



Institute for
**Protein
Innovation**

2021

**Annual
Report**

From the interim executive director



As the world struggled to live in and through a seeming “forever pandemic,” 2021 was a year that demanded global resilience. The potency of delta followed by fast spread of omicron variants might have led to despair. At IPI, we fought back, digging deep into expertise and mission to find ways to work, rebuild and connect.

For us, 2021 was a time of renewal.

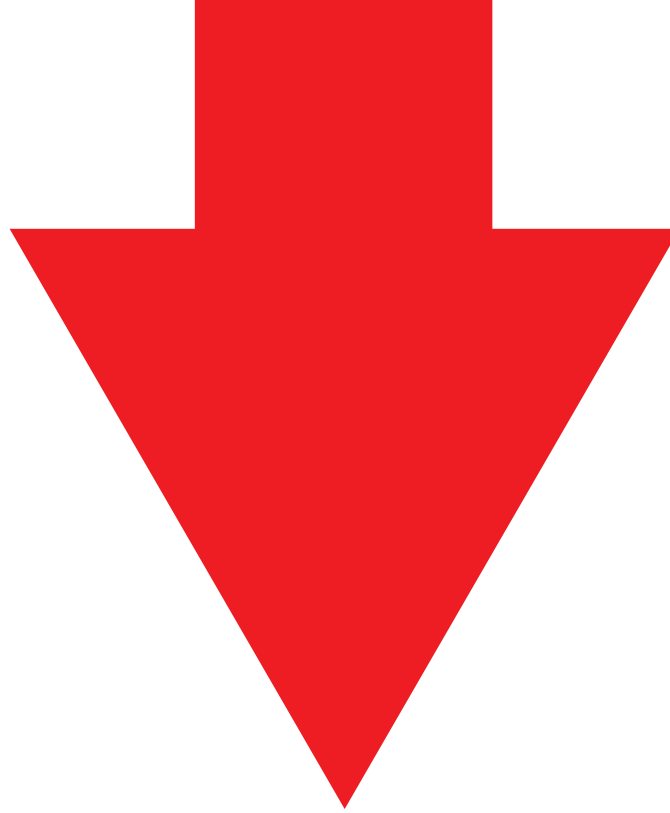
We hired record numbers of new staff from across the world for all parts of the organization: highly skilled scientists to renovate our Antibody Platform; writers to promote our scientific progress; administrators to support our rapid growth on all our teams.

We created a culture of diversity, knowledge-sharing and teamwork through retreats, celebrations of heritage and processes meant to bring people together. We learned to do our research in a way that keeps each other safe, while showing our dedication to the scientific community.

At the highest levels, our Board elected a new chair, Samantha Singer. With a background in consulting and executive operations, now CEO of her own startup biotech, Singer brings to IPI insightful leadership and strong operational skills that will be critical in steering us through our transition from an early to growth stage organization.

“We created a culture of diversity, knowledge-sharing and teamwork through retreats, celebrations of heritage and processes meant to bring people together.”

We redoubled our efforts to create and produce fit-for-purpose antibodies directed against extracellular and secreted protein targets, distributing them to collaborators for validation. Quality control was a theme. Data integration between the teams enabled better understanding of how to optimize the platform for efficiency. Antibody engineering is now emerging as a near-future strategy. Overall, the goal for 2022 is to optimize the technology and platform still further, adding in necessary application development and production processes to begin scaling for full distribution.



To focus its activities on this antibody effort, IPI spun out its Protein Design Laboratory, headed by Christopher Bahl. He launched a startup, called AI Proteins, that uses artificial intelligence and protein design to create synthetic proteins for therapeutic application.

Back in the lab, we embarked on new frontiers in antigen and antibody discovery. We’re intrepidly hunting down an elusive form of an opioid receptor in the hopes of inspiring painkillers without side effects. We’ve also launched another antibody discovery campaign focused on a tough-to-target family of cell signaling proteins.

We reaffirmed our commitment to promoting training and career development. We’re thrilled to send off two of our research associates to top graduate and medical schools to earn their doctorate and medical degrees.

As we look back upon such a historic year, we’re grateful for the many ways we have found to move forward as one team through volatility with creativity. One of the things I enjoyed most was listening to a recent episode of our newly launched training series, dubbed “IPI 101.” One of the research associates was teaching the group about the history of human embryonic kidney cells, throwing in a spontaneous quiz with cupcakes for the right answer.



As she singled out our new director of people and talent to try and answer her largely scientific question — whose incorrect response evoked a “maybe you’d better phone a friend” response—I laughed. We’re all laughing again. It’s time to feel lighter and for the future of protein science to be brighter. I am looking forward to the opportunities ahead.

Warmest Wishes,

Rob Meijers

Director of the Antibody Platform & Interim Executive Director

Five years on, IPI sits in an ‘exciting landscape’ for protein research

A Q&A with co-founder Timothy Springer



When Harvard University professor and eight-time entrepreneur Timothy A. Springer co-founded IPI in May 2017, the world was a very different place.

X-ray crystallography was still the go-to method to piece together protein structures. Gene-editing techniques were advancing, and researchers were seeing early success in correcting DNA and RNA point mutations. Attention to science’s reproducibility crisis was increasing, with particular focus on bettering antibody research.

Since then, revolutionary techniques have revealed never-before-seen molecular structures. New computational methods have opened once unimaginable pathways to structural and functional understanding. Display technologies have matured and antibody libraries have grown more and more vast, signifying great therapeutic potential.

These changes — plus a biotechnology boom and a global pandemic — have played out as IPI has built and rebuilt its synthetic Antibody Platform. Now, five years on, Springer reflects on IPI’s journey into a nonprofit making high-quality antibodies and ready to ride the current biotech wave.

IPI: YOU FOUNDED IPI BACK IN MAY 2017. NOW, NEARLY FIVE YEARS ON, HAS YOUR VISION FOR THE INSTITUTE EVOLVED? IF SO, HOW?

SPRINGER: The reason I started IPI was to go beyond the limitations of antibodies made in animals with a new type of antibody made in yeast. That vision hasn’t changed.

I really am excited that we can do this both in a high-throughput way and make really high-quality antibodies. I would say we’re not quite working at biotech speed yet, but I think we can do this.

IPI: WHAT CHALLENGES HAS IPI FACED ALONG THE ROAD? HOW HAS IT OVERCOME THEM?

SPRINGER: The challenge with IPI was that it really started de novo. If you look at other institutions, like the Dana-Farber Cancer Institute or the Broad Institute, they grew out of people’s laboratories. I didn’t grow IPI out of my laboratory — I started it from scratch. I knew how to start a company, so I thought we could start a brand new institution. And it’s still an experiment that is in the process of being realized.

IPI: IPI APPROACHES PROTEIN SCIENCE AND ANTIBODY PRODUCTION FROM BOTH AN ENTREPRENEURIAL AND AN ACADEMIC ANGLE. WHAT CAN IPI DO THAT A COMPANY OR ACADEMIC LAB CANNOT?

