanded during your career as a professor?

The idea is, just like genome sequencing opened the floodgates of genomics by allowing us to read an entire genome—where you basically press a button and get a string of DNA, which is a text file on your computer of A's, T's, C's, and G's—that operation is now kind of routine in terms of reading and assembling genomes. The key is that the genome is just one tiny part of the entire biological system. DNA is packaged inside a chromosome, which is packed inside of the nucleus, which is inside of cells with all of their machinery like the Golgi apparatus and vacuoles, and of course cells make up different cell types, which make up tissues and organs. Wouldn't it be great if we could press a button and get the structure and function of the entire cell, or the entire functioning organism? That's really when people talk about systems biology, what we are trying to do. Of course as you start to understand more of the structure and function of the rest of the system outside of the nucleus, then that does shed light on disease, and disease mechanisms. So for COVID-19 and any of these diseases, the idea is that just like DNA sequencing is kind of the core factory operation that one does in lab, it's been automated, there's another set of automated tools we apply called protein interaction mapping, where you identify all protein-protein interactions that interconnect the system. So the genome itself is just a number line, or a string of letters, from which you can find genes; but the genome doesn't necessarily tell you how those genes function together in pathways and protein complexes in cells. And of course almost all genes don't act alone: almost all genes work together to encode parts of molecular machines, kind of like your IKEA manual, where the first page is always the parts list, and pages 2-7 are how you assemble those parts into making the piece of furniture. That's sort of true for any machine that

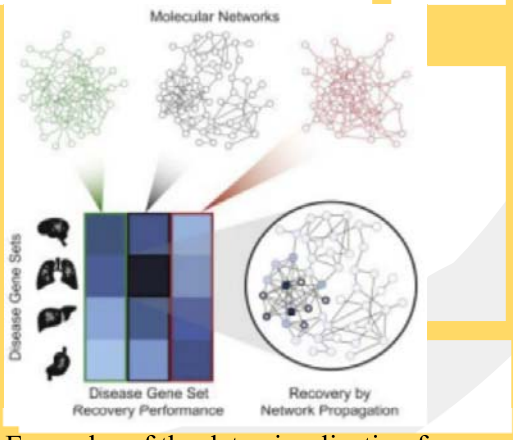
must be assembled; what we work on is what proteins, since proteins are the parts, what proteins are connected to other proteins, and that's what's determined by protein interaction screening. Given all those data, you then want to infer what is that assembled machinery to be revealed.

Q: What is the power of computational/network based strategies in understanding the mechanisms of the novel coronavirus?

So for the COVID example, the idea is you take every viral protein: the viral genome encodes viral genes which make proteins just like our human genome—it's far fewer; most viruses have just a dozen at most proteins, and for those proteins you now perform an affinity purification experiment and you pull proteins down from the human cell, and what you find is that each viral protein is incorporated into multi-protein machines involving both virus and human proteins. That's the sort of tricky thing about viruses, is that they use as much of the human cell as they can. So the papers you read this year on COVID are a map of not just what are the parts of the virus—because that's what the genome tells you—it's a map of how those parts connect to all the parts of human cells to co-opt its function and produce more of the virus. If you're trying to pioneer these approaches which aren't just automatically reading genomes, but are carrying out the rest of the IKEA manual, then viruses are not just important as a public health issue, they're a perfect model system because they're small. And then maybe one day when we figure that out we can scale it up to a whole human cell.

Q: As a co-director of the Cancer Cell Map Initiative [which synergizes the talents of several professors at UCSD and UCSF] , what is your goal for the organization moving forward?

Now that I've explained what we do, we want to do the same thing for cancer. Cancer proteins don't act alone; now that's a very interesting question: is cancer more



Examples of the data visualization for cancer studies, provided by Dr. Ideker

complicated than viral infection? There certainly are more proteins that have been implicated in cancer than are encoded by a virus. There's hundreds of so-called cancer proteins—what causes a protein to be called a cancer protein? There's lots of reasons, but the most common is that the gene encoding that protein is mutated in most tumors. So what we're doing is we're starting with each of those mutated proteins in cancer; so far we've looked at 61 genes that are the 'most mutated' in cancer, and what we do is to extract the wiring diagram, so pages 2 through 7 of the furniture assembly manual. We try to develop an exhaustive list of what other proteins those cancer proteins bind to, then use all of this data to really start to see if we can assemble all of the parts of a cancer cell. Some of those parts end up being quite well known—we have a story where collagen is a complex of about 40 different proteins. It turns out that any one of those genes is rarely

mutated in tumors, but almost all tumors mutate one of those collagen genes. And you don't see that unless you have the whole machine of collagen, and you're staring at it, and you see that at the machine level, that thing is mutated like gangbusters in most people who have cancer. To understand diseases that are diseases of the genome you need to have that map; so when mutations tinker with that wiring diagram, what are the implications of that? Until you have that wiring diagram, it's going to be hard to make progress.

Q: The 2018 Nobel Prize in Physiology for immunotherapy research sparked incredible interest in pushing forward CAR-T therapies. What do you believe the implications of the Nobel Prize in CRISPR will be on the field of bioengineering?

In the case of CRISPR, I think the impacts have already very much been felt, significantly. It's great that the Nobel Prize Committee recognized both Doudna and Charpentier's contributions earlier—sometimes it will take 40 years when the Committee will realize 'Oh we never gave the Prize for CRISPR'—so it's great that they did that. On the other hand, maybe they don't want to give the prize too soon because they might be worried that CRISPR is just a fad, and it doesn't really work. But I actually agree with the timing of this because it's clear that CRISPR is here to stay and it's utterly changed the field. We (the Ideker Lab) use CRISPR all the time to knock out genes. Once you've assembled the wiring diagram, so if proteins A, B, C, and D connect, you need to understand the impact of that machine. CRISPR is a shotgun that basically kicks out different systems and you see what the consequence of having done that is. And to be clear, the ability to snip a gene out of the genome had existed for a while, but it wasn't very efficient. It was much more efficient in model microbes like budding yeast and bacteria; CRISPR makes all of this possible in humans.

