



2021-2022 Student Newsletter

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About CBB

Computational Biology and Bioinformatics (CBB) is an interdepartmental program partnered with many departments across Yale's Graduate School of Arts and Sciences and Medical School. The CBB program itself is involved in a wide range of initiatives, including but not limited to: a Biomedical Informatics Research Training Grant from the National Library of Medicine, the Yale Center for Genome Analysis, the Yale Systems Biology Institute, the Yale Center for Medical Informatics the ENCODE & PsychENCODE projects, the Department of Pathology Informatics Group, the Institute for Biological, Physical, and Engineering Sciences, the Program in Physics, Engineering, and Biology, and Yale's Cancer Biology Training Program.

Students in the program complete laboratory rotations while taking classes in their first year. In their second year, students concurrently complete their course requirements while conducting research. In their third year, students qualify and advance to candidacy. From there, candidates diligently conduct their research until their defense and submission of their dissertation. More information about the program is available on the CBB website: <u>https://cbb.yale.edu/</u>.



About this Publication

In this inaugural year of publication, CBB neither solicited nor commissioned the present: it was initiated by current students on a volunteer basis with the hopes of connecting the past, present, and future CBB community together by establishing a medium through which CBB can promote and celebrate itself.

This publication was drafted by current CBB student, J Nick Fisk, a 5th year in the lab of Jeffrey Townsend. Fisk, together with fellow students Raghav Sehgal and Vimig Socrates, brainstormed the idea for this publication as a way of following up with recent graduates of the program, celebrating recent successes of students, and making public some of the personalities present in our community. Sehgal and Fisk solicited recent achievements from the current students. Only students who voluntarily submitted their achievements and consented to their publication are featured, but the successes of other students are no less laudable.

Fisk contacted recent graduates of the program. Again, only graduates who responded and consented to the dissemination of their information are featured, but other graduates not featured are still celebrated by the community.

Socrates interviewed and attended the lab meeting of Dr. Serena Tucci for her feature. Fisk conducted the interviews for Dr. Steven Kleinstein, Wes Lewis, and Kriti Agrawal. The interviewees were all given a chance to ensure the textual of their interviews accurately reflected their views.



Student Achievements



Yale CBB

Maryam Zekavat

Zhao/Natarajan Labs, 3rd Year MD/Ph.D

Grants:

Leducq Early Career Investigator Award

Awards:

Massachusetts General Hospital Scientific Advisory Committee - Poster of Distinction Award



Recent Publications:

Zekavat, S.M., Lin, SH., Bick, A.G. et al. Hematopoietic mosaic chromosomal alterations increase the risk for diverse types of infection. *Nat Med* (2021). https://doi.org/10.1038/s41591-021-01371-0

Other:

Patent application (serial no. 63/079,74) on prediction of infections from mosaic chromosomal alterations



Guannan Gong

Krumholz lab, recently graduated

Awards:

2020 Startup Yale Rothberg CatalyzerAward, CT Innovations BioPipeline Award,2021 Tsai CITY Summer Fellowship

Male CBB

J Nick Fisk

Townsend Lab, 5th Year

Grants:

NIH Ruth L. Kirschstein National Research Service Award NCI F31

Awards:

3rd Place New York City Life Sciences Case Consulting Competition

Recent Publications



Fisk JN, Mahal AR, et al. Premetastatic shifts of endogenous and exogenous mutational processes support consolidative therapy in EGFR-driven lung adenocarcinoma. *Cancer Lett*. (Jan 2022) doi: 10.1016/j.canlet.2021.11.011.

Ho M, Thompson B, Fisk, JN. et al. Update of the keratin gene family: evolution, tissue-specific expression patterns, and relevance to clinical disorders. *Hum Genomics* (2022). https://doi.org/10.1186/s40246-021-00374-9 Fisk, J Nick. "Navigating Evidence and Knowledge Equity" *Exploring How We Teach* Edited by Samantha Clem. Utah State University Press. May 2022 (in-press)



Yaro Markov

M. Levine Lab, 3rd Year **Awards:**

CBIT Healthcare Hackathon — Audience Choice Award (together with Vimig Socrates, fellow CBB Student) Wes Lewis *Kluger Lab, 3rd Year*

Internships: Protein Evolution Inc. (PEI)

Other Distinctions: Blavatnik Associate





Sarah N Dudgeon Schulz Lab, 2nd Year

Internships: FDA Center for Devices and Radiologic Health

Recent Publications:

Durant TJS, Dudgeon SN, McPadden J, et al. Applications of Digital Microscopy and Densely Connected Convolutional Neural Networks for Automated Quantification of Babesia-Infected Erythrocytes. *Clin Chem*. 2021 doi:10.1093/clinchem/hvab237

Dudgeon SN, Wen S, Hanna MG, et al. A Pathologist-Annotated Dataset for Validating Artificial Intelligence: A Project Description and Pilot Study. *J Pathol Inform*. 2021 doi:10.4103/jpi.jpi_83_20

Joseph S, Varadaraj V, Dave SR, et al. Investigation of the Accuracy of a Low-Cost, Portable Autorefractor to Provide Well-Tolerated Eyeglass Prescriptions: A Randomized Crossover Trial. *Ophthalmology*. 2021 doi:10.1016/j.ophtha.2021.05.030



Raghav Sehgal *M. Levine lab, 2nd Year*

Internships:

Yale University Office of Cooperative Research Fellow; Yale Accelerator for Innovation Development Fellowship

Grants:

Impetus Aging Grant

Other Distinctions:

Semi Finalist Yale Life Sciences PitchFest; Yale CBTP





Egbert Castro Krishnaswamy Lab, 4th Year

Publications:

Learning Meaningful Representations of Life Conference Poster Acceptance

Other Distinctions:

Acceptance into the Nucleate Accelerator Program to work on a startup called AscentBio.