SPRINGER: IPI is a place where a scientist can discover. It can make its discoveries readily available to other people. It can really enhance what companies and academics can do in a way that a for-profit cannot because a for-profit has to maximize its value.

“IPI is a place where a scientist can discover.”

IPI: OVER THE PAST FEW YEARS, BIOTECH INVESTMENT BOOMED AND STARTUPS SKYROCKETED. THOUGH THE PACE HAS SLOWED IN RECENT MONTHS, THE MARKET IS STILL HOT, PARTICULARLY IN THE BOSTON AREA. HOW DO YOU SEE IPI FITTING INTO THIS NEW BIOSCIENCE SPACE?

SPRINGER: It is just much more competitive. A lot more people clamoring for attention and wanting to be heard. There are many other companies hiring good scientists. And, to be honest, there is a lot of good research being done in academia and a lot of good drugs being developed at companies.

It’s a very exciting landscape and IPI has much to contribute.

IPI: WHAT VALUE, SPECIFICALLY, CAN IPI ADD TO THE INDUSTRY?

SPRINGER: We’re working on proteins. Nucleic acids are much faster, and you get publications more quickly, but I think there is a realization of how important working with proteins is. There is much, much more need for what we can offer.

From bench to business

Samantha Singer brings a unique profile and perspective to the IPI board

By Caitlin Faulds

When a young scientist looks out at the world, they typically see a career in academia or industry. Rarely does the view include running operations at a high-growth nonprofit, holding leadership roles in a multitude of companies or chairing the board at a fledgling protein institute.

But Samantha Singer is rare.



Photo: Marissa Fiorucci, courtesy of Third Rock Ventures

She's followed an unconventional path and amassed skills and insights far more comprehensive than is typical in a science and tech-heavy world. In a space that is traditionally male, academic and competitive, Singer, chair of the Board at [IPI](#) and president and CEO of her own company, [Abata Therapeutics](#), has made it.

Looking back on her success, she cites the value in seeking advice, gathering a wealth of experience and focusing on impact. But the most important thing: "You should love what you're doing," she says.

THE ROAD LESS TRAVELED

Singer's first love was biology. She found that passion as a middle schooler in Kansas and carried it on to a graduate program at Rockefeller University in New York City.

Midway through the program, she hit a "hard truth" that lab work wasn't for her. She left with the institute's first master's degree — the "door prize for dropping out," she says, jokingly.

"The idea of using science to impact and alter people's lives still meant a lot to me," she says. "I just wasn't going to be doing the science itself."

Instead, she leaned into team building and business strategy, working as a management consultant and later completing an MBA at Harvard Business School. She loved bridging science and business to positively affect human health.

As a consultant, she was the perfect person to act as a "midwife at the birth" of the [Broad Institute](#), helping to draft the nonprofit's original business plan. She also forged a long-lasting consulting relationship with an early client, [Biogen](#), later taking an "in-house" position in its executive ranks in 2007.

There, she gained insight into the inner workings of a global company, before moving back to the Broad as chief operating officer, playing a pivotal role in the Broad's transformation from startup to thriving research center.

After successfully managing major growth, she looked for ways to more directly impact patients. The opportunity

"You should love what you're doing," she says.

came through a healthcare venture firm, [Third Rock Ventures](#). As an entrepreneur-in-residence, she nursed a contingent of young biotechs into existence before fostering her own, [Abata Therapeutics](#), to transform [regulatory T cells](#) (Tregs) into transformational medicines.

It was during a lunch-time conversation with Timothy A. Springer that Singer learned of IPI, the nonprofit protein institute he'd co-founded with the mission of accelerating protein research and improving human health.

Singer was intrigued. When he offered the chance for her to join the board, Singer sprung at the opportunity to help bring that vision to fruition.

"It was the mission. It was Tim," she says. "It was the passion and the opportunity again for me to learn and to bring something to the table."

BUILDING A DIVERSE TEAM

What could she bring? In an [increasingly competitive biotech climate](#), any effective organization needs "great people working together in a culture that allows them to be more than they could be individually," Singer says.

Diversity also plays a part, she says. There's a powerful impact when junior employees see themselves and their identities reflected and valued in a biotech's upper levels.

Despite long-standing calls for diversity, equity and inclusion — and the demonstrated impact of diversity on innovation and [financial strength](#) — a 2020 Biotechnology Innovation Organization report found the representation of ethnic minorities on executive teams and company boards hovered around 15 percent. A similar 2021 report by [Bedford Group/TRANSEARCH](#) showed gender equality also lagged in the industry; women made up 14 percent of board members and just 6 percent of CEOs in biotech.



As she's moved up the ranks of biotech, Singer has seen this dearth of diversity reflected in comments on how she balanced work life and time with her daughter — comments that weren't equally directed at her male colleagues. Though it hasn't stopped her, it's hard to tell how much those unconscious biases have shaped her journey. That impact is something she's deeply cognizant of in setting the foundations of both Abata and IPI.

"We're being mindful of bringing a diversity of people into leadership positions," she says, "and I think it will snowball from there."

LEADERSHIP AT IPI

At the Board level at IPI, she is already orchestrating the interactions of a "remarkable group of people," high-level players with deep knowledge in their domains. She's simultaneously working closely with IPI's leadership team to build out all aspects of the nonprofit. In developing both the science and the operations at the same time, she says, IPI can quickly maximize its potential.

Equally important, Singer says, is making room for growth by giving employees the chance to step out and "even risk failing." Through calculated risk, she believes teams can expand their capabilities and employees can grow both personally and professionally.

"As a leader, the things I'm most proud of are the times in my career when I've been able to literally hear someone say, 'Wow, I didn't think I could do that,'" Singer says. "But they did because my leadership team was able to provide them with that opportunity."

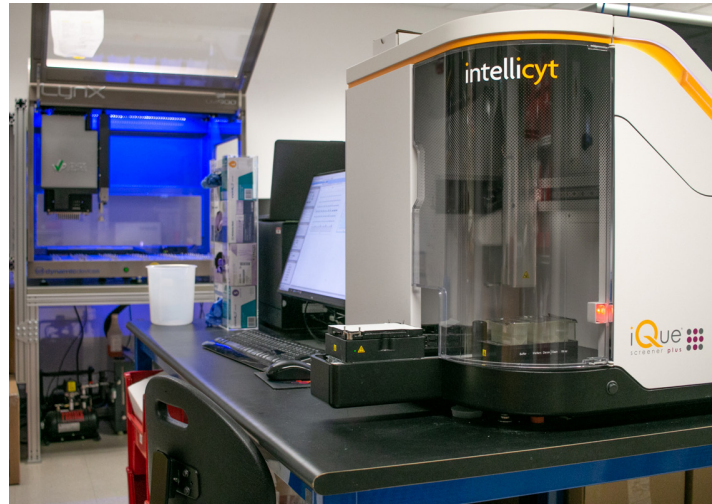
News from the lab



Bahl lab takes bold machine-learning design methods to a bigger market

The year 2021 marked a boon for computational protein designers. As technologies like AlphaFold won awards, Christopher Bahl, head of Protein Design, and his team seized the momentum to launch AI Proteins, a startup that uses artificial intelligence and high-throughput drug discovery to create new synthetic proteins with therapeutic potential from scratch. IPI wishes Bahl and the former IPI Protein Design team the best of luck in their new venture!