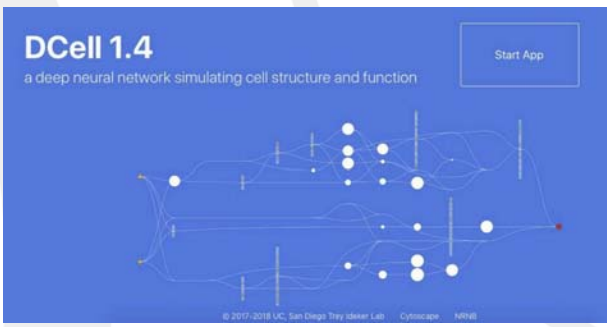
Q: Cytoscape (an open source bioinformatics platform) has been widely implemented by systems biologists around the world. In your own words, could you explain how you would like to see scientists incorporate it into their own work?

The success of Cytoscape is really based on not us, but it's everyone out there who uses the tool. The reason why it got heavily used is first of all it was timely, so it was the first tool that let you visualize these wiring diagrams that you could read out using protein interaction mapping technologies, along with others. For example, another technology you may have heard about is ChIP-seq (chromatin immunoprecipitation combined with DNA sequencing), which is measuring binding between proteins and DNA as opposed to proteins with other proteins. So it draws a wiring diagram of what transcription factors bind to what gene enhancers and promoters, and Cytoscape can help visualize this. It came out around 2003, and over the years we haven't rested; we continually improve the tools and have added lots of new functionality. A lot of software is hard to make work even, especially academic research code that someone publishes with their papers—it's very hard to pick up someone's code and make it useful. But in the case of Cytoscape, we've really invested into making it user friendly and robust, and having a community of users

and groups around Cytoscape. The last thing I'll mention is that we've made it extendible through what we used to call plug-ins but are now called apps. The ability to write an app in Cytoscape is what attracted a lot of developers along with users. The most modern incarnation of that is that rather than having to write your app in a full coding language like Java or C, you write your 'app' in Python or R and use the 'REST communication protocol' (representational state transfer, a method for creating Web services between devices) to interface to Cytoscape. You could be running an electronic notebook like Jupyter and writing Python code, and have that Python code invoke network analysis visualization in Cytoscape.

Q: How do you see cancer bioinformatics research in particular progressing in the future, i.e. new research methodologies or theories/areas of interest?

I think what's going to be possible is the level of automation we've seen with sequencing in DNA and RNA is essentially going to happen with other aspects of biology. So the ability to push a button and just read out the structure of a tumor—now, you can kind of just look at the histopathology of the slide of your tumor cross section and look at cells, but imagine if you could peer into each of those cells and understand its unique structure, and moreover, how that structure differs from the normal cells that surround it. That's going to all become possible, and by extension or as a consequence, treating disease is going to be based on those 'shop manuals', or wiring diagrams of your particular disease. It's like, can you imagine debugging your radio if you didn't have the blueprint?



Web page of DCell, a cellular biosystem modeling software developed by Ideker Lab.
Access via http://d-cell.ucsd.edu/

Interviewer's Notes:

While there is immense power in applying computational strategies to understand biology across all levels of interaction, the Ideker lab remains dedicated towards applying wet lab techniques to validate and expand experimental findings. This versatility is what has propelled the researchers to explore topics that are relevant to all of us: not only is precision medicine on the horizon, but also hierarchical modeling and mapping cell fate decisions.

Dr. Prashant Mali

Gene Therapy: CRISPR, RNA Editing and mRNA Vaccine

By Wei Ji Chen | Interview Writer

Introduction: *Dr. Prashant Mali is an Associate Professor at the Bioengineering Department and the Principal Investigator of Mali Lab. He received his B.S. and M.S. degrees at the Indian Institute of Technology, Bombay in Electrical Engineering. Dr. Mali completed his PhD in Biomedical Engineering at Johns Hopkins, where he started his research in gene therapy and regenerative medicine. After 3 years of a postdoc fellowship at Harvard Medical School, Dr. Mali came to UCSD in 2014. His expertise in various gene therapy approaches led us to insightful discussions about CRISPR, RNA editing via recruitment of endogenous enzyme, and mRNA vaccines.*

Q: What influenced you to become a professor and work in academia?

I was always interested in the research and development of engineering tools, however I didn't begin my undergraduate studies knowing that I would eventually become a professor and conduct academic research. After I graduated, I did an industry job at an oil rig in the middle of the ocean so evidently, my path to academia was not linear. It was only after a while did I decide this is a potential interest I should explore a little more thoroughly. Once I was settled in my PhD I realized that I was happy here and the rest is history.

Q: At what point did bioengineering research become your focus?

In my undergrad, I was an electrical engineering student, but I became interested in building physics based tools for studying the basic physical properties of biomolecules. At this point, I had no formal training in biology. After my stint on the oil rig, I decided to apply for a bioengineering PhD at John Hopkins and it was then I had a year of life science courses taught at the medical school. Initially, I did rotations in labs that had an interest in electrochemistry and physics, however the way the professors presented biology at Hopkins made a deep impression on me and I switched completely to a STEM cell biology lab. Of course, It was not the easiest of transitions to move from an electrical engineering background to biology focused research but I was fortunate in that I had many great mentors who were patient in my training.

Q: What research is done in the lab?

