

A complete press & media kit for journalists

About us

The Institute for Protein Innovation (IPI) is a nonprofit research organization co-founded in 2017 by Harvard Medical School professors Tim Springer and Andrew Kruse. Its mission is to advance protein science to accelerate research and improve human health.

Surrounded by the momentum of genomics but immersed in protein science, Springer understood the need to connect the many genes uncovered by the Human Genome Project to their ultimate function in the body via proteins. He founded IPI to fuel a next generation of protein science that might fill the gaps genomics cannot reach.

Specifically, IPI is providing scientists with antibodies and other protein tools, as well as the expertise to use those tools to illuminate fundamental biological processes and therapeutic leads. The Institute also advances protein science by supporting applied protein research, technology development and educational outreach in the life sciences.

Quick facts

- IPI was founded in 2017 by scientists Tim Springer and Andrew Kruse of Harvard Medical School.
- The Institute is headquartered on the Harvard Medical School campus.
- IPI is making synthetic recombinant antibodies and distributing them to scientists through its nonprofit partner Addgene.
- IPI is financially secured by substantial gifts from co-founder Tim Springer, revenue from antibody distribution, sponsored research and federal funding.
- IPI is a nonprofit 501(c)3 organization.

Anchored by Springer's philanthropy, IPI stands apart from traditional life science companies in its freedom to pursue long-term and high-risk projects without funding limitations or profit constraints. The Institute is uniquely sustained by revenue from its antibody distribution, sponsored research and federal funding.





At IPI's core is a scientific platform producing synthetic, recombinant antibodies against sets of related extracellular and secreted protein targets. Combining yeast display technology with rigorous quality control, the Institute targets highly conserved proteins that have eluded traditional animal-derived antibodies.

IPI also aims to address the scientific reproducibility crisis and the lack of comprehensive information provided with typical reagent antibodies. IPI validates its antibodies in key research applications with standardized protocols based on user feedback to create a repertoire of reproducible and well-validated protein tools.

The opportunity

At IPI, we see a critical need for:

- · Cutting-edge protein science to enable new tools and technologies that support biomedical discovery and therapeutic development.
- A home for talented protein engineers and technology-focused scientists to better convene and innovate without the constraints of an academic or industrial setting.
- Access to reproducible, well-characterized antibodies and information on the conditions and contexts in which to use them.

IPI is poised to address these unmet needs through its nonprofit status, organizational structure, expertise and strategy.



Visit us at: https://proteininnovation.org/forjournalists Contact us at: communications@proteininnovation.org



Protein Innovation



History

The Institute for Protein Innovation (IPI) is the brainchild of scientist and entrepreneur <u>Timothy Springer</u>, the Latham Family Professor of Biological Chemistry and Molecular Pharmacology in the Blavatnik Institute at Harvard Medical School and Boston Children's Hospital.

Springer teamed up with co-founder <u>Andrew Kruse</u>, a professor at Harvard Medical School and expert on synthetic antibodies, to launch IPI in 2017 as a nonprofit institute. The pair aimed to create a means for basic research scientists to access antibodies directed against cell surface and secreted proteins, the key targets for most successful drugs.

In 2018, the Institute moved to the Harvard Institutes of Medicine in the heart of the Boston Longwood Medical and Academic Area. That same year, IPI launched its first campaign to help scientists validate their antibodies using high-throughput technology.



Celebrating the launch of IPI in 2017. Photo courtesy of the Springer Lab



IPI co-founders Timothy Springer, left, and Andrew Kruse, right. Photo courtesy of the Springer Lab

In 2021, IPI's board of directors, previously led by Springer, <u>elected</u> a new chair, Samantha Singer, formerly an entrepreneur-in-residence at Third Rock Ventures and now president and CEO of Abata Therapeutics. Singer brings these experiences, as well as her time as chief operating officer of the Broad Institute, to help IPI realize its vision as an academic-industry hybrid institute dedicated to accelerating biomedical research.

Kenneth Fasman, formerly senior vice president for research at The Jackson Laboratory, joined IPI as president and CEO in 2022. Beginning his career in computational neuroscience, Fasman designed and implemented the original Human Genome Project database at the Johns Hopkins School of Medicine. He then pivoted to bioinformatics, drug discovery and research strategy, spending more than three decades with top pharmaceutical companies and nonprofit genomics institutes. Under his guidance, IPI takes on a three-fold mission to build resources, aid research and empower education within the protein science and biological research communities.