Kyra Thrush

M. Levine Lab, 4th Year

Grants:

Ruth L. Kirschstein National Research Service Award Individual Predoctoral Fellowship (NIH F31)

Recent Publications:

Higgins-Chen AT, Thrush KL, Levine ME. Aging biomarkers and the brain. *Semin Cell Dev Biol*. 2021; doi:10.1016/j.semcdb.2021.01.003





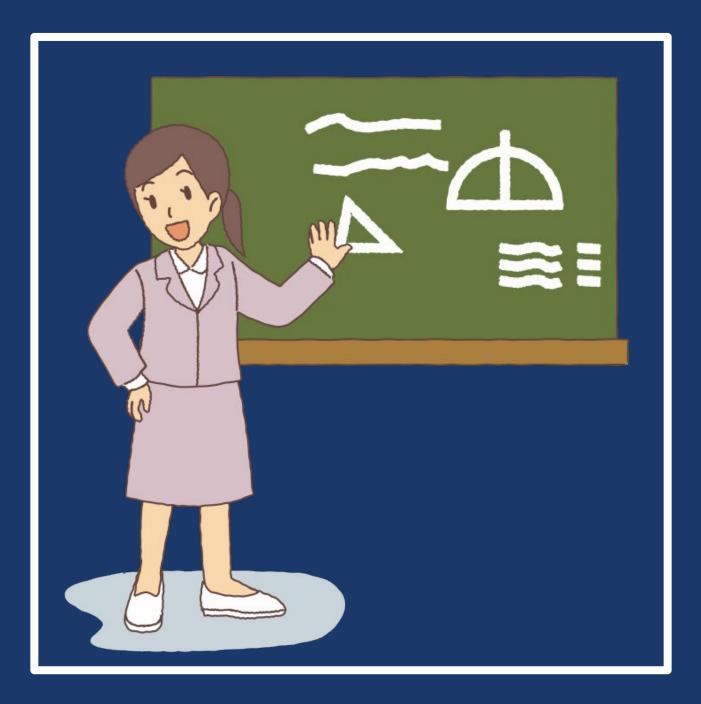
Biqing Zhu

Zhao Lab, 3rd year

Internships: Clinical and Biostatistics Intern at Boehringer Ingelheim



Faculty Features



Yale CBB

Dr. Serena Tucci

Research

Dr. Tucci's investigates fundamental questions in human evolution and population history using DNA from both present-day and ancient humans.She combines expertise from anthropology, population genetics, and computational biology to reconstruct past demographic events and disentangle the genetics of human adaptation. By synthesizing lab, field, and computational approaches, her work sheds light on mechanisms of evolutionary change, and on the genetic legacy that extinct humans - such as Neandertals and the enigmatic Denisovans - left in the genomes of human populations in Island Southeast Asia and Oceania.

Before Yale:

Previously, she conducted postdoctoral research at the Department of Genome Sciences at the University of Washington and the Lewis-Sigler Institute for Integrative Genomics at Princeton University. She was supported by the Lewis and Clark Fund for Exploration and Field Research from the American Philosophical Society. Tucci received her Ph.D. in Evolutionary and Environmental Biology from the University of Ferrara in Italy

Website:

https://campuspress.yale.edu/stucci/

Yale CBB



Teaching:

At Yale, Dr. Tucci has mainly instructed hands-on, experiential learning courses in Methods and Research in Molecular Anthropology. She was also the organizer of the first Yale workshop on ancient DNA data analysis

Fun Facts:

Dr. Tucci loves expresso, samba, and grunge music. She is a proud Italian immigrant to the United States and has a large pet cat named Alice!

Dr. Tucci is currently recruiting graduate students and postdocs to work on large scale genomic projects that are highly collaborative. Interested parties should contact Dr. Tucci at serena.tucci@yale.edu

Dr. Steven Kleinstein

Background

Dr. Steven Kleinstein received his B.A.S. in Computer Science from the University of Pennsylvania and his Ph.D. in Computer Science from Princeton. He is presently a Professor of Pathology with a secondary appointment in Immunobiology. He is also a member of the Interdepartmental program in Computational Biology and Bioinformatics (CBB) and has recently taken on the role of co-Director of Graduate Studies for CBB. His research focuses on multimodal approaches to probing immune signatures and profiling B cell repertoires. His lab contributes their computational expertise to many collaborations at Yale and beyond.

What is your favorite part about New Haven?

Over the past 15-plus years, I've really grown to love New Haven. it's not too large, so you often meet people you know just walking down the street, but it is also big enough that there is always something interesting going on. We like to go to the theater — at least we did before the pandemic – and there are multiple good groups around Yale including Long Wharf, Yale Rep and the Yale Cabaret. And there are also many excellent restaurants. The community here is great too. Plus, it's just a short drive to get to beaches or forests. It's got a lot to offer.



What made you decide to work at Yale?

The first reason was location. My wife and I are very family oriented, and we knew we wanted our kids to grow up near their grandparents and other family who are mainly in the New York City area. So, when we were job hunting, we drew a radius around NYC and focused our search there, which still provided a large number of possibilities. After location, it was the science. I do computational immunology research and Yale is very strong in both the computation and immunology sides with plenty of strong collaborations.



What made you decide to work at Yale? (cont.)

I also knew Yale had a great collaborative environment since I had already started working very closely with one of the faculty here when I was still a graduate student.

What scientific innovation or advancement on the horizon and in your field are you most excited about?