We're primarily interested in two areas, one is the space of gene therapy and the other is regenerative medicine. We're fundamentally a technology development lab with a curiosity based approach, what we find novel or exciting is what we focus on in the lab. Much of the work in the lab is a combination of basic science and tool development. By understanding the intricacies and nuances of, say,

a stem cell's behavior, and understanding the function of a particular genome, you can then build a new tool from the ground up. It's very much a self-perpetuating cycle when you have a foundational understanding of the basic science. The basic science will drive the development of technology and that opens up more basic science and subsequently, more technology, and so forth. Half of my lab is in gene therapy and half my lab is in stem cell biology. For stem cell research, we work with human pluripotent stem cells as our model system and we're very interested in how early development takes place. As for CRISPR, although strides can be made to improve the system itself, we're much more focused on using the CRISPR system from a gene therapy perspective. Only a small fraction of my lab is working on pure CRISPR development. Everybody else is more interested in gene therapy as a whole. However, in order to successfully enable gene therapy, it necessitates improvements on various aspects of the pipeline. Gene therapy by itself is a complicated package, composed of the payload, the route of administration, the delivery vehicle, fully understanding the workings of an organism and its individual subtleties. Each step of a therapeutic pipeline requires technology development and research to ensure what you deliver and how you deliver it is functional and safe.

Q: What are specific challenges with gene therapy that are different from traditional medicine?

The prevalent medicine we use today is based on small molecule drugs in the form of a pill. However unlike small-molecule based drugs, gene therapy does not focus on the molecular tool alone, but the delivery modality for the same is an equally critical component to build the full therapeutic. In gene therapy, one of the important tools is CRISPR and while there's always room for improvement, CRISPR is already quite effective and easy to use. Even prior to CRISPR, we had TALENs and ZFN (Zinc Finger Nucleases) so the problem lies not in the molecular tool, but in the delivery of the package. Delivery is a big unsolved challenge in the field right now and if we can solve delivery then that opens up greater potential in gene therapeutics and beyond.

Q: What has made CRISPR receive the attention it has in comparison to past genetic editing tools such as TALENs and ZFN?

For a tool, there are two attributes that make it extremely valuable. One is does it work? Two, the ease of use. The previous genetic editing tools such as TALENs and ZFN along with CRISPR all satisfy the first criteria. However, the ease of using CRISPR has democratized the tool. Everybody can use it, every single lab can do it, and it can literally be a high school experiment. What otherwise could have been a tool that mandated years long experiments of only a handful individuals can accomplish, it is instead universal to any lab that wishes to utilize it. It enables basic research due to its broad variety of applications, making it an indispensable method. To ask someone if they use CRISPR is the same as asking if someone uses PCR. That's what makes CRISPR different from all previous genome engineering technology. It's powerful and it works for everyone. Beyond CRISPR's obvious implications on therapeutics, I personally believe it'll be most impactful in basic

Q: Can you speak about your experience in RNA editing? What are the similarities and differences between DNA and RNA editing?

For DNA, we have CRISPR, but for RNA, we've been working on a system called ADAR (Adenosine Deaminase Acting on RNA). Unlike CRISPR that is found in the genomes of prokaryotic organisms, bacteria and archaea, the ADARs are already present in the human body, thus working with these is safer in that unlike CRISPRs they won't elicit an immune response upon delivery. The ADAR enzyme binds to double stranded RNA and converts adenosine to inosine and the ADAR protein functions as an RNA editor by making post-transcriptional modifications on mRNA transcripts. What we've been doing is developing tools that allow us to redirect ADARs to make specific RNA edits in order to repair a gene. RNA editing can be very exciting because it's tunable, reversible, and no off target is permanent, which is a notable difference from the binary nature of DNA editing, once edited, it's permanent. Our long-standing interest is in being able to build programmable targeting tools for DNA, RNA, and Protein i.e. at each level of the central dogma. In doing so, this gives us greater flexibility in tool selection since targeting on each level of the central dogma has its own advantages and disadvantages and is suited for different circumstances.

Q: Pfizer and Moderna have recently released two COVID-19 vaccines. What is your opinion on an mRNA based vaccine compared to the standard vaccines used up till now? Do you think this will become the new standard within the industry?

Developing a vaccine involves multiple steps, the first is creating the vaccine itself and the other is mass producing it economically. I think the future challenges of mRNA based vaccines lie in biomanufacturing as they have turned out to be much more expensive than some of the classic vaccines. When it comes to biotechnology, an important aspect to consider is its accessibility. For developing countries, cost is a limiting factor and while mRNA vaccines are exciting because they can be easily programmed and directed to a pathogen of interest, it is necessary to continue refining the technology while lowering the cost. The challenge and goal of the field is to keep producing and making it an affordable commodity. Different parts of the world have different needs and constraints and vaccines need to reach the whole world.

For example, some of the RNA vaccines need to be stored at -80 celsius and need to be transported in low temperature as well which makes it heavily reliant on the availability of infrastructure. The manufacturing process may also require technology and reagents that is prohibitively expensive outside of developed countries. As thrilling as it is to have another tool on the market, it is always a good policy to have many distinct options.

Q: Being someone who's experienced in academia and has also deep connections with industry, what is your perspective on the intellectual property of research once it's moved beyond the academia space?

Hypothetically, suppose as an academic one invents a tool. Given that the tool is useful, that tool will now be widely used in academia. If I want to take that tool and have it translate to the clinic, then companies are an important vehicle to do so because labs are not designed for product commercialization. To move a product away from the laboratory space requires a different level of funding, approach, and work, so having a very healthy connection between academia and industry is important to achieve translational research. Companies for their own safety and ability to commercialize their work effectively will need to have access to patents and license it from whoever the inventor is. It's an important incentive for them to be protected as the path to the clinic is a long one, and entails considerable resource investment as well as tacking of a host of additional challenges.