Today, IPI remains an independent nonprofit research institute, partnering with researchers at Harvard Medical School, Boston Children's Hospital and more. Aligned with Springer's founding vision, IPI seeks to use protein tools and resources to impact biological research and ultimately, improve human health.







All about antibodies

Nature's protection

Antibodies are powerful, Y-shaped proteins that are key to immune system function. They help orchestrate the response of a variety of specialized proteins against foreign invaders in most vertebrates. The most common antibodies are immunoglobulins (IgGs), which are globular proteins that circulate in mammalian bloodstreams.

Antibodies are produced by white blood cells to identify and bind to targets, called antigens, which include foreign invaders such as viruses and bacteria. Though IgG antibodies are much smaller than a virus, they're essential to guiding white blood cells to find and destroy microbes and other invaders.



A computer model of an immunoglobulin. IPI image by Christopher Bahl

How scientists use antibodies in research

While the human immune system naturally makes antibodies to target foreign invaders, biologists have spent decades engineering ways to exploit their binding and homing abilities.

Scientists can use antibodies to illuminate the locations of proteins in living cells and tissues, identify mutations in a microbe's structure, track proteins in cells at various stages of a disease and more. Also capable of blocking protein functions, antibodies can uncover the biological impacts of diseases and, ultimately, inform therapeutic cures.

Some of the most common uses of antibodies in laboratories include:

- Immunohistochemistry, a technique that uses antibodies to detect proteins in a tissue sample
- · Western blotting, a technique to identify a specific protein in a mix of others
- Enzyme-linked immunosorbent assay, a technique to detect and quantify biological molecules, including peptides, proteins and hormones.
- Flow cytometry, a popular way to analyze the chemical and physical properties of cells



Despite their promise, antibodies face major hurdles

Antibodies have helped basic scientists achieve new levels in their experiments thanks to decades of progress. But time has also revealed the limitations of contemporary antibody technologies.

Initially, scientists relied on polyclonal antibodies, naturally made by immune cells. Researchers produce polyclonals by injecting the protein they want to study into an animal - usually mice, rabbits or llamas - to induce its immune system to produce antibodies against that protein.

But with that method comes major hurdles. The animals produce a unique mix of antibodies against the injected protein, severely limiting specificity. When the animal dies, so does that collection of antibodies, making the reproducibility of results impossible from study to study over time.

A breakthrough came in 1975, when Georges Köhler and César Milstein, once a mentor to Institute for Protein Innovation (IPI) co-founder Timothy Springer, invented hybridoma technology, the first way to produce long-lasting antibodies. Researchers could immunize a mouse and extract a single antibody-producing cell, fuse it to a cancer cell and create a hybridoma, an immortal cell culture that churns out identical antibodies in perpetuity.

The finding earned them the Nobel Prize and spurred a new class of antibodies - monoclonal antibodies — capable of much higher specificity.

But researchers, including Springer, learned that hybridomas change over time as they divide, resulting in a mix of antibodies that drifts away from the initial one. Also, hybridoma technology still requires the immunization of animals, raising a key technical challenge: Some proteins are so central to the functions of their systems that they've persisted against nearly 100 million years of evolution. Known as conserved proteins, they make for challenging targets in basic science because animal immune systems cannot recognize them as foreign and fail to generate antibodies. It's a major barrier for scientists studying complex human systems that are highly conserved among mammals, such as the brain and stem cells.

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Moreover, many life science companies don't thoroughly validate their products, resulting in antibodies that don't recognize the targets they're intended to or bind to other antigens with similar structures, called cross-reaction. This dearth of validated antibodies helped spur what's known as science's reproducibility crisis, a trend recognized around 2010 in which key studies — many using flawed tools - can't be verified by other researchers.





IPI aims to revolutionize biology with new technology and open science

IPI scientists specialize in generating synthetic, recombinant antibodies, which are made in organisms such as yeast using synthetic DNA. IPI scientists engineer yeast cells to make antibody fragments, capable of binding target proteins, and display them on their surfaces. Researchers create "libraries" of billions of yeast, each making its own antibody fragment. The diversity mimics what happens in the human body, which houses billions of cells, each carrying a potential antibody displayed on its surface.

In a well-tuned sorting process, IPI scientists tap the libraries to find the best yeast binders for a target of interest. Those binders become candidates for further testing, characterization and ultimate packaging into recombinant antibodies. Because the technology is reliant on knowledge of the DNA sequence of the antibody binding fragment, synthetic antibody approaches ensure reproducibility. The method is among the best ways to generate reproducible antibodies for highly conserved targets. Protein scientists can also use advanced engineering techniques to generate antibodies with specific abilities beyond binding, such as function blocking or locking protein shapes for researchers to study.