Interested in working with the Institute for Protein Innovation? Our team is still growing. Visit our careers page or contact us at careers@proteininnovation.org for more information.

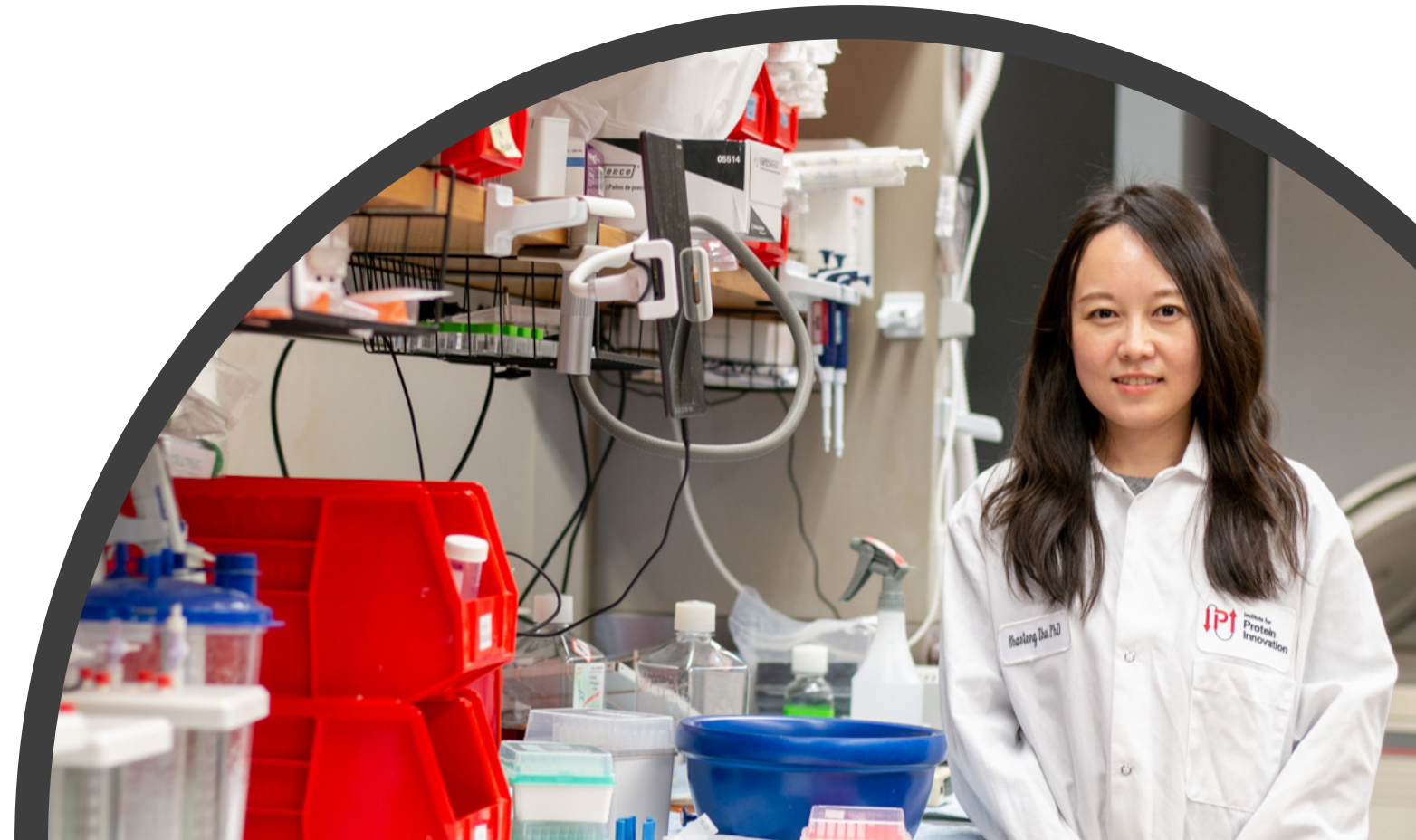


SARS-COV-2 variant studies

As coronaviral variants continued to infect global populations, IPI forged a timely collaboration with Boston Children's Hospital virologist Bing Chen. Joined by IPI principal scientist Haisun Zhu, research associate Krishna Anand and former director of Target Discovery Wei Yang, the team studied how ensembles of mutations in viral spike proteins affected the transmissibility of SARS-CoV-2, variant to variant.

From alpha through delta to omicron, each variant has evolved a different strategy of infection, the team found, whether binding more tightly to the viral receptor, angiotensin-converting enzyme 2, or evading neutralization by immune system antibodies.

IPI researchers characterized the binding of each variant's membrane-bound spike trimers to the viral receptor, while Chen's group conducted in-depth structural studies. Overall, the results — published in three successive papers, including two in *Science* — showed one particular region of the virus that remains the best target for vaccines.



IPI jumpstarts collaborative opioid receptor project

In the fall, IPI's growing Protein Research team, headed by principal scientist Shaotong Zhu, launched a new project on the complex opioid-receptor_pain-signaling_pathway. Supported by a \$410,000 grant from the National Science Foundation, the project will investigate a major controversy surrounding the opioid receptor — a prominent G protein-coupled receptor subfamily.

Simulation-based studies have hinted that the receptor can change its conformation when it senses a pH drop in injured tissues. If Zhu and collaborators can confirm the existence of the receptor and create novel antibodies to it in this "pathological state," these antibodies open up new avenues to painkillers that selectively target only injured tissue, minimizing the side effects and the addictive qualities of common narcotics.

"You can see how the project actually will benefit public health," Zhu says. "That's very exciting for me."

"You can see how the project actually will benefit public health," Zhu says.

Building domain expertise




Matthew Salotto
Antibody Discovery Principal Research Associate
START
February 2021
HOMETOWN
York, Pennsylvania, USA

For Pennsylvania-native Salotto, the lab is a place to indulge in curiosity-driven experimentation. Each method or condition he tests reveals a new path for exploration; each path leads to promising new antibody candidates.

Salotto studied the thermodynamic stability of cell membrane receptors and the effect of epidermal growth factor (EGF) binding on EGF receptor dimerization at Johns Hopkins University, graduating with a master's in materials science and engineering. He then spent five years managing antibody campaigns at Adimab, focused on platform optimization, nanodisc testing and whole-cell selection for G protein-coupled receptor targets.

He is a formidable addition to IPI's Antibody Discovery team, busy improving sorting and selection methods to optimize antibody binding and quality.