Similar to a lot of other research areas, computational immunology is being transformed by the advent of single cell multi-omics technology. It is driving the need for new computational methods and expanding the scientific questions we are able to ask. It is also bringing subfields together. My lab used to be somewhat split, where some people focused specifically on methods for analyzing B cell receptor sequencing data, and others were focused on different types of high-throughput immune profiling data transcriptional states, cytokine profiles, proteomics, metabolomics, etc. Now, with platforms like 10x, we are profiling multiple modalities from the same individual cells, so everything is integrated. In particular, the ability to pair information about the B cell receptor with the transcriptional state of that cell has been very powerful in understanding immune responses to vaccination and infection.

What are some of the strengths or unique features of CBB?

First of all, I think the faculty and students in general are incredibly strong.

Yale CBB

The research that is being done—the science—is top notch. One of the unique aspects of our program is that it is interdepartmental. It means there is a diversity of faculty involvement and a variety of training that people are getting. Also, the close connection between the medical and clinical research with the more data science side is a real strength. Here at Yale, having the medical school in such close proximity to the rest of the campus is conducive for generating those collaborations.

"The research that is being done—the science—is top notch"

You've recently taken on a bigger leadership role in the program as DGS. What are some priorities or initiatives you want to focus on in your tenure?

My first priority has to be to make sure we continue to provide the best possible training to all of our students. We want to put everyone in the position that they are able to get a job doing what they want when they leave Yale. Among other impacts, the pandemic has really created some challenges in terms of community and collaboration. So, remedying that is a priority. Being an interdepartmental program has a lot of strengths, but one challenge is that we don't have a single, physical home or building.

What are some priorities or initiatives you want to focus on in your tenure? (cont.)

Our faculty and students are spread out across many locations—different labs, departments, and so forth. So maintaining connection and building a vibrant community takes continuous effort and is even harder with the pandemic. At the same time, it has created some opportunities, in the sense that people are a lot more open to virtual meetings and using technology. Still, I am a big believer in the importance of in-person activities, so I hope that we can, as it becomes safe, facilitate more in-person events like seminars and social activities.

You can't live here for long before you are expected to have a New Haven Pizza hot-take. What's yours?

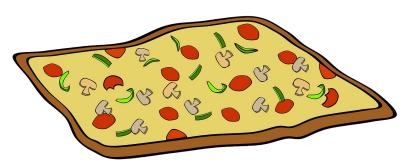
I like New Haven Pizza, but I grew up in New York City, so... actually, I won't say anything to compare the two! As for New Haven, I'm partial to Modern, though BAR is pretty good too. Generally, I am just a big pizza fan. I like it all.

How would you describe your mentorship style? Is it different from your advisor's?

As a Ph.D. student I was given a huge amount of independence. My advisor was in parallel computing, and did not really know much about immunology and the specific research I was doing. Even so, he was always able to ask really good, probing questions. Still, I had to be very independent and find my own collaborators. I thought it was good for my development, so I try to give my students as much freedom as they want to pursue their own collaborations and interests. At the same time, I want to pass along the things that I have learned. I try to meet with each member of my lab every week. I don't want to micromanage the individual steps, but rather try to offer guidance on the bigger picture-the broad trajectory of their work. Overall, I would say that I try to provide a bit more structure than I had, but still a lot of freedom. That said, I also try to adapt my style to the needs of individual students.

Any advice on how to approach an advisor about mentorship styles?

I think having an explicit conversation with your advisor, preferably before joining a lab, is the best way to go about it. Talking to current members of the lab is also effective.





Yale has a lot to offer outside of research and classes. Do you have any recommendations for things to do outside of CBB?

Go to talks. CBB is an interdisciplinary field so exposing yourself to the work going on in applied math, data science, statistics, computer science as well as the different areas of biology is critical. You have to be careful, though... Yale is such an active place that you could easily spend every hour of every day in seminars and that is a bit much! But I think it's important, even if the talk isn't precisely related to your work because there are a lot of advancements to be made by making connections across different fields.

What do you do in your free time? Any hobbies?

Hiking, walking and just generally getting out into nature. I love swimming in the warmer weather, and we also go skiing as a family every year. I grew up doing a lot of camping, so this is also a big part of our summers. If you don't yet know about it, the Yale Outdoor Education Center is a hidden gem.



Besides the program, what else about Yale should be appealing to students?

Faculty and students are very willing and eager to share ongoing research pre-publication and even in the not-yet-fully-formed idea stage. That is something I've really enjoyed, this collaborative problem-solving environment. Yale is big enough that there's probably a research lab that touches on any area you're interested in, but not so large that labs are overlapping which can create a hyper-competitive and secretive environment.



What should prospective students consider about where to do their Ph.D or whose lab to join?

To me, the most critical thing is to find an area of science and a problem that is inspiring to you. A Ph.D. isn't easy—you put in a lot of hours every day and it is many years of work. You really want to work on a problem that is inherently interesting to you. You want to wake up every morning excited about what you might learn that day. If the science isn't inspiring to you, well, you're not going to have enough fuel. So, find a place where there are faculty working on problems that sound exciting to you.

I have to ask, because I ask everyone I interview, do you think math is invented or discovered?

Oh, I'm going to stay out of that one.

*Oh, I'm not going to let you go until you give me *something*.*

Laughing Well, from my computational research perspective, I will say that it is invented, but used to make discoveries.

Is there anything else you'd like the potential audience of this interview to know?

There is a huge amount to learn, so be curious. I hope we can continue to foster an environment where people are curious and interested not only in their own research niche, but are also comfortable asking questions about other students' projects. This makes all the science better.

I've been at Yale since 2006. Overall, I've found it to be a very exciting and engaging intellectual environment. Yale is putting a lot of resources now into building up an even better data science community. It's a really exciting time to be working in computational biology and bioinformatics, and Yale is a wonderful place to carry out this work. Website: https://medicine.yale.edu/lab/kleinstein/

Twitter @skleinstein

Immcantation



immcantation.org

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This has been an edited transcript of an interview between J Nick Fisk and Dr. Steven Kleinstein. The conversation has been edited for brevity and clarity.