Q: Any advice to undergraduate students who are interested in pursuing research?

Most importantly, if you choose a lab for research, choose a lab that excites you, where the research being done fascinates you. For an undergrad there's a constant juggle of homework and research, but equally important is experiencing life, and extracurriculars. So at the end of the day you should choose something you're most passionate about or intrigued by. But, don't ignore your coursework at the cost of research, because your coursework builds your fundamentals and a strong resume. Additionally, this knowledge will become necessary as you start formulating your own hypotheses and venture deeper into the complexities of your research topic.

INTERVIEWS With Industries

Dr. Teriete from TumorGen

Circulating Tumor Cell Clusters and Targeting the Root Cause of Cancer

By Yichen Xiang | Editor-in-Chief

Introduction: *After Dr. Teriete received his Bachelor of Science from the University of Leeds in Biochemistry, he went on to earn his D.Phil. from the University of Oxford. Now he is a research assistant professor at Sanford Burnham Prebys Medical Discovery Institute and the Chief Scientific Officer at TumorGen, a biotech start-up company in San Diego. Dr. Teriete is an expert in cancer research and works with TumorGen following their vision: Fighting the root cause of cancer. As a researcher active in many fields including bioengineering, Dr. Teriete has been involved with the UCSD Bioengineering department for many years.*

Dr. Peter Teriete

Q: How did you hear about and become involved with our Departmental events?

I got to know Isgard Hueck, your Director of Industrial Relations Office, because my children and her child went to the same Saturday German school. Therefore, as a Bioengineer working in both, academia and industry, naturally I was invited to participate in those programs involving industrial members. I have always been excited to work with student interns from UCSD bioengineering, because they have proven to be really good students and make excellent interns.

Q: What is the Vision of TumorGen that makes the company different from others?

TumorGen is a startup biotech company utilizing among other things bioengineering in the field of cancer research. We are trying to address a specific need scientifically, medically, as well as commercially. TumorGen was co-founded by Dr. Jeff Allen and me in 2016 based on a vision Jeff had addressing what is often considered the root cause of cancer, which is the spreading of the disease to distal organs, in a process mostly referred to as metastasis. A main driver of this process are circulation cancer cell clusters, and some of my early PhD work played a major role in this research direction.

I find it boring to introduce a company with numerical statistics, and thus would like to talk about why Jeff's this vision is important to us. Jeff lost his wife 17 years ago to cancer. She was diagnosed with widely spread tumors all over her body and sadly passed away not too long after the diagnosis. Taking care of their two sons didn't leave much time, but over time a vision was ignited in Jeff, driving him to do what he could to fight this disease. We crossed path when he came looking for a lab space to use for a fundraising campaign. I found his specific interest fascinating, studying the drivers of metastasis, the circulating tumor cell clusters, and how to eliminate them.

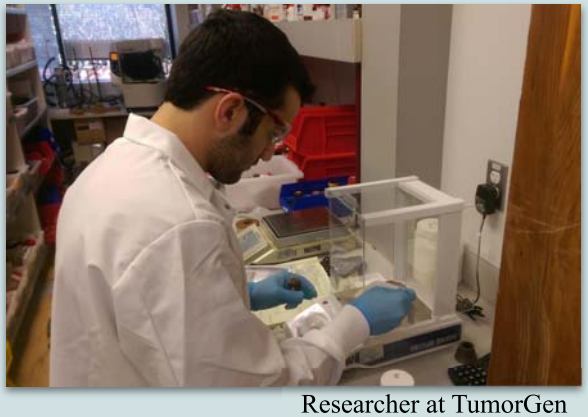
Q: TumorGen focuses on targeting circulating tumor cell clusters to cure cancer. What are circulating tumor cell clusters?

Tumor cell clusters are entities that leave the primary tumor

as an already formed cluster. They enter the circulation either via the bloodstream or lymphatic system. What distinguishes them from single cancer cells found in the circulation, is that single cancer cells do not typically contribute to the development of metastases. However, clusters were found to be a major culprit of cancer spreading. So, TumorGen started looking for method to analyze and target those entities.

Q: What are the most interesting breakthroughs/technologies developed by TumorGen?

As a rule of thumb, you can't target anything that you don't see. You need the right technology to actually capture them, then you can characterize them on a molecular, genetic, and functional level. We needed tools. So, the first step we took was to develop the tools used to capture the clusters. Other researchers found some ways to capture them, but rather inefficiently. We noticed a common up-regulation of an important cell surface marker, CD44, across many publication, and in fact I have studied this one extensively during my PhD. This biomarker is relevant in cell adhesion and cell migration; thus it is not surprising that it plays an important role in metastasis. Utilizing natural occurring interactions with this marker we found a way to isolate the clusters and then used secondary adhesion steps, such as antibodies, to actually bind them. As a foundation for our capture process we employed a microfluidics approach, the core of our technology. We collaborated with Dr. Sam Kassegne, a professor in the Mechanical Engineering department at SDSU, and his students helped us to prototype some of the device we designed. The next step we took is to optimize the ability to capture the clusters and turning



Researcher at TumorGen

hypothesis into functional devices. This is where the UCSD interns we had over the years came in very strong and helped us a lot to continue this journey.

Q: What do interns do at TumorGen?