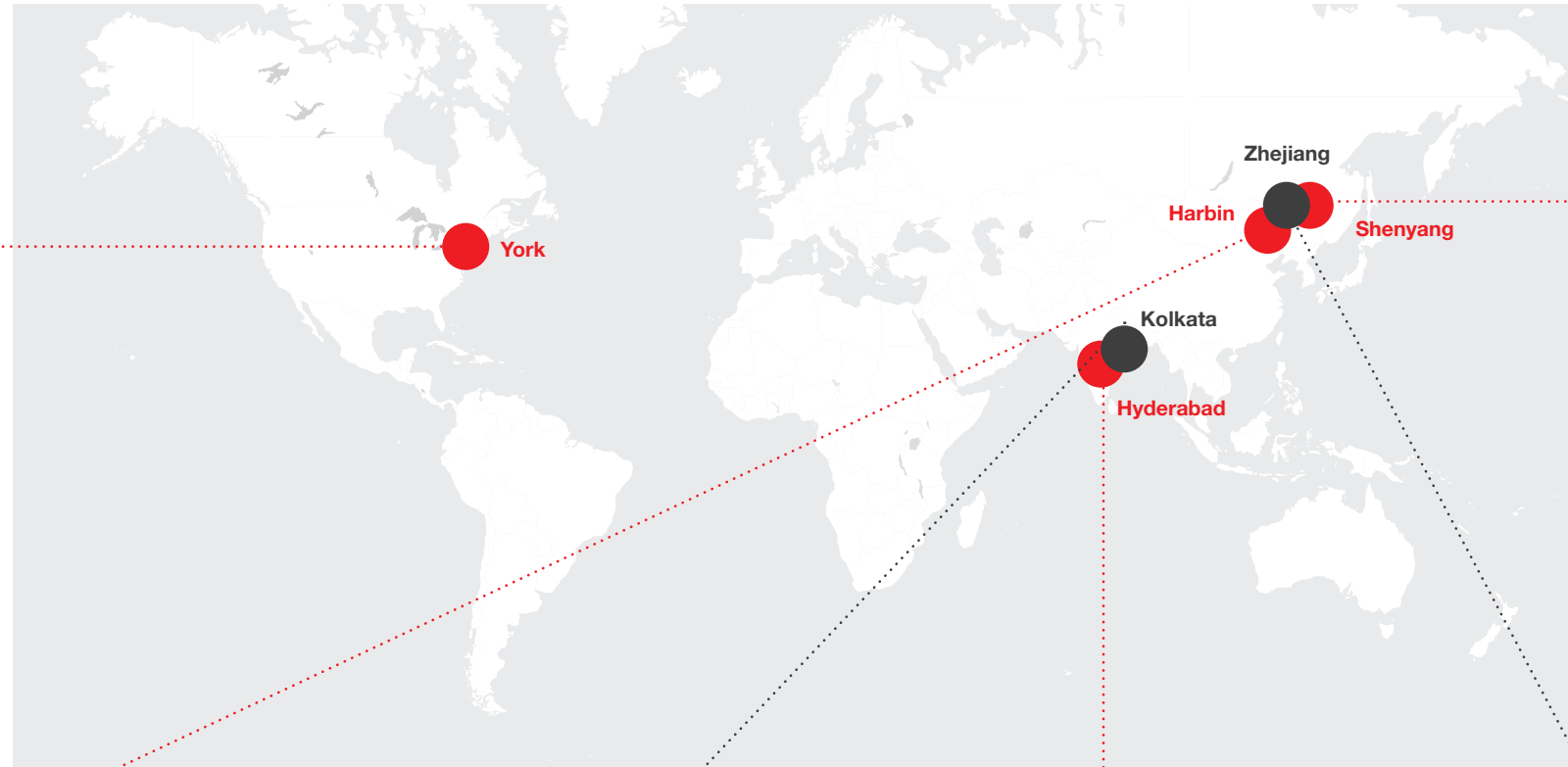


Roushu Zhang
Protein Production Scientist
START
March 2021
HOMETOWN
Harbin, Heilongjiang, China

Growing up in China, Zhang shared a love of biology with her mother, a physician. But instead of becoming a doctor, she found her place in the lab developing tools for diagnosis and drug development.

She launched her career at the University of Maryland, studying glycosylation and fucosylation in SARS-CoV-2 infection. Earning her Ph.D., she also worked on HIV-1 viral evasion and vaccine design, analyzing the fundamentals of glycoproteins in modulating structure, function and later therapeutic development.

With the Antibody Production team, she dissects pieces of DNA, inserts plasmids, and invents biochemical assays to optimize protein expression, validation and purification. She also serves as a mentor, eternally expanding early scientists' knowledge and enhancing IPI research.




Shaotong Zhu
Antibody Production Principal Scientist
START
August 2021
HOMETOWN
Shenyang, Liaoning, China

Zhu is a problem solver who's made her way to IPI from China, via Texas. She likes unraveling protein structures, including the notorious GABA_A receptor, for which she published the first high-resolution structure, appearing on the cover of Nature in 2018.

She completed her Ph.D. at Southern Methodist University in Dallas, focusing on membrane proteins, then landed a postdoc at the University of Texas Southwestern, where she raised monoclonal antibodies and used cryo-electron microscopy to achieve her GABA_A success.

As head of IPI's growing Protein Research team, she's applying her structural biology and biochemistry strengths to express shape-shifting opioid receptors and ancient cell signaling molecules, and generate hard-to-reach functional antibodies to the membrane proteins.




Anita Ghosh
Protein Production Scientist
START
July 2021
HOMETOWN
Kolkata, West Bengal, India

Ghosh is the kind of scientist with all-round knowledge of structural, biochemical and biophysical methods. She's employed that expertise to understand proteins' role in disease pathogenesis and drug resistance.

Originally from Kolkata, India, Ghosh completed her Ph.D. in structural biology and biochemistry at Purdue University. As a postdoctoral researcher at Johns Hopkins University and later Boston University, she characterized a wide range of protein structures, from the *M. tuberculosis* transpeptidase paralog, Ldt_{MIS}, to oyster and clam galectin sequences.

As leader of IPI's Antigen Production team, she focused on standardizing workflow to ensure efficiency. With that capacity to scale, she's led IPI to develop and implement a new Benchling-based laboratory information management system.



Murali Anuganti
Biophysics Scientist
START
November 2021
HOMETOWN
Hyderabad, Telangana, India

Since his childhood in Hyderabad, India, Anuganti has been fascinated by biological mysteries. He investigated one during his Ph.D. at the University of Connecticut, developing a surface plasmon resonance-based approach to explain how a mix of enzymes break down cellulose. The results set the stage for more economical cellulosic biofuels. As a postdoctoral scholar at the University of Nevada, Reno, Anuganti continued to hone his sleuthing via biophysical characterization. There, he engineered novel labeling strategies and used total internal reflection fluorescence microscopy to track the behavior of muscle motor proteins.

At IPI, Anuganti has applied his deep understanding of biophysics to improve quality control and analyze how well IPI antibodies bind their targets.