Alumni Features



Yale CBB

Scott Gigante

Dissertation Title:

Diffusion-based methods for exploration and visualization of high dimensional data

What was your favorite thing about Yale?



Free food? Um. Probably all the wonderful and fascinating people I met from all over the world.

Where do you work?

Immunai, a NY based startup using machine learning and single-cell genomics to improve our understanding of the immune system.

What is a piece of advice you have for incoming students?

Your time is your most valuable asset. Not just the time you spend working, either; ensure you set aside quality time to spend time with yourself, your friends, and your family.

What is something about you outside of work/school that you'd like to share?

As Yale Students and alumni, we bear immense privilege. Yale as an institution controls over \$34 billion in assets and wield a formidable reputation. Use it for good and do all in your power to convince others to do the same.



Donghoon Lee

Dissertation Title:

Leveraging Function Genomic Data: Modeling Transcriptional Dynamics and Interpreting Disease Genomes



What was your favorite thing about Yale?

I really liked all the people I worked with and the quaint college town vibe at Yale. You don't get that in NYC.

Where do you work?

I am an assistant professor at Mount Sinai working on psychiatric genomics.

What is a piece of advice you have for incoming students?

You've chosen the best program at Yale. Now try your best to finish the Ph.D as early as possible. There are lots of opportunities waiting in the field right now!

What is something about you outside of work/school that you'd like to share?

I started investing after college and mostly hold long positions. I rarely sell any positions and I just buy dips and hold. It has been a bumpy ride but it has been fun to collect stocks of my favorite companies whenever I can.

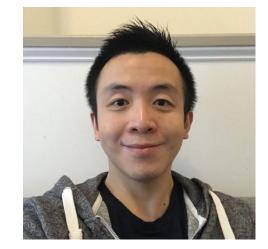
Male CBB

Julian Zhou

Dissertation Title:

B Cell Clonal Lineage and Somatic Hypermutation Profiling Analysis.

What was your favorite thing about Yale?



I liked that social science and the humanities have a big presence at Yale. It helped give me perspective and reminded me that there's more to one's intellectual pursuits than just research in natural science. I also really enjoyed (and miss dearly) Yale's unbeatable geographical location: day trips to NYC and Boston were the best!

Where do you work?

I worked in industry as a bioinformatician at AbCellera before returning to academic research. I'm now a staff scientist working remotely from Canada for Washington University in St. Louis

What is a piece of advice you have for incoming students?

Keep an open mind about research directions. Value collaborations they make science a lot more fun and you might be surprised how many doors collaborations could open.

What is something about you outside of work/school that you'd like to share?

I have a giant pup (an Irish wolfhound) and he's v.e.r.y. tall!



David Chang

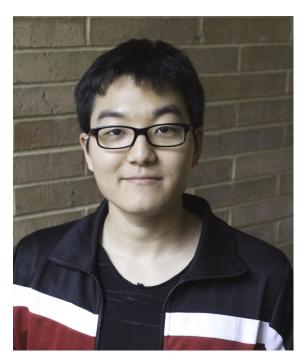
Dissertation Title:

Natural Language Processing and Graph Representation Learning for Clinical Data

What was your favorite thing about Yale?

There are a lot of smart and interesting people in every field. It doesn't hurt that it's also very close to New York City!

Where do you work?



I'm working at a mature startup called nference in Cambridge, doing biomedical and clinical natural language processing, which is exactly what I studied during my Ph.D. So it worked out perfectly for me.

What is a piece of advice you have for incoming students?

Put a lot of effort into planning your time at Yale and talking to as many people as you can.

What is something about you outside of work/school that you'd like to share?

I have the best dog. One extra tip for grad school is to try and get a dog if you can manage it somehow. It is life changing.



Kevin Lopez

Dissertation Title:

Machine Learning with Multimodal Data

What was your favorite thing about Yale?

Friends, and exploring campus.

Where do you work?

I am a faculty data scientist at the Yale Department of Emergency Medicine.



What is a piece of advice you have for incoming students?

Be ready to do a lot of work, a lot of stress, and a lot of pain. But it will be one of the most enjoyable, fulfilling, and exciting parts of your life. Oh! And be sure to ask for the rubric on any of your presentations.

What is something about you outside of work/school that you'd like to share?

I like anime, I read deep learning papers for fun, and I like video games!



Ryan Powles

Dissertation Title:

Picking Targets: Exploring Genomic Biomarkers of Breast Cancer Across Trials, Treatments and Tissues.

What was your favorite thing about Yale?



The many different backgrounds and perspectives that come together in a place like Yale.

Where do you work?

I'm a senior scientists in the informatics and predictive sciences department of Bristol-Myers Squibb and am located in Cambridge, MA.

What is a piece of advice you have for incoming students?

Find non-science hobbies to invest in during school! Your brain needs time away from work to rest and reflect in order to do the kind of creative problem solving you'll need for a dissertation project.

What is something about you outside of work/school that you'd like to share?

I put together my first custom PC build this year!



Dingjue Ji

Dissertation Title:

Integrative Analysis of Neuroimaging, Cognitive Functions and Genetics Data

What was your favorite thing about Yale?

Friendship with my fellas.

Where do you work?

Working for an AI pharma startup. I am planning to start my own business at some point, though.

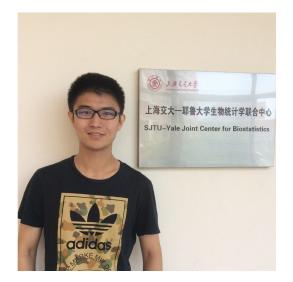
What is a piece of advice you have for incoming students?