Interns are often involved in tissue culture. There they learb to grow varies cell models, modeling artificial clusters, 3D cultures or spheroids, out of cell types that would mimic the molecular clusters in patients to optimize the system. I always tell my interns that an internship is a great opportunity to observe what people actually do in a field of their interest. It is not always relevant what you do yourself, but what you see other people in various stages of their career, do and if this interests you. On the other hand, I believe internships also enable personal development, and an opportunity to demonstrate drive, the ability of a person to tackle a problem with a team. I believe in the field of bioengineering a team is the central piece. We always place our interns into a team of at least two, so they can help and rely on each. Interns at TumorGen are tasked with real problems with no known answers. We show them the tools

we are using and teach them the existing knowledge relevant to the issue, and we provide the opportunity for them to be trained professionally such as techniques for tissue culture, microfluidics, microscopy, but in essence they have to find the solution of the problem they are facing. From the interns we have had, two went to highly coveted grad school placements, two from our last year's intern programs recently got entry-level positions in industry. We provided very strong support such as letters of reference and answered phone calls, which I am always very happy to do. I think our approach works. I think people appreciate being tasked with a problem instead of being used as a technician.

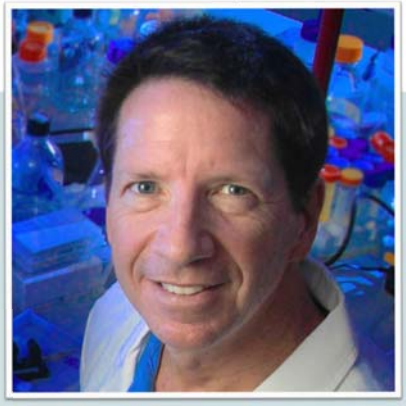
Q: How does TumorGen collaborates with other research institution on cancer studies?

We are at the fortunate position that TumorGen is strongly supported by the Sanford Burnham Prebys Medical Discovery Institute, one of the local nonprofit research institutes where I am also a research assistant professor. This not only provides us amazing infrastructure at the institute but of course by extension keeps us well connected to the academic research sites in San Diego. For example, we collaborate with the Moores Cancer Center at UCSD on cancer research. As a mentor of mine always says, we are building the plane while flying it.In practice you will often find that in order to make progress you have to develop and test a so-called MVP, minimum viable product. This means you build something which just fulfills what needs to be done and you keep testing and improving it along the way.

When we approach challenges in this manner, it often feels like the pace might be slower, but we feel it allows us to come up with a better product that provides a better solution.

Q: How is the academic environment different from industry?

In an academic setting if you have an idea, you basically have to generate some preliminary data and then you will apply for some funding, and you repeat this cycle every few years. It is focused on idea, hypothesis, and proof. There do not have to be any commercial justifications in your idea. Which I think is fantastic. Imagine you were a PhD candidate ten years ago and you studied algae, looking at some plankton in the ocean and its life cycles, which did not really look profitable or even related to fuel industry at the first glance. However, a few years later you would probably have a secure job opportunity in a dozen companies focusing on algae fuel technology. Looking at novel unusual things, you often don't know where it will lead and what comes out of it. I am a big believer in broad funding of basic research, even in areas we don't necessarily see an immediate benefit. To use a metaphor, when extracting cream from milk, in order to get more cream, you will have to produce more fresh milk.



TumorGen Founder
Dr. Jeff Allen

Q: Which events hosted by Bioengineering Student Orgs/ the Department are the most interesting/important to you as an industrial member?

BE day. What I love about BE day are the senior projects. I was able to attend as a judge a couple times (I hope I didn't judge too harshly). Because I am able to see how the students executed and presented their projects and its actually more interesting if they worked on something that I don't know much about. I look forward to learn if they are able to teach me something and convey their ideas to me. Individually and when interacting as a team. When I see the respective contributions I always ask them how they divided up the teamwork and how did that work out. I want to hear how they co-operated and benefited from each other. The UCSD Bioengineering Department has been able to invite some amazing keynote speakers as well. BE day also provided me with network opportunities and I was able to build connections with other judges and attendees from the local biotech area.

Q: What do you and TumorGen seek in those events?

Apart from the quality of student population in UCSD as seen in the senior projects, seeing how well those events are organized, I was truly impressed. I think those events speak volumes of how engaged students are in the year, and it is another reflection on the student population itself. Every student should be aware of that, especially those who are reluctant in lending a hand in organizing these events. I attended the career fair before "the end of the world", back in February 2019, which I enjoyed very much.

I received a lot of resumes for the past summer's internship program, which as you can imagine, didn't happen, and if you are one of the students that reached out to me, my apologies. The careers fair is another good networking opportunity for me with other industrial members at the events and not just for the students.

Q: How can UCSD Bioengineering Department do better in those industrial related events? Do you have any suggesting as what we should try during this global pandemic?

I think the BE department at UCSD is on the right track and if the student population remains as engaged and active as it has been over the last few years, I have no concerns. The current pandemic has forced us all to rethink the ways how we engage with others, how we learn, and how we apply for new opportunities after receiving your degree. If I could impart some advice, I would encourage all students to reach out to each other and find ways to support each other. In particular it might be important to reach out to not only the first or second person you can think of, but the third and the one you almost forgot about. I am looking forward for future interactions with the BE department and very much enjoyed talking to you.

Student Spotlight

Maya Holay

Adventures in Nanomedicine

By Wei Ji Chen | Interview Writer

Introduction: Maya Holay attended Carnegie Mellon University, graduating with a bachelor's degree in Chemical and Biomedical engineering in 2017. She began her graduate studies in UC San Diego's Nanoengineering department and is currently a fourth year PhD candidate working in Dr. Liangfang Zhang's lab. Her current research aims to expand the biomimetic therapeutic toolbox by developing novel cell and extracellular membrane coated nanoparticles.

Q: What is your research focus? Why did you choose this research focus?