Haiying Li
Biophysical Characterization Principal Scientist
START
January 2022
HOMETOWN
Zhejiang, China

Li has always been curious about the unknowns in science. Beginning with her Ph.D. at the University of Southern Denmark, she's tapped that inquisitiveness, along the way developing an impressive skillset in liquid chromatography mass spectrometry-based proteomics. She sees the technique as the means to enable novel discoveries — a powerful tool to uncover those unknowns.

As an assistant professor at ShanghaiTech University, Li developed and directed the institute's new Multi-Omics Core Facility. At Boston Children's Hospital and Harvard Medical School, she worked in glycan and protein biomarker discovery related to urologic diseases.

Now, Li is bringing high-tech methods in mass spectrometry and native mass spectrometry to the table to revolutionize quality control at IPI.

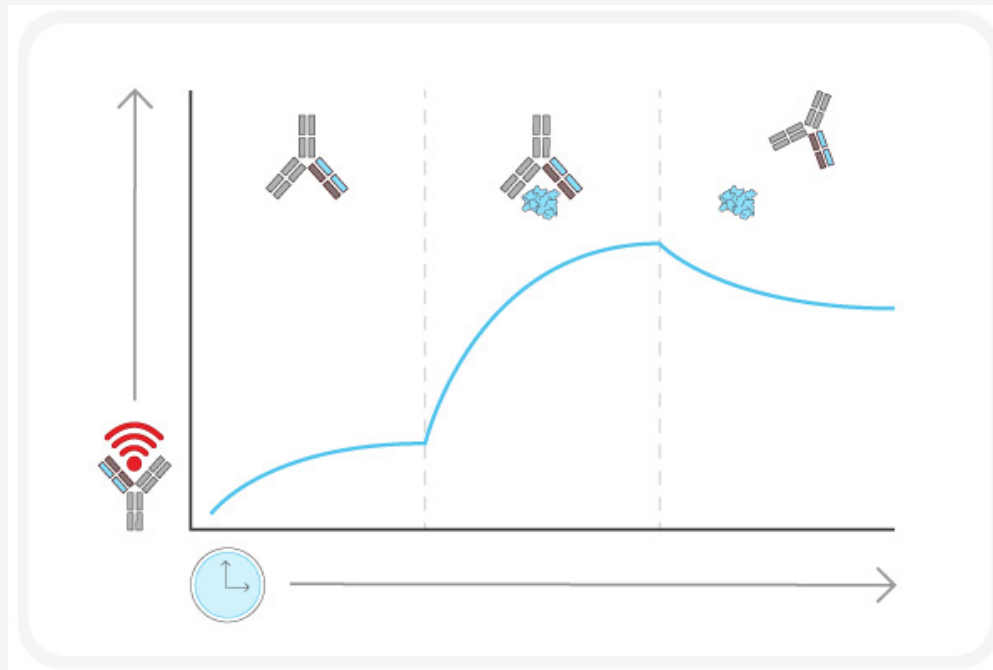
Enhancing characterization capabilities

With the addition of new talent to the Antibody Platform, IPI gained the expertise in 2021 to make difficult antigens and the beginnings of antibodies to target them. To further optimize those antibodies, the pipeline doubled down on antibody characterization, yielding new and better methods to precisely gauge antibody affinity and specificity.

KINETICS OF BINDING

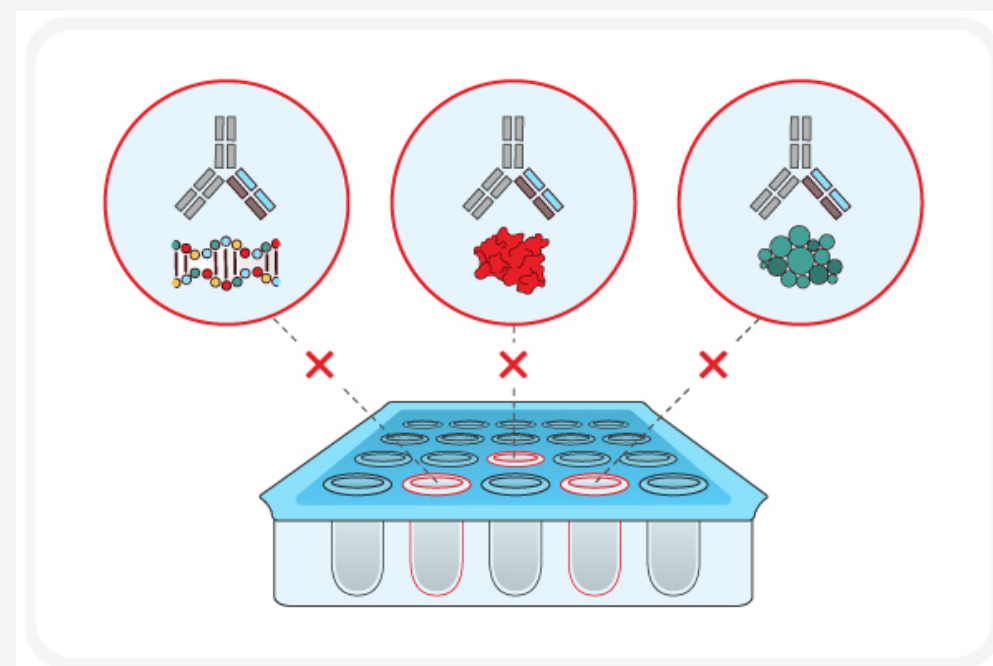
To measure how antibodies bind to their target antigens over time, we use two complementary, real-time biosensing technologies: high-throughput biolayer interferometry (BLI) and highly reproducible surface plasmon resonance (SPR).

- We introduce and anchor an antibody to a sensor.
- We add antigen and measure the intensity and timing of binding, or on rate.
- Over time, the antigen dissociates. We measure this detachment, or off rate, yielding a measure of binding affinity.