Invest in the basics: Statistics, calculus, linear algebra *before* deep learning; do more, and think much more.

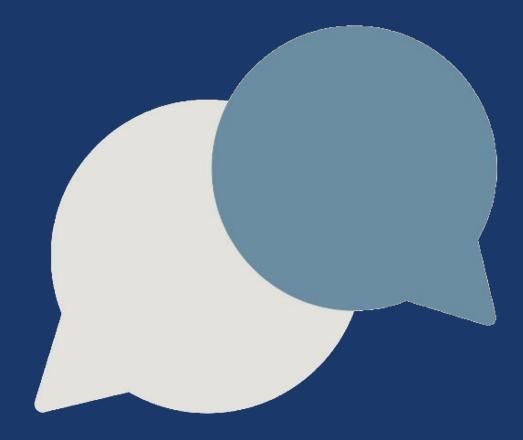
What is something about you outside of work/school that you'd like to share?

I hate corporate life though I don't hate the people. Now I realize happiness always comes first, especially when I spend most of my time with some people from work. I think I should and I could choose better.





Student Interviews



Yale CBB

Kriti Agrawal

Background

Kriti is a first-year graduate student in the CBB program at Yale still completing her lab rotations. She mostly grew up in Southern California. Kriti completed a BS/MS program in Bioinformatics at University of California San Diego (UCSD) where she also conducted research in her undergrad and graduate years.

The following is an abbreviated and edited transcript of a conversation between Kriti Agrawal and J Nick Fisk. The unedited audio is available at: <u>tinyurl.com/CBB-Agrawal</u>

UCSD is well-known and regarded for their computational biology programs. Did you consider attending UCSD for your Ph.D.? Why choose Yale?

I did apply there. I really liked it—I was comfortable there. Maybe too comfortable. I felt like I would be limiting myself to one location and hadn't ever lived in the Northeast before. I was interested in exploring myself by living far away. After all my interviews, I narrowed it down to two schools—one in California and then Yale. I chose to come here because I was ready for a big change—to take a bigger leap.

You majored in bioinformatics. I didn't even know it was a field entering undergrad. How did you discover the field and decide to enter it?



When I was applying to college, I knew I was interested in science, but hadn't really taken any computer science. My parents, who are researchers, recommended I look into bioinformatics and programming. So I spent my first year taking CS classes and some biology classes. I liked it and really kept going. I really wanted to experience how the coursework was applied in a research laboratory. So I joined a lab and from there got to work on many exciting projects.

Can you tell me a little more about your research experiences?

At UCSD, I was in the lab of Dr. Tariq Rana and focussed mostly on single-cell RNA sequencing projects.



Tell me about your research (cont)?

I worked on a variety of projects, though. My first project examined the T-cell populations between high and low viral load patients with HIV. I also worked on some CAR-T cell therapy, methylation analysis, and cancer treatments. But eventually I transitioned to my thesis project, which centered on word done in the lab with human cerebral organoids, which were meant to model the developing fetal brain. We exposed these organiods to different chemicals. I performed analysis for the organoids exposed to THC and Methamphetamine.

Outside of my work in the Rana lab, I also had an internship at the Center for Computational Biology and Bioinformatics at UCSD where I worked on merging ATAC-seq and RNA-seq in a meta-omics project. So I worked on a pretty wide variety of projects.

Speaking of a wide variety of projects, at Yale in the BBS and the CBB program, we do rotations our first year. Can you tell me a little bit about how your rotation experience has been?

My rotation experience so far has been great. The faculty really work on a wide variety of projects in a wide variety of ways. The Rana lab was mostly a wet-lab, so it has been interesting working with labs made up entirely of dry-lab scientists. They have been able to guide me more directly as to the specific skills and techniques of computational research.

The faculty here also have amazing projects in many different fields.

I've gotten to do one in immunology and realized I do have an interest in it, but that you can approach it in many ways. I've really enjoyed the unique ways the labs are set up.

So, would you say that you are glad that rotations are required for the program?

Yes, definitely! Coming in, I didn't know exactly what I wanted to focus on, but these rotations have been great at guiding me towards what I want to focus on for the next four or five years.

"Rotations have been great at guiding me towards what I want to focus on."

It is maybe a little early to vest too much into this, but do you have a sense of what you want to do after the program?

I always get asked: "Industry or Academia?" I am not 100% sure what I want to do. I think I want to do a postdoc, because after that I can still pivot to either industry or academia. I think there is a lot of value in that. It is a question I am definitely considering right now.

You've been at Yale a little while now. Is there anything about being here that surprised you or caught you off guard?

Things are done a little differently here than at UCSD. UCSD was a public institution, so the availability of resources is very different, in a good way.



Laughing Is that just a kind way of saying that Yale has a lot of money? Yeah! I guess I'm so shocked by

that, but I can really see how useful it is.

I still get that way now! It happens that it is my first year actually living *in* New Haven. I lived in East Haven and then Hamden before that. But now when I walk to lab or just walk around, I'm still amazed by how much Yale looks like Harry Potter!

Really! 100%! There's that one part of the library that looks like the hall from the movies!



You've been in New Haven for a bit now. What do you think about the city??

I definitely have found places I really like. I live about 30 minutes walking from the medical school, but I like to walk down. Walking down Prospect is one of my favorite things right now.

I have to ask the quintessential New Haven question. Best pizza?



I've only gone to Frank Pepe's so far—I haven't made my way to Sally's or Modern yet. It was a little too burned for my taste.

It is! That East Coast Brick Oven Pizza is always a little crispy on the bottom.

Yeah, it's definitely not something I'm used to. I don't have a solid opinion yet, but I'm looking forward to getting around to try them all out.