I believe Dr. Liangfang Zhang's work in cell membrane coated nanoparticles is an ideal platform to combine my skills in chemical and biomedical engineering. Chemical engineering follows a classic engineering school of thought, multi-step planning, solving problems in discrete phases, and real world applications. Biomedical engineering is simply the application of such principles to medical use. In nanomedicine, my work in cell membrane nanoparticle bridges what I was taught in chemical and biomedical engineering; it draws from the systematic approach of chemical engineering while requiring creativity and innovation to successfully translate my drug delivery research to address medical needs. My work is focused on exploring novel cell and extracellular membrane materials to expand the biomimetic toolbox for targeted drug delivery and mucosal vaccination applications.

Q: Can you elaborate more on cell membrane coated nanoparticles?

Because of the increasing threshold in what is considered safe and effective drug delivery, nanoparticle development offers a new standard in precision medicine by targeting sites in the body to minimize side effects or harm to patients. By cloaking nanoparticles with a cell membrane, nanoparticles are able to evade the immune system and stay in the body for an extended period of time to deliver the therapeutic payload. Due to the breadth of cell membranes available, the synthetic nanoparticle platform provides incredible versatility, i.e. by coating the nanoparticles with red blood cell membranes, nanoparticles gain immunomodulatory proteins while using the cell membranes from platelets will ensure an antibiotic load to reach the site of infection. Because of the endless combinations in cell membranes and nanoparticle payloads , the possibilities of nanoparticle functions are endless. Genetic modifications can even be made to a cell line in order for it to express particular or necessary receptors before the membranes are extracted and utilized.

Q: What are the challenges and advantages of nanomedicine compared to the standard pharmaceuticals?

The nanomedicine fabrication process is very different from the current drug development pipeline in the pharmaceutical industry, since we are working at the nanoscale. The characterization and formulation of nanoparticles require different procedures, protocols, and equipment.We often struggle with polydispersity, which means nanoparticles are not always the same size, which is a barrier to clinical translation of these platforms Due to the novelty of the field as a whole, there's still a need to establish methods to create consistency and replicability in nanoparticles. Another challenge is the lack of comprehensive understanding of how nanoparticles react once in the body, leaving us apprehensive to administer novel formulations to humans prior to more in-depth study.

Nanoparticles have a significant advantage over the small molecule based drugs in pharmaceutics because of their functionality. While drugs are quickly cleared by the body, nanoparticles are formulated to be delivered with greater precision with less side effects. A current clinical example is Doxil. Doxil is a nanoengineered chemotherapeutic drug composed of nanoscale liposomes capable of targeting tumor tissues via the EPR Effect (Enhanced Permeability and Retention) and penetrates deeper into tumor tissue compared to macromolecule drug delivery.

Q: Recently, Jennifer Doudna and Emmanuelle Charpentier have won the Nobel Prize in Chemistry due to their work in CRISPR. Do you believe CRISPR's recognition on the highest level affects the field of bioengineering and if so, how do you think it will?

Indeed it's exciting to see CRISPR being acknowledged on this level. The speed of CRISPR's validation goes to show that academia is accelerating in its research. There's already been thousands of papers on this technology and to have this much progress before the nobel committee's recognition is an achievement on its own. Increasing open access to science means that we, as an academic community, can further technology before it brings the attention of something as monumental as the Nobel Prize. I believe one of CRISPR's greatest impacts in the bioengineering field is by providing researchers with tool building technology. There are many rare diseases that are without a competent model system and without a model, there's no accurate way to test out potential therapeutics before it is pushed to human trials. CRISPR provides a particular method to modify our systems to model rare genetic diseases through cell culture and animal models. It's powerful not just for therapeutic applications as a solution to cure genetically deprived diseases, but also its ability to develop complex systems to create more accurate and representative models of previously untouchable diseases.

Q: What does it mean for women involvement in STEM for these two distinguished scientists to be celebrated on such a stage?

This is the first time that a Nobel prize in STEM has been awarded solely to women - which is a bit mind blowing! It's 2020 and we feel like we've broken down a lot of gender barriers but the fact that this is the first time shows that we're still experiencing those gender barriers. It's absolutely exciting because it demonstrates that the Nobel Prize committee is committed to recognizing women who are working hard to discover new scientific concepts and

making these concepts accessible to the public. It's a big win for gender equality in STEM and demonstrates that we can be recognized just like men can.

Q: Who is your faculty advisor? How does he/she help your research?

Being a well-established tenured professor with connections to local nanomedicine companies, Dr. Liangfang Zhang has offered me many exciting opportunities to engage with industry and various collaborators. He has extensive experience in writing grant proposals, securing funding for the lab, and that has led me to working on cutting-edge projects with a rich pool of resources. Because of our industrial collaborations, I'm invigorated and inspired when I see the translation between academia papers to the industrial pipeline in pre-clinical trials, clinical trials, and ultimately a product that makes a real world impact . Along with Dr. Zhang's personal expertise, the lab houses many individuals with different experiences and backgrounds so if I have a question, there's usually someone with the answer. Whether it is about a specific assay or a new technique, there's always someone who can help me with my inquiry.

Q: What is the work-life balance of a PhD student? What do you do in your free time?

For me, the work-life balance happens when I have scheduled time to invest in my other interests. I've swam since I was a kid so being in San Diego gives me a chance to indulge in that venture by swimming with the Masters swim team here at UCSD. I also volunteer with the San Diego House Rabbit Society. Both these extracurriculars have scheduled practices/shifts, so it necessitates me to plan my schedule ahead of time and make time to do things I enjoy. Unlike a 9-5 job, graduate students are not expected to be in nor out at a certain time, so many feel they have to constantly work and this can create a stressful cycle of work, eat, sleep, and repeat. I combat this by treating my research like a job - and trying to limit my work hours to time I've already set aside . While others may think this is too little time, this limit actually forces me to be more efficient in planning out experiments, eliminating wasted time at the bench, and setting up internal deadlines for minor tasks improved my ability to be in a constant flow of work. Moving between classes, research, and teaching became much more of a smooth transition in my daily schedule instead of a painful juggling act of sleepless nights and headaches.