POLYSPECIFICITY REACTIVITY ELISA

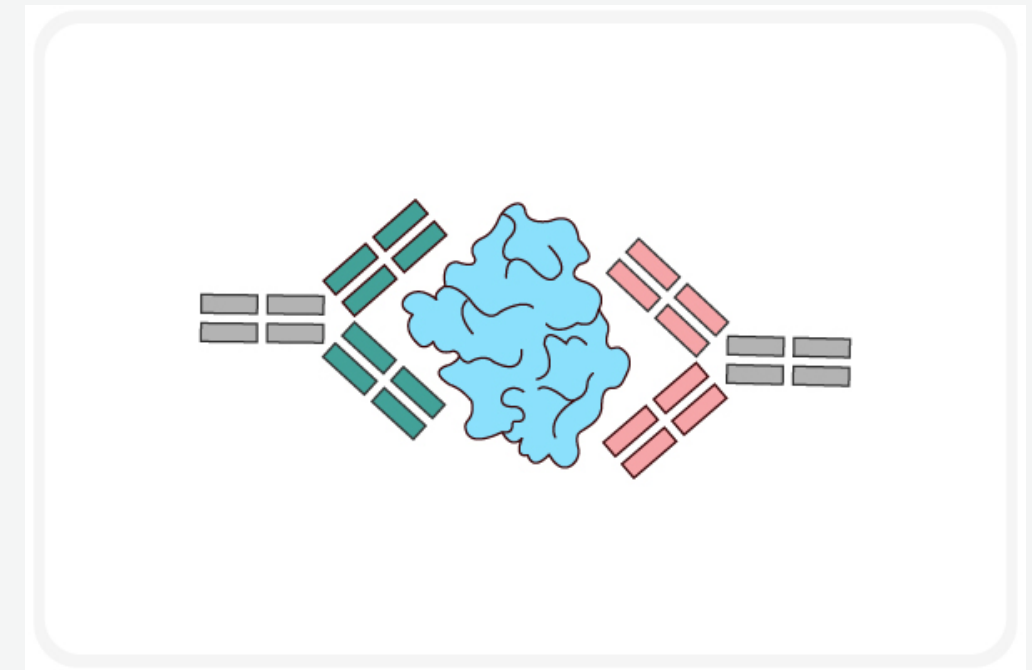
To test antibody “stickiness” and ensure antibody specificity, we use enzyme-linked immunosorbent assay (ELISA) to measure antibody affinity to nontarget substances, including genomic DNA, a nontarget protein or a mix of digested insect cell membranes. Antibodies that bind to this protein medley are dropped out because they don’t recognize their targets specifically.



EPITOPE BINDING

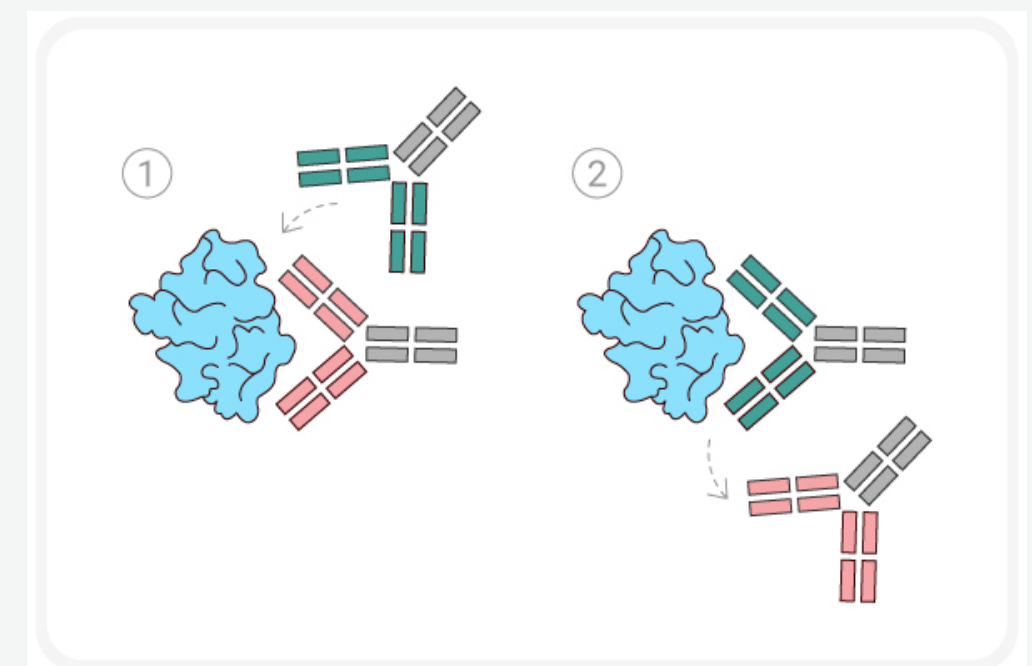
Noncompetitive binding

When two antibodies do not share a binding site, or epitope, both can simultaneously bind to the same antigen. If the antibodies are noncompetitive, we’ll detect an increase in light reflected by the protein layer using SPR.



Competitive binding

When two antibodies share an epitope, the addition of the second antibody will displace the first. We’ll see no change in signal using SPR.

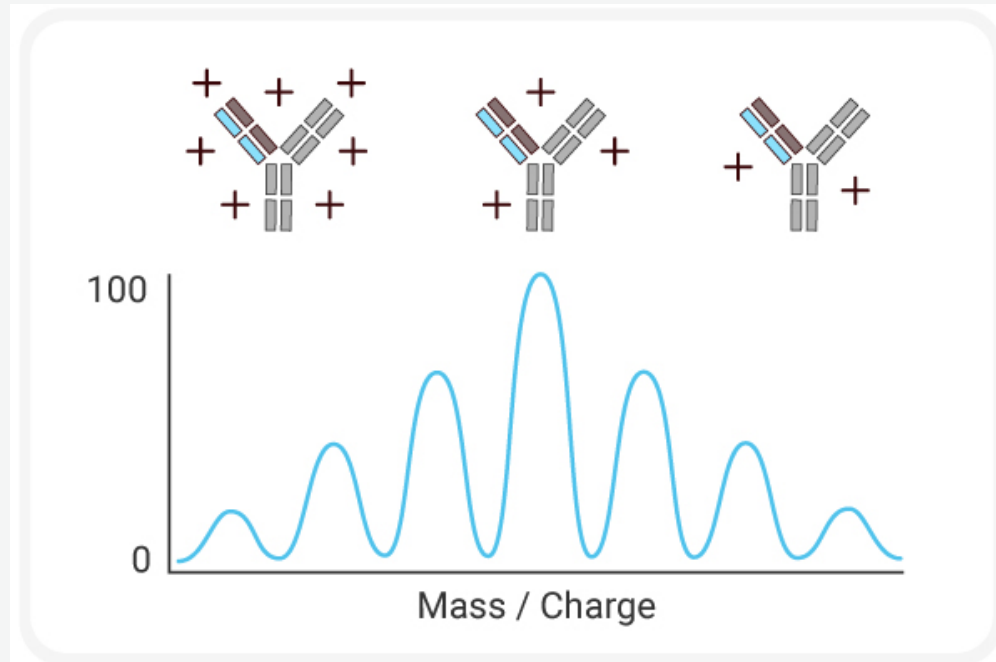


Ensuring quality and quantity

IPI has invested in the people and tools necessary to prioritize antibody quality and determine antibody yield. These measures help ensure that IPI antibodies are of verifiable quality and provide the best possible protein tools to global bioscientists.