You just finished your first semester of classes. What do you think?

In my Masters, we only had to take like one class and I had a gap year before starting here, so getting back into the mindset of class—like homework and everything—was a bit of an adjustment. We were also on quarters and Yale is on semesters, which meant the semester felt a bit long to me. Otherwise, it was really nice. I like that we can take classes and I am really excited for some classes in the future. I have a lot on my list.



Now that you've been a part of the program for a while, what is a real strength or selling point of CBB?

CBB is very supportive in the sense that you have the flexibility to explore. The core classes are pretty flexible and you are encouraged to interact with a lot of different faculty to figure out exactly what you want to do, rather than being guided to a restricted path. I think it is a big strength of Yale and of the program.

No program is perfect. What is one challenge CBB faces and do you have any thoughts on how to face it?

The pandemic has introduced a lot of challenges. I really wish we had more events. We have our nearly weekly Wednesday research in progress talks and journal club, but it would be nice to have more events where the whole CBB community can just sit and discuss among each other. I really enjoyed our welcome barbeque and the student-faculty picnic. It was great to hear the perspectives of other students and get advice from them. I wish we had a little more of that.

What is on your mind as you consider different labs to join?

I would like a lab with good infrastructure where I have someone I can ask questions to easily, like a senior student or even the PI. I really want someone who can be a mentor—give me advice and direction—but isn't holding my hand. Moreover, I want my thesis to focus on a specific biological question, not just abstract method development.



What are some of your hobbies and have you been able to continue them here?

I like to do artistic things. I tend to develop a "focus of the month" if that makes sense. It varies. I used to do a lot of painting and things like that, but I didn't bring many of my supplies. Right now, I am knitting. For the most part, I've been able to do my hobbies here, but am still working on getting them set up and built into my routine. I also really like to go for walks, which was really lovely until about the end of November when it started getting cold.

It is understandable that you want to get situated in a lab before you think about it, but have you gotten involved with any student groups? Or planning on it?

I haven't. As you say, I'm trying to focus on which lab to join. But once that uncertainty is gone, I would like to get involved in some. I'm interested in some of the student outreach groups with New Haven youth and the Biotech Investment Group—I have a minor in business, after all!



I'm going to ask you a question I ask everyone I interview: Do you think math is invented or discovered?

Interesting. No one has asked me that question before. I think...I think that math is invented, because the basis of math is numbers and I feel numbers are arbitrarily created, so I am leaning towards invented. It is something that we can use effectively. And I do think there are discoveries to be made in math. I'd have to think about this a little more, because boiling it down to numbers is definitely not giving many of the many amazing mathematical theorems due credit. This is an interesting question.

I think it is especially interesting to ask scientists to see what they say about this. I took a philosophy of mathematics course here and now I can't get the question out of my head.

It is. I mean, just look at p-values in probability and statistics. I'm not saying statistics is in bad shape or anything, but the number—this threshold—is just a number that we've chosen. They have some backing and make some practical sense, but ultimately they were just chosen. I feel like a lot of mathematics is that way.

Is there anything else you want to add? Any tips or recommendations for this audience?

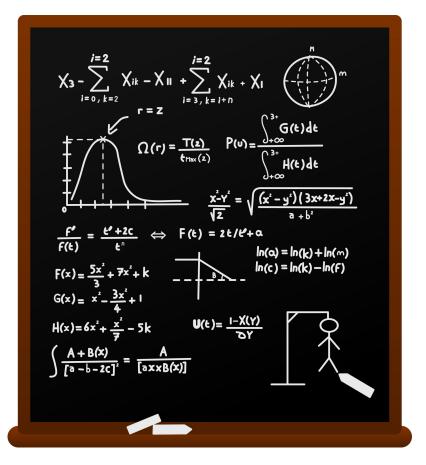
I would say to prospective students, the best way to learn about a faculty, their work, and their lab is just to set up a meeting with them. Actually, even more than that, I recommend reaching out to



the current and past students. When I got here, I got to hear their point of view and it was really informative for me. It's helped me make decisions for my rotations. The current students in CBB had a good sense of how a lab is run and how well it fit with my interests. Network and talk to everyone right away. Get going on that.

Yeah, I think a way of saying that might be that science isn't just the science we do or a dogma of discovery. It's a community.

Yes, exactly.



Wesley Lewis

Background

Wes is a third-year graduate student in the CBB program at Yale in Dr. Yuval Kluger's lab. Originally from the Buffalo, New York area, Wes attended the University of Rochester, where he graduated with a degree in Computational Biology in the spring 2019 and started at Yale that Fall. He is a Blavatnik Associate and a Trainee of Yale's Cancer Biology Training Program (CBTP).

The following is an abbreviated and edited transcript of a conversation between Wes Lewis and J Nick Fisk. The unedited audio is available at: <u>tinvurl.com/CBB-Lewis</u>

Did you always want to study Computational Biology?

No, I didn't. It arose from different and more niche interests. When I started undergrad, I felt like I had only really experienced engineering in high school in the Buffalo Engineering Awareness for Minorities Program, where I got to exprierence parts of the engineering programs at different colleges around me. I was, and still am, very interested in music, so I convinced myself I really wanted to study audio and music engineering. But when I started undergraduate coursework, I released audio engineering didn't seem focused on the aspects of music that I loved.



What'd you do next?

I drifted for a little bit, not knowing what to study. But during my general coursework as a freshman I was exposed to psychology which fostered an interest in brain and cognitive sciences—for neuroscience. But as I had that revelation, I realized I found myself in the position of not having taken any of the prerequisites for that track during my first year, so I had to do them my second. I felt behind, but also really discovered this consistent desire to be a researcher in some capacity, which led to my involvement in some neuroscience and pathology spaces doing computational work, though I didn't become a computational biology major until spring of junior year.