Because IPI is a nonprofit, sustained in part by philanthropy, we're poised to make antibodies widely available to biological researchers and share our data. This commitment reflects IPI's contribution to the open science movement, which aims to enable accessibility to research data, samples, software and tools.



Nicholas Hollmer, a research associate on IPI's Antibody Discovery team. IPI photo by Pat Piasecki



Mina Abdollahi, left, and Filmawit Belay, right, of IPI's Antibody Production team. IPI photo by Pat Piasecki



Shaotong Zhu, principal scientist. IPI photo by Pat Piasecki.

Protein Innovation





Leadership

- IPI's Board of Directors is chaired by Samantha Singer and includes a strong team of scientific, industrial and financial talent.
- IPI's Scientific Advisory Board includes an impressive group of world-class scientists and biotechnology experts.
- Kenneth Fasman is IPI's president and CEO.



Kenneth Fasman, president and CEO

Kenneth Fasman, formerly senior vice president for research at The Jackson Laboratory, joined IPI as president and CEO in 2022. After earning his Ph.D. in biomedical engineering from the Johns Hopkins School of Medicine, he founded a bioscience laboratory systems company, BME Systems Inc., and went on to design and implement the original database for the groundbreaking Human Genome Project.

Fasman later pivoted to bioinformatics, drug discovery and research strategy, spending more than three decades with top pharmaceutical companies and nonprofit genomics institutes. Under his guidance, IPI takes on a three-fold mission to build resources, power discovery and enhance education within the protein science and biological research communities.

Read our profile



Samantha Singer, chair of IPI's Board of Directors

After earning her master's degree in molecular biology, Samantha Singer completed a master's in business administration at Harvard Business School. She served as an executive at Biogen before becoming chief operating officer of the Broad Institute and an entrepreneur-in-residence at Third Rock Ventures. Singer is currently president and CEO of Abata Therapeutics.

Read our profile







Timothy Springer: Altruist, scientist and philanthropist

For more than four decades, Timothy Springer has wanted to do good, practice good science and support basic research.

Now, the Institute for Protein Innovation (IPI) embodies his long-held desire, grounded in a mission to advance protein science to accelerate research and improve human health.

Early idealism

Springer, Latham Family Professor of Biological Chemistry and Molecular Pharmacology in the Blavatnik Institute at Harvard Medical School and Boston Children's Hospital, is not a typical academic scientist. Early on, he attended Yale University but left after a year to pursue more altruistic ideals. He spent a year with the domestic Peace Corps program, VISTA, serving on a Shoshone reservation in Nevada. That experience seeded a desire to do good in the world that he would later fulfill in more philanthropic pursuits.

He transferred to the University of California, Berkeley, where he earned his bachelor's degree in biochemistry and first used antibodies in independent research. Springer next earned a Ph.D. in biochemistry from Harvard University, working under the guidance of immunologist Jack Strominger on proteins residing on the surfaces of immune cells.



Timothy Springer in his office at Harvard Medical School. IPI photo by Caitlin Faulds.

His work continued as a postdoctoral student with César Milstein in Cambridge, England. Milstein personally taught Springer how to make monoclonal antibodies, made possible by a technique Milstein invented that later won him and Georges Köhler the Nobel Prize. This would be the inspiration for Springer to launch IPI 40 years later.

Scientific success

After studying briefly under Milstein, Springer returned to Harvard in 1977 as an assistant professor at Harvard Medical School. There, he used monoclonal antibodies to discover cell surfacebased molecules that immune cells require to recognize and bind other cells, <u>including</u> the protein LFA-1. He then <u>showed</u> that LFA-1 was related to two other molecules on myeloid cells, <u>Mac-1</u> and <u>p150,95</u>. Further, these three molecules were members of a <u>family</u> with one identical subunit, called beta, and distinct but related subunits, called alpha.



Unbeknownst to Springer, Richard O. Hynes at the Massachusetts Institute of Technology and Erkki Ruoslahti at Sanford Burnham Prebys Medical Discovery Institute had independently identified and sequenced <u>fibronectin</u>. As a result, they uncovered a cell surface protein, glycoprotein IIb/IIIa, that helps affix cells to the surrounding material, or the extracellular matrix.