MASS SPECTROMETRY

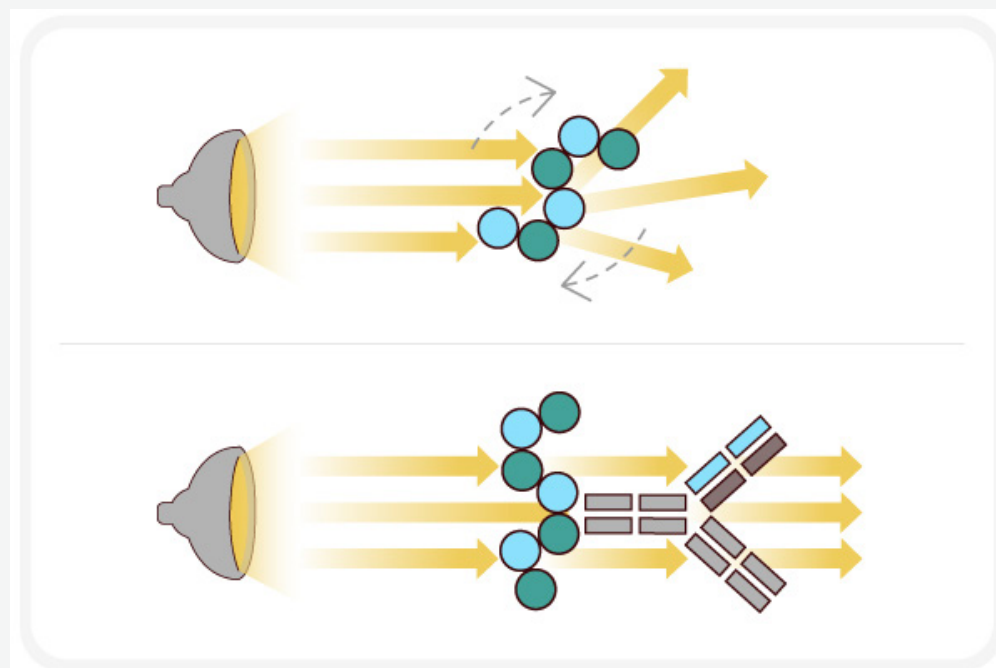
The highlight of our quality control effort is mass spectrometry, an invaluable technique used to measure the mass-to-charge ratio of an antibody that has different charged states. Using these measurements, we can calculate the antibody's molecular mass, thereby confirming its identity.



ELISA TITER ASSAY

To quantify antibody yield, we add an antibody to a solution of peptides.

- A. If the peptides do not bind to the antibody, they'll spin. When a fluorescent beam is shot through the solution, the rotation will depolarize the light to indicate low antibody yield.
- A. If the peptides bind to the antibody, they'll fix in place and polarize the fluorescent beam. We measure the level of polarization to quantify the amount of bound antibody present.



Research, clinical care and community

Eliza Gavin balances three medical strategies as a prospective physician-scientist

By Caitlin Faulds



Eliza Gavin was always the kid who wondered why. As a middle schooler, she'd look at a piece of crystallized rock candy, hypothesize how it formed and then learn how to make a supersaturated solution on the stovetop.

In high school, she learned about DNA replication and watched through a light microscope as amoebas consumed bacterium in front of her eyes. Her early inquisitiveness was quickly directed toward biology.

"This whole universe was right underneath my nose," she says. "I was just so amazed by all of the things that are going on in a cell."

Now, as a research associate at IPI, she's focused on structures that she cannot see: antibodies stabilized through strategic disulfide bonding. Quirky receptors with a key role in brain wiring. The path of her future in medical school.

"IPI has really helped me deepen my research knowledge," she says, "and the people have all been extremely supportive, in both my research endeavors and career development."



GROWING UP

As the only child to a single mother, Gavin knew the ways her helping hands could ease her mother's stress. From a young age, she'd find small means of lending support, whether setting up movie nights, doing laundry or serving dinner.

"It would make my mom smile and feel better," she recalls.

That was the initial point when she realized, in addition to doing science, "I really want to heal," she says. "I really want to help people."

She caught her first glance at her dream job as a rising freshman at Georgetown University. She heard about the [Clinic for Special Children](#), a clinic tucked at the end of a single-lane road in southeastern Pennsylvania that treated Amish and Mennonite children with rare genetic conditions.

"I told them, 'Please teach me. I will do whatever you need,'" Gavin says.

She spent her summer stationed in a community-raised clinic amid cornfields writing blogs about the treatment and research around her — high-tech genetic analyses downstairs and patient services upstairs. The whole enterprise, Gavin says, was steeped in a striking blend of research, clinical care and community building.

"Being immersed in that and being able to help out in that environment — I really wanted to do that with my future career," she says.

Since then, for nearly 10 years, Gavin has triangulated her every move based on that three-pronged approach to medical care.

As an undergraduate researcher at Georgetown, she repurposed FDA-approved drugs to improve cervical cancer treatments with the [Schlegel Lab](#) and studied transcription factors and neural development with the [Silva Casey Lab](#). In the [Umemori Lab](#) at Boston Children's Hospital and Harvard Medical School, she looked at the effects of biomolecules in the brain.

After graduation, she got her first taste of family medicine working at Atrius Health in downtown Boston. As a medical assistant, she helped treat patients of all ages, perform in-office procedures and take patient histories. Gavin's mentor, Meredith Amos, would review patient labs and notes with her every morning and together they'd develop treatment plans that Amos would bring to the patients.

"I felt like I was actually having an impact," she says. "In addition to all of that learning, I was also really connecting with my patients."

Then COVID-19 hit.

"For Gavin, joining IPI was an opportunity to provide answers — at a time when answers were in short supply."

PROVIDING ANSWERS

Patients were coming in with sore throats, respiratory issues and other mysterious ailments. The clinic moved online, offering telemedical appointments to limit transmission. In those early stages, Gavin — and the medical community at large — knew next to nothing about this rapidly spreading, novel coronavirus.

"We were frustrated that we couldn't do more, and we didn't have more answers for the patients," she says.

Asking why, Gavin came to IPI.

She knew from her clinical work and previous research that antibodies, like those in development at IPI, were extremely powerful therapeutic tools: highly specific, broadly applicable and used in all forms of research. IPI's yeast-borne antibodies were poised to go beyond the limitations of traditional, animal-based antibodies to make life-altering discoveries.

For Gavin, joining IPI was an opportunity to provide answers — at a time when answers were in short supply.

"I wanted to do something impactful in the middle of this pandemic," she says.

As a research associate on the Protein Production team, she jumped into an antibody stabilization project, designing and testing constructs for thermal and chemical stability and antibody denaturation.

She then began working with [roundabout receptors](#) (ROBO), a family of transmembrane receptors that play

a key role in the wiring of the brain and central nervous system. Previous IPI research had uncovered ROBO antibodies that were highly specific — "which is great," Gavin says, "but we didn't have enough affinity."

To rectify that, she learned under the tutelage of protein production scientist Roushu Zhang how to develop bispecific antibodies. These composite antibodies are assembled from the severed heavy chains of two moderate binding antibodies — essentially borrowing "half of one and half of another," Gavin says.

While the ROBO bispecifics are still in their testing phase, the process promises to aid in the rescue of other candidates with subpar affinity, increasing the odds of viable antibodies.

In between designing and testing antibodies, Gavin has been busy. For years she's had medical school in her crosshairs, studying for the MCAT, writing applications and prepping for interviews.

Finally, after a last push at IPI, that work has paid off. In August 2022, Gavin will head off to Philadelphia, with a full-tuition scholarship to attend the University of Pennsylvania's [Perelman School of Medicine](#) — less than 100 miles from the clinic that inspired her journey.