Interesting, so your path here was a little bit winding. In an alternate timeline, what might you be doing?

Once I started on those more medically oriented prerequisites, I really held myself to the high standards of the heavily pre-med community around me. I even worked in surgical pathology, so I did see a future as a pathologist or a psychiatrist. There was maybe even a world in which I returned to engineering.

You have mentioned that you're interested in music and have been for a long time. Can you tell me more about that? Was there ever a world in which you dropped out and pursued that instead?

I grew up being very interested in jazz music, listening to my dad's collection and having him burn CDs for me. As I got older, I found myself interested in different subsections, some of the more eclectic stuff. I think I admired my dad and his taste, but I also wanted to be my own person and forge my own way as I developed my own identity. So I ended up taking to jazz and fusion and funk. Towards the end of high school especially, I joined a band and used to play pretty heavily, at local coffee shops and the like. But given the financial insecurity and the creative inflexibility of the industry, I decided I wanted to explore—I was young, after all, and maybe I could find a way to blend my interests together.

Are you still involved in music now?

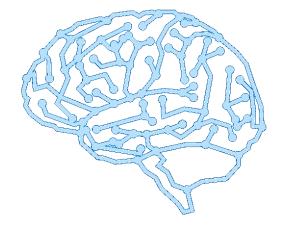
Yes! Part of my decision to come to Yale was influenced by the proximity to the NYC jazz scene and Yale's own resources for the arts. In my first year, before the pandemic started, I was part of the Yale Jazz Combos Program, which allowed me as a tenor sax player to be coached by a world renowned tenor sax player from Harlem, who'd generously come up here and coach and teach us in a hands-on and personal way. But it really surprised me at just how thoroughly I could really follow my passion for music while here pursuing a scientific Ph.D.

So you mentioned that you did this neurology and pathology research in undergrad. Is that what you do now?

No, its not. Though my research was already very computational, I actually forged my relationship to that research more through music. I worked in an fMRI lab where a major case study I worked on was a patient who had a peculiar neurological deficit and was a music teacher.

"It really surprised me at just how thoroughly I could really follow my passion for music while pursuing a scientific Ph.D."





Is that what you do now? (cont.)

The ephemera and narratives of the lab were very computational and other members of the labs included bioinformaticians and mathematicians. Because of this experience, it seemed more feasible to move in that direction. I've since found myself interested in statistical learning with genomic data, but also in data agnostic ways. I find myself interested in social media or epidemiology and public health datasets, for example. Right now feels like a frontier of information sciences.

Though now that I think about it, my advisor—Yuval Kluger—has appointments in both Applied Math and Pathology, so I guess I do still technically work in pathology. But it's very different, for sure: novel, interesting, and ever-expanding.

Is doing research as a grad student here different than you expected, then?

Yes. Coming into grad school, I had this expectation that I would enter a program and become immediately almost fully differentiated where I couldn't go back or contextualize new things. Instead, it feels like a radical broadening of contexts and of my interests actually. Where my skills and interest are not just relevant, but essential.

So you're pluripotent then?

Laughing Yeah. Absolutely. Still just a little stem cell.

Did you feel prepared or confident that you could become prepared when you got here?

I'm not sure. Imposter syndrome was a defining part of my undergrad, especially since I started my prerequisites there later than my peers. And since it was very pre-med heavy, my classes felt like they hammered fundamental concepts through memorization tasks. I came in feeling essentially inadequate in a lot of ways.

But here I realized that there were so many different things I could possibly do and possibly do well, but that I couldn't possibly be an expert in all of them. The ability to realize that and let go and accept that has been a humbling experience I didn't anticipate. It feels like I've matured and that feeling like you are behind has been very centering because it feels like a common experience shared by my peers.





You mentioned proximity to the NYC Jazz scene as a factor choosing Yale. What were some other factors?

Family was a factor too. I've had family in NYC for a while. And though he hadn't when I committed, my brother ended up moving to the city, too. But, really, it was more about my interview experience. Before I interviewed, I was invited out as part of Yale's Diversity Preview Day from the Office of Graduate Student Development and Diversity. They kind of showed us a day in the life of a Yale graduate student. They showed us Gryphon's and Friday Night Karaoke. But I was told that I was someone who should be applying and that I would be considered. At the time, I was especially lacking direction and was at the height of my imposter syndrome. So it was incredibly supportive and validating.

When I came again to interview, I was able to get a greater familiarity for all the things Yale and New Haven has to offer, like being near the Long Island Sound and the nearby natural spaces.

You're a little bit less than half-way through the program, more or less. Do you have any sense on what you want to do after you graduate?

That is a little bit like asking "what do I want to be when I grow up?" I've been slowly whittling away at the list of things I want to do. In the academy, we get to see the life of academics through our collaborators and advisors, but we don't necessarily get to see what else is out there. But there are plenty of options and opportunities out there. So as I was exploring these options myself, I became interested in other careers intimately revolving around science, but not academically hosted. So, I became a Blavatnik Associate, where I work with faculty-led groups that Yale funds to create start-ups based on their research and interests, which has exposed me to venture capital and how science intersects with IP.



I've also been involved at a startup around New Haven called Protein Evolution, which is part of an incubator founded by Jonathan Rothberg called 4Catalyzer. Recently, we've been examining questions of sustainability with Al—plastics accumulation in the environment, for instance. I never thought I could do this sort of thing, but it has been more straightforward than I expected to follow these exciting opportunities as I've encountered them. So, on the topic of sustainability would you say that in addition to your intellectual interests, you've found space at Yale to express more of your political, moral, and ethical interests?