Q: If you could give one piece of advice to undergraduate students who are pursuing research, what would it be?

Set boundaries and set expectations. Once you've found a lab, be sure to establish clearly what you wish to gain from the experience, whether that be familiarizing yourself with the research field, learning techniques, or gaining publications. It's completely fine to change your initial expectations once you're more experienced but at least having an idea of potential expectations you have for yourself is important so your expectations align with your mentor's expectations of you. Setting boundaries, such as desired work hours or days ensures you can work at your best pace and limit burnout. Never be afraid to set boundaries, it demonstrates maturity and an unspoken understanding that you are committed to what you promise.

Hope Leng

Philosophy, STEM, and the Genentech Outstanding Student Award

By Maria Sckaff | Deputy Editor-in-Chief

"I started off as a Philosophy major before transferring to UCSD. I have a really strong inclination for the humanities, and I still love to read and dance whenever I have time. I am planning to graduate as a dance minor as well. I think that humanities and STEM go hand in hand, and I love bringing creativity from the humanities to experimental design."

Q: What are you most passionate about?

I am passionate about finding solutions. Instead of temporary treatments, I want to find long-lasting solutions for unmet needs through addressing root causes. Animal studies and 2D monolayer cell culture, currently used in preclinical and clinical studies, have poor prediction of human health. I hope to reduce the costs and failure rates of drug discovery through developing more predictive stem cell-based models, such as organoids and organs-on-chips. Many injustices and imbalances in society could be mitigated through proper education, which is why I have been actively involved in educational outreach both in community college and at UCSD. As a response to climate change, I began composting, eating more plant-based, and reducing my use of disposable plastics. If a problem comes to my attention, I follow my curiosity to see how I can make some sort of meaningful change. Although I cannot personally tackle every single issue, I try to take personal actions that could make an impact for a healthier planet.

Q: What is your field of interest in academics/research? How does that relate to the research you currently do?

I am interested in advancing organ engineering and organs-on-chips technology for my graduate research. After transferring to UCSD, I joined the Kwon Lab and began working with a graduate student Julia Kudryashev on an activity-based nanosensor that responds to hyperactive biological activity in the brain after traumatic brain injury (TBI). My senior design project--to make a device that can be used as a point-of-care diagnostic for TBI in humans--is an extension of that research. I am working with a team of 3 other bioengineering students--Maria Sckaff, Nabaan A. Mir, and Max Pendleton--to build a computational model that will streamline the optimization of such a device, hopefully to decrease costs by narrowing down the range of parameters that make the device more sensitive for detecting biomarkers. Throughout my undergraduate research experience, a common theme emerged: experiments are often limited by the models used. Although the activity-based nanosensor was validated in mouse models, it is still a long way from clinical trials due to the inherent species differences in mice versus humans. Similarly, the computational model we are building is limited by simplifying mathematical assumptions. The issue is that brain tissue is largely inaccessible, limiting our fundamental understanding of

neural mechanisms and thus our ability to develop effective theranostics for neural diseases. Organoids and organs-on-chips are a promising method for addressing those limitations by providing a physiologically relevant 3D platform derived from stem cells.

Q: What does your research experience at UCSD and in the industry mean to you?

Both my research experience at UCSD and in industry have helped me develop the intuition to solve real-world problems. Critical thinking--thinking like both a scientist and an engineer--has been an invaluable part of my training at UCSD and industry. Working in almost every part of the drug discovery pipeline, I have found that every step is very closely interconnected to one another; I was able to connect the dots between basic, translational, and preclinical research. Communication has been a key skill that I have focused on developing to improve translation of basic research to preclinical settings. Through working with diverse teams in academia, hospitals, and industry, I am confident that we can address any scientific problem to address unmet needs in our society.

Q: How did winning the Genentech Outstanding Student Award inspire you?

I was one of those applicants that was unsure about applying due to having limited qualifications. I transferred to UCSD in Fall 2018, and started working in the Kwon Lab in January 2019. When I applied for the 2019 Genentech Outstanding Student Award (OSA) in October, I had less than 6 months of full-time research experience. However, during the interview, I showed the interviewers that I was ready and eager to learn whatever I needed to make significant contributions during the summer internship. As a Genentech intern, I was exposed to the phenomenal capabilities of the biopharmaceutical industry, as well as the rate-limiting steps in drug discovery. Now, having a more complete picture of drug discovery gives me more motivation to bring life-saving theranostics to patients faster. I hope that my winning the OSA can inspire other students to take advantage of the breadth of research opportunities that UCSD presents. I am also happy to announce that this year's OSA winner, Delina Kambo, is a fellow transfer student!

Q: What did you get to work on as the Genentech Outstanding Student?

As the Genentech OSA recipient, I developed a web-based application called the "Study Tracker Tool (STT)." The STT facilitates cross-group communication and semi-automates data management and analysis for stability and toxicity studies that can last 6-12 months. I had to learn JavaScript in 3 weeks, because I was originally going to conduct cell-based assays in a different sub-department at Genentech. Due to the pandemic, my internship was completely virtual, and I collaborated with a software engineer in the U.S. Pharmaceutical Development Department to design and create a user-friendly application that could be integrated with electronic lab notebooks and also shared with the Pharmaceutical Development department in Europe. The project required many iterations based on user feedback and was the first time that I combined creative design with practical applications.