These initially disparate lines of inquiry converged and expanded after all three investigators realized that the proteins — now called integrins — belong to the same molecular family. Its members play central roles in an astounding array of processes in embryonic and adult organisms. For example, Springer and others <u>found</u> that a group of individuals with leukocyte adhesion deficiency, marked by recurrent life-threatening bacterial infections, bear mutations in the shared beta subunit of LFA-1, Mac-1 and p150,95. The integrin discovery <u>won</u> the trio the prestigious Albert Lasker Award for Basic Medical Research in 2022.

Continuing this high-discovery pace, Springer's lab in 1991 <u>elucidated</u> a three-step process by which white blood cells traffic from the bloodstream to tissues to find and fight infections. The work <u>won</u> him and Eugene Butcher the 2004 Royal Swedish Academy of Sciences' Crafoord Prize. In 2019, those findings and his ability to translate them into clinical impacts also <u>earned</u> Springer Canada's Gairdner Award, nicknamed "Canada's Nobel." Since 1996, Springer has been a <u>member</u> of the National Academy of Sciences.

Clinical impact

Despite the tremendous scientific success, Springer felt he could do more. His lab had shown that each of three steps in the immune cell trafficking process required a unique receptor and receptor partner, called a ligand, for each type of white blood cell involved. The combination of the steps in this process, like the digits in an area code, encoded the type of cell that left the bloodstream and the location in the body to which it trafficked.

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By extension, each receptor and ligand represented a target for drug discovery. Theoretically, an inhibitor to any molecular player in this three-step process could enhance the flow of a specific immune cell type to sites of pathogen invasion or block it during autoimmune disease.

To go after this plethora of potential targets, Springer founded his first company, LeukoSite, in 1992. In the mid-1990s, one promising monoclonal antibody inhibitor entered preclinical trials, resulting in the blockbuster drug vedolizumab, known commercially as Entyvio. This humanized monoclonal antibody selectively thwarts an integrin that promotes immune cell migration into the gut. thereby ameliorating ulcerative colitis and Crohn's disease. The agent was approved by the Food and Drug Administration for both conditions in 2014. Since then, more than 100 integrin-targeted therapies have entered clinical trials or been approved by the FDA, including interventions for autoimmune diseases, endometriosis, and carcinoma and other cancers.



Entrepreneurship and philanthropy

In 1999, Millennium Pharmaceuticals, now owned by Takeda Pharmaceutical Company, acquired LeukoSite for stock that later appreciated to \$3 billion. Thinking he could never successfully develop another company of that stature, Springer devoted his time to his research laboratory. But, in 2008, his interest in biotech was rekindled. Since then, while remaining a full-time academic, Springer has invested in three companies and founded and invested in another four, including Moderna Therapeutics and Scholar Rock, the latter attempting to generate therapeutic antibodies to cell surface receptors.

While successful thus far, Springer still recognized the limitations of using monoclonal technologies, particularly that they fail to produce antibodies against identical — and even similar — molecules between humans and mice. He began to read and hear around his scientific circles about a technology where one could generate antibodies synthetically using genetically engineered yeast. The technique mimics what happens in the human body when it encounters a microbe and needs to generate an antibody defense. Excited, he teamed up with Andrew Kruse, then a rising star at Harvard and now a professor there, who specialized in making libraries of these yeast display synthetic antibodies.

The two launched IPI in 2017 as a nonprofit venture to create a means for basic research scientists to access antibodies directed against membrane and secreted proteins, the key targets for most successful drugs.

"There are all these molecules on cell surfaces and outside cells, and many of them can't be identified with traditional antibodies," Springer <u>said</u> in 2017. "We want to put these antibodies in the hands of investigators to make new discoveries."







Let our proteins power your next discovery.

IPI is now developing high-throughput methods that leverage yeast display and other technologies to generate high-quality antibodies for challenging protein targets, particularly in neuroscience and developmental biology. Unlike most commercial entities, IPI scientists also characterize those antibodies to determine their fitness for purpose before distribution in an open science model. The work and the distribution model will provide reliable antibodies to the scientific community, bolster research initiatives and inspire new treatments in the clinic.

Protein Innovati

"IPI is my legacy project," Springer <u>said</u>. "It encapsulates, in a practical, integrative way, all that I have accomplished in researching the functions and interactions of biomedically important proteins to create treatment advances in immunology, hematology, infectious disease and cancer."



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Timothy Springer, IPI co-founder