Yeah, absolutely. I feel like an emblematic example is when I was working to make podcasts for Yale's Journal of Biology and Medicine. We were able to feature many faculty members at Yale that have incredible research talking about health equity and, racial impacts on health, for instance. Participating in things like this, I feel, has been feasible and encouraged as a graduate student.

You've been in New Haven for a few years now. I have to know your New Haven Pizza hot-take.

I really like Sally's, but the takeout experience at Modern might be superior. Actually, I've really gotten into Da Legna recently. It is a little bit of a newer contender. Their pie has a slightly thinner crust and it is marketed as a fun, upscale place. Plus, they have an in-house brewery!. You know, still being able to engage in this cultural discussion of New Haven pizza has been nice during the pandemic, because there are still some things that aren't back to normal.



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Any other thoughts or recommendations on food in New Haven?

The real highlight for me has been the food trucks and carts that are always present at the medical school and likewise by Science Hill. They have a good variety, are affordable, and give me a reason to get up and walk outside. I'll often run into my friends grabbing food there, too.



Are there any strengths of the CBB program you'd like to highlight?

There is this really robust community of numerous investigators at different levels. There are labs that have been around for decades and some that have only been around for a few months. There are always new people to work with. I mentioned before that I was worried I'd become hyper-differentiated in a way that I could change what I was doing, but I feel like the ability to follow my curiosity has been well facilitate by this collaborative environment. In an interdisciplinary program like ours, it might feel a little formless, but I've yet to encounter any weaknesses in the excitement and opportunities.

As you allude to, CBB certainly faces some challenges as a program. What do you think some of those challenges are and what can we do about them?

Yeah, so I think our program is still trying to figure out how to best formalize the support it gives. For instance, because the faculty we can work with span so many departments, we have been working to get some templates and guidelines of what is expected of advisors of CBB students. There are many people who have great experiences, while there are others who nonetheless have a good experience, but kind of have to start from the ground up because there are fewer templates. It is especially difficult with newer faculty.

But this is something that has been noticed and speaks to a challenge Yale and CBB are working to solve. Especially with the pandemic, new students and faculty haven't been exposed to as many of the cultural aspects of graduate school and academics, with a lot of remote work being done. So it has been a little bit more difficult to see the senior students' and your peers' progression and learn from that. Recently, the leadership in our program has taken renewed interest in meeting these challenges.

What is a technology or advancement on the horizon that has you excited?

Spatial transcriptomics, definitely. Though I've also become more interested as of late in protein design and high throughput screening using deep learning methods.

What advice would you give to a prospective student searching out labs?

I would say to make sure and reach out to previous students, if there are any, and get a sense of lab expectations and timelines that the mentor tends to expect. And, of course, finding a mentor who you think is aspirational but who can also manage and integrate the different ideas that you both, as two separate thinkers, will be working on together for a long time. I would also say to follow your excitement. There is always the aspect of safety to consider, but I tend to think there is nothing wrong with dreaming a little bit. The wonderment will help you get through the harder times.

Yale is a dream school for some. What advice to you have to people who are intimidated by the thought of applying?

The summer before my senior year, I had a mentor tell me I should apply because it was an option that I could have, if I wanted it. It was something that had never, in so many words, been said to me. I was still struggling with my esteem and struggled to trust them. So for me applying was learning to trust and to self-advocate and to ask for that trust myself. I was daunted by the financial difficulties of applying to many different schools, but was also genuinely worried about facing a lot of rejection. At a conference, I discovered that fee waivers exist for many graduate programs so that helped and that there are plenty of resources to help people struggling with the same issues I was.



Yeah, I think Cientifico Latino has collated a lot of those resources, no ?

Exactly, I think that is one of the best resources. It started small but has sort of been embraced all over now.

What else did you look for in a place to do your Ph.D?

For me, it really was trying to find a university that didn't just have one project or one faculty who I could see myself working with. And, as I mentioned, being close to family—a support system—was important to me too.

I'm going to end the interview with a question I always ask: Do you think math is invented or discovered?

I'm going to go with invented. I feel that by formalizing and making understandable tangible things on paper requires and is dependent on the person—the inventor, I guess—it feels like it is more correct to say that the person invented it than discovered it.

Is there anything else you want to add?

Oh, man, I feel like it's the end of the interview show *Hot Ones* where they plug what they're doing right now, but I don't really have anything like that to plug.

I can say that I hope this next class of people coming to Yale and going to grad school in general are able to have a similar experience in their first year that I had, where you are able to find community and closeness. There are very hard times in grad school. Finding and maintaining an enriching community takes work, but will help you thrive and find yourself.

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Referenced Resources

Blavatnik Associate Website: https://ocr.yale.edu/Blavatnik-Fellows Yale Cancer Biology Training Program: https://medicine.yale.edu/pathology/training/ cbtp/ Cientifico Latino: https://www.cientificolatino.com/ Kluger Lab: https://medicine.yale.edu/lab/kluger/ Yale Diversity Preview Day: https://gsas.yale.edu/diversity/prospective-s tudents Yale Jazz Combos Coaching Program: https://bands.yalecollege.yale.edu/fall-2020vale-jazz-initiative-jazz-combo-coaching-pro gram Yale Journal of Biology and Medicine https://medicine.yale.edu/yjbm/ **Protein Evolution**

https://www.pei.bio/



Community Photos



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Entering CBB class of 2021 meets their upperclassmen at the CBB Welcome Picnic

Lisa Sobel (left), CBB and YMCI Registrar, and Dr. Mark Gerstein, CBB co-DGS, enjoy the 2021 CBB welcome picnic







Entering CBB class of 2017 enjoys the Molecular, Cellular, and Developmental Biology retreat at Woods Hole, MA

happy hour on the patio





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