"I want to get back to at least the concepts of when I was at the Clinic for Special Children. I love the research, I love the clinic and I know I like connecting with communities," she says. "If I can get back there, then I know I'll be in the perfect place for me in my career."

Becoming a research scientist

Krishna Anand takes IPI lessons to biomedical graduate school

By Caitlin Faulds

Krishna Anand spends her weekdays at the tail end of IPI's middle bay. Multichannel pipettes hang in a line down the wall. Test tube holders, buffers and buckets of still-wrapped serologicals — her tools for protein expression — lie in wait on the shelves and worktop, poised for upcoming experiments.

It's a lab space that feels lived in, one that has served as the home base to Anand, research associate on IPI's Protein Production team since she joined in 2019. There, she's moved from the pipeline's end to beginning, grown from contract researcher to published molecular biologist and picked up an attractive repertoire of academic and industrial skills. Equipped, she'll soon leave for the next step: a doctoral program in biomedical sciences at the University of Massachusetts Chan Medical School.

"I've learned a lot at IPI," she says. "And even after three years, I'm still growing."

As a teenager in Lexington, Massachusetts, Anand always pictured herself as more of a "studio art person," she says. Her first few years as an undergraduate at Reed College in Portland, Oregon, straddled a passion toward illustration and a pull to science.

When she could no longer see a "practical way" forward in art, she pursued a biology major, joining [Janis Shampay's](#) telomere lab. She spent her senior year enthralled by the power of research and busy constructing an epitope-tagged clone of the telomere-associated protein, TIN2, in the model organism *Xenopus laevis*.

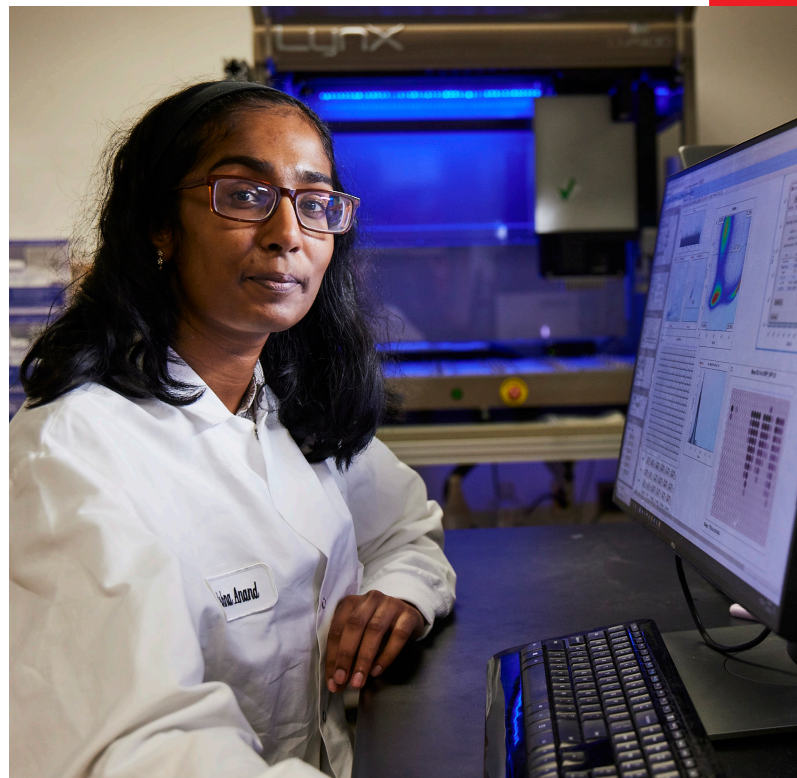
Shortly after graduation, she joined IPI as a part-time researcher performing characterization assays. Immediately, she was drawn to the unique environment — creative, ambitious and research-oriented.

"I felt like it was okay to ask a lot of questions," Anand says.

Day by day, she found herself becoming more deeply invested in the research process. Biology, she realized, was no longer a "backup choice." She was determined to pursue it as a passion — and quickly excelling.

In January 2020, she became a full-time research associate, working with principal scientist Haisun Zhu to pressure-test IPI antibodies for their target-binding abilities. She also mastered cell display, in which she tested and characterized antibodies in bulk — up to 1,200 antibodies at a time — using the lab's Beckman Coulter Biomek FX[®] and Intellicyt iQue Screener PLUS, watching over the robots to ensure they stayed on track.

"The best part," according to Anand, was always the eureka moment of reading fluorescence emission plates from flow cytometry experiments, learning whether the antibodies worked.



"I've learned a lot at IPI," she says. "And even after three years, I'm still growing."

SPURRED INTO ACTION

Months after Anand was hired full-time, the novel coronavirus SARS-CoV-2 swept the globe, infecting millions and spurring those with the tools to study infectious disease mechanisms into action — IPI researchers among them.

Anand and Zhu joined a research effort led by Boston Children's Hospital and Harvard Medical School virologist [Bing Chen](#) to study how mutations in the viral spike protein affected the transmissibility of SARS-CoV-2 variants.

Using flow cytometry, Anand characterized the binding of membrane-bound spike trimers to the viral receptor, angiotensin-converting enzyme 2 and monoclonal antibodies isolated from COVID-19 patients. Her analytical results helped the Chen lab assess the antigenic properties of the spike proteins and better understand the mechanisms of infectivity and immune invasion.

The group's study on the alpha, beta and gamma variants was published in *Science* in June 2021. As additional variants rose to dominance, the team reassembled to investigate the [transmissibility of delta](#), also published in *Science*, and the omicron variant.

As the coronavirus restructured society outside the lab, inside, IPI was also undergoing a reorganization under the new management of Rob Meijers, newly appointed as director of the Antibody Platform at IPI.

The lab previously worked in two main groups; one concentrated on antigens and their target antibodies, while the other focused on the discovery of synthetic antibodies. Everything was in place to meet IPI's ambitious goals, but the two halves functioned as disjointed parts, according to Meijers. In May 2021, Meijers began "streamlining" the lab by arranging it into four teams: Protein Production, Biophysics, Antibody Discovery and Bioinformatics.



This reordering — which has improved quality control throughout the pipeline and enhanced cross-lab communication, Meijers says — allowed Anand the opportunity to cross-train and continue learning. She moved from endgame characterization to the frontline Protein Production team.

From the same bench, Anand now transfects cells with plasmids containing fragments of DNA that harbor the code for antigen targets of interest. She judges their yield and quality before testing variant plasmid vectors to optimize their production. Her goal is to make a large selection of high-quality antigens to hand over to the Antibody Discovery team. There, her antigens are used to screen and optimize strong binding antibodies, which IPI then produces for future use in research and therapeutic discovery worldwide.

In August 2022, Anand will start a biomedical Ph.D. program at the [University of Massachusetts Chan Medical School](#). She aims to study intercellular cancer signaling, armed with an arsenal of techniques picked up at IPI.

"Knowing that I can grow even more?" she says. "It's really freeing."



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