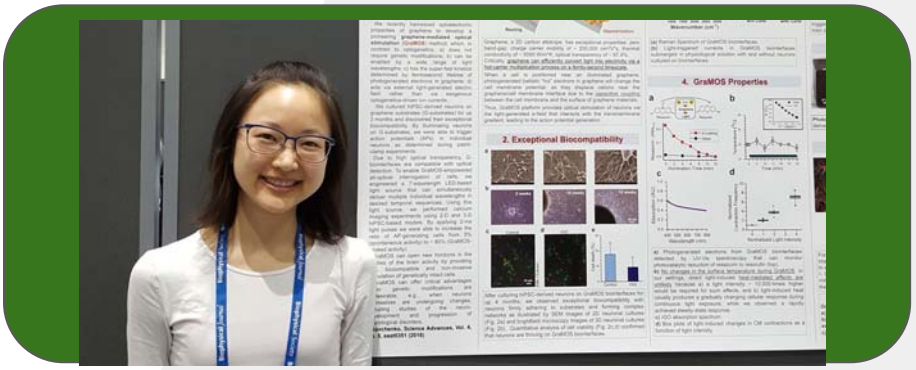
Q: How do you pick which internship opportunities fit you best?

Internships are an opportunity to learn new skills and explore different fields of research, so I like to apply for a really wide range of internships. Since I work in an academic lab during the school year, I wanted to experience working in industry, and I was lucky to experience two sides of industry--a small start-up and a large pharmaceutical company--during my first two summers at UCSD.

Q: How do you balance your academics with your extracurriculars/research?

Probably the greatest takeaway from college is the ability to connect my academics with my extracurriculars and research. Participating in extracurriculars and research is an extension of what I learn during lecture, so all my activities support one another and are all conducive to my development as a scientist and an engineer. I would not be able to design reproducible experiments without taking chemistry, physics, biology, and math. Further, extracurriculars that are not directly related to research, such as dance, can provide the mental breaks I need to approach my academics with greater clarity. Mental health is extremely important, and conducting research on the brain has only made me a stronger proponent for mental health!

Q: What is the biggest challenge you have faced during the lockdown?



One of the biggest challenges I faced during lockdown was focusing outward. Although we were physically self-isolating, I learned to connect with others through virtual platforms and maintain some perspective on the takeaways from a global pandemic. Instead of waiting for others to solve the problem, I began educating myself on best practices to reduce viral transmission. I followed scientific advances in characterizing the virus so that I could relay the information to friends and family. I also tried to clear up some of the misinformation around the origins of the virus, especially since some accusations were directed at the Chinese community. Most importantly, I became poignantly aware of how deeply imbedded racial injustice is in our society, and the actions I need to take to promote equity.

Q: How do you hope to contribute to your field or the world through your life?

One of my biggest goals in pursuing organ engineering is to reduce reliance on animal-based assays. With more predictive, cell-based models for drug screening, we can reduce the cost of drug discovery and deliver more effective drugs to the patient population. As academic researchers, we need to work closely with industry to improve translation of improved drug screening methods for clinical applications. By using cells taken from the patient, we are very close to making personalized medicine a reality. As a professor in the future, I want to inspire my students to continue seeking solutions rather than just treatments.

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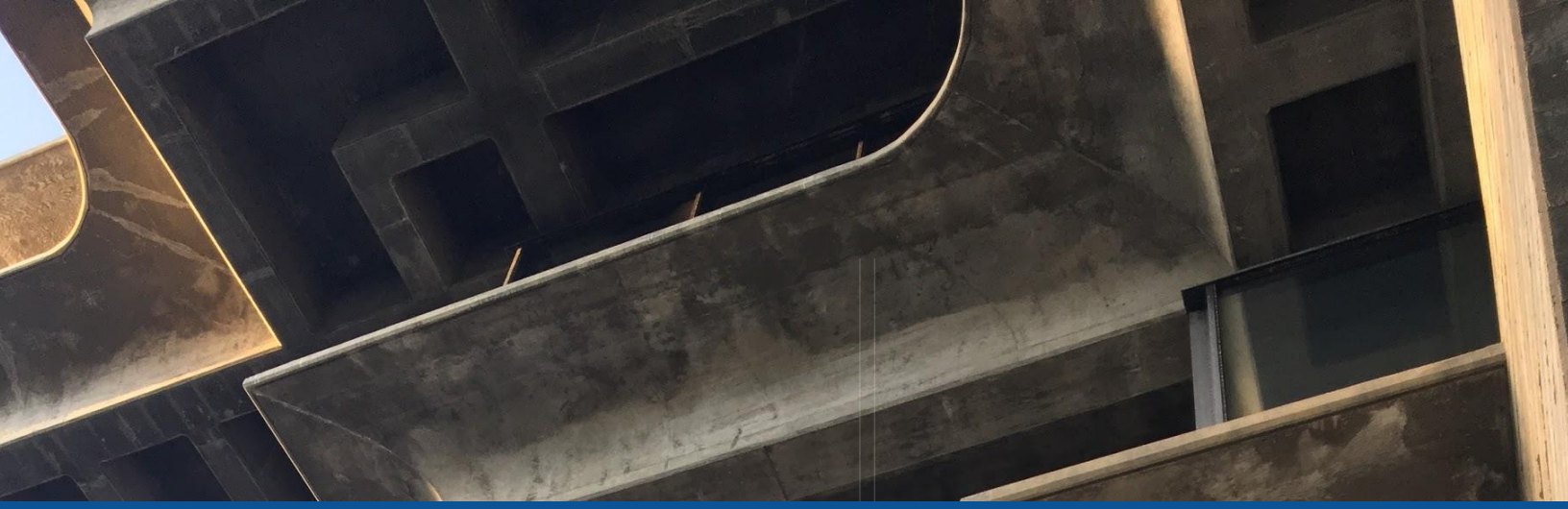

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