



ADDICTION	NEURODEGENERATION
ALS	NEURODEVELOPMENT
ALZHEIMER'S	OBESITY
ANXIETY	PAIN
AUTISM	PARKINSON'S
IMMUNE FUNCTION	PTSD
INFLAMMATION	SCHIZOPHRENIA
ITCH	SOMATOSENSATION
MEMORY	STRESS

METABOLISM







GILL CHAIR Richard DiMarchi



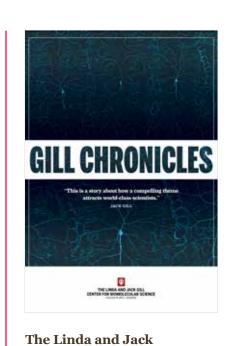
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A MESSAGE FROM THE EXECUTIVE DEAN OF THE IU COLLEGE OF ARTS AND SCIENCES

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"To raise new questions, new possibilities, to regard old problems from a new angle, requires creative imagination and marks the real advance in science."

ALBERT EINSTEIN



The Gill Center is a compelling example of what is possible when talented scientists are granted agency to work in community.

As a synergistic team of neuroscientists, they are

able to combine their knowledge, creativity, and skill to venture far beyond the boundaries of what is known, and return with new insights into the nervous system that could only be found through collective effort. Their life-enhancing discoveries belong to all of us, and their wonder, persistence, and desire to create a better world reflect the better angels of our nature.

The Indiana University College of Arts and Sciences is forever grateful to Linda and Jack Gill. They understood from the beginning the wisdom expressed by Albert Einstein: "To raise new questions, new possibilities, to regard old problems from a new angle, requires creative imagination and marks the real advance in science." There is no doubt that the success of the Gill Center traces back to their compassion and foresight. The Gill Chronicles celebrates all who have strived to make the Center an extraordinary place.

Congratulations! We look forward to many more years of awe-inspiring science.

Larry Singell

Executive Dean

College of Arts and Sciences

Indiana University Bloomington



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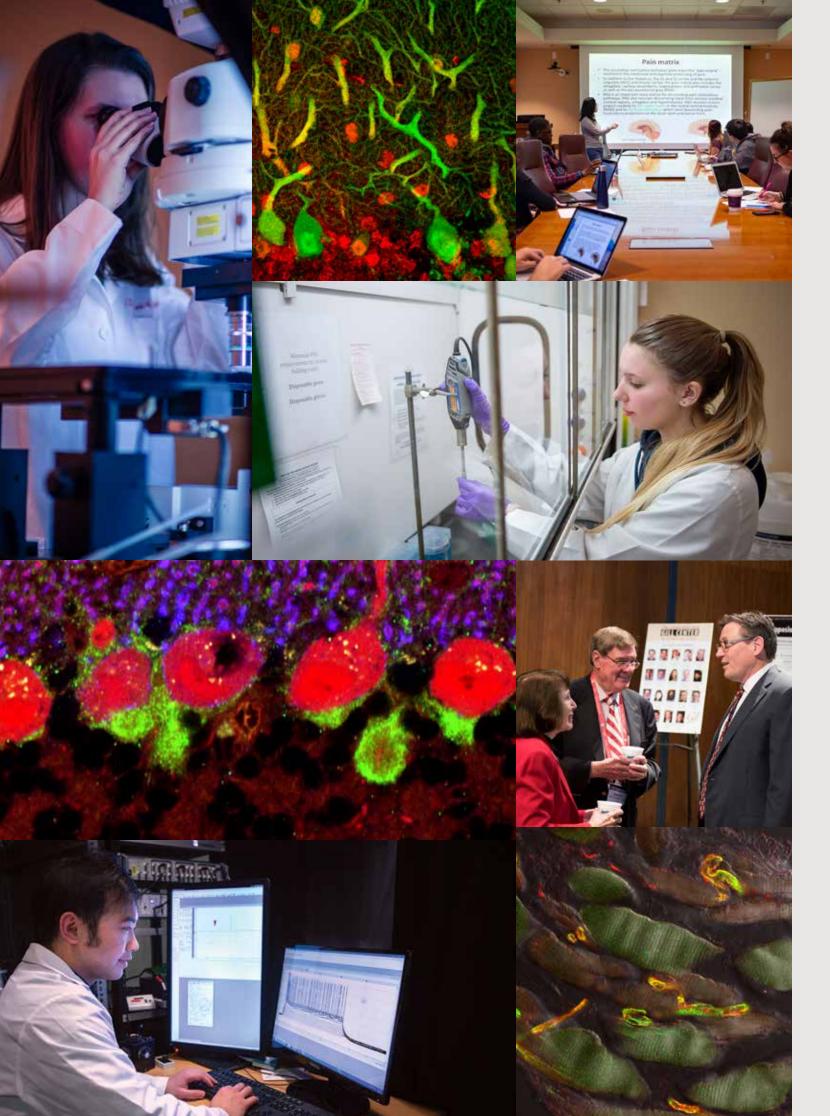
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FOREWORD



The Linda and Jack Gill Center for Biomolecular Science is one of Indiana University's great success stories. It stands as a beacon for 21st-century research, demonstrating how

interdisciplinary efforts can, through collaboration and ingenuity, deliver insights with the potential to solve urgent problems and dramatically change lives.

As a result of the Gill Center's work, we now have a deeper understanding of how the brain's communication networks develop, operate, and maintain themselves. We've gained a far clearer picture of the mechanisms of pain, and particularly of the endocannabinoid system's roles in alleviating pain. Moreover, we have new hope for prevention of dependence on opioid drugs, recovery from addiction, management of metabolic disorders, and even protection against the ravages of neurodegeneration.

The Gill Center is also an extraordinary site for teaching and learning, in which undergraduate and graduate students alike participate in – and often lead key aspects of – groundbreaking research. It is exceedingly rare for undergraduate students to have the opportunity to participate so meaningfully and intimately in neuroscience research, yet at the Gill Center it has become the norm to welcome dozens of these young scientists.

Educational initiatives also extend beyond the campus, sharing neurosciences discoveries with K-12 students, teachers, and the broader public through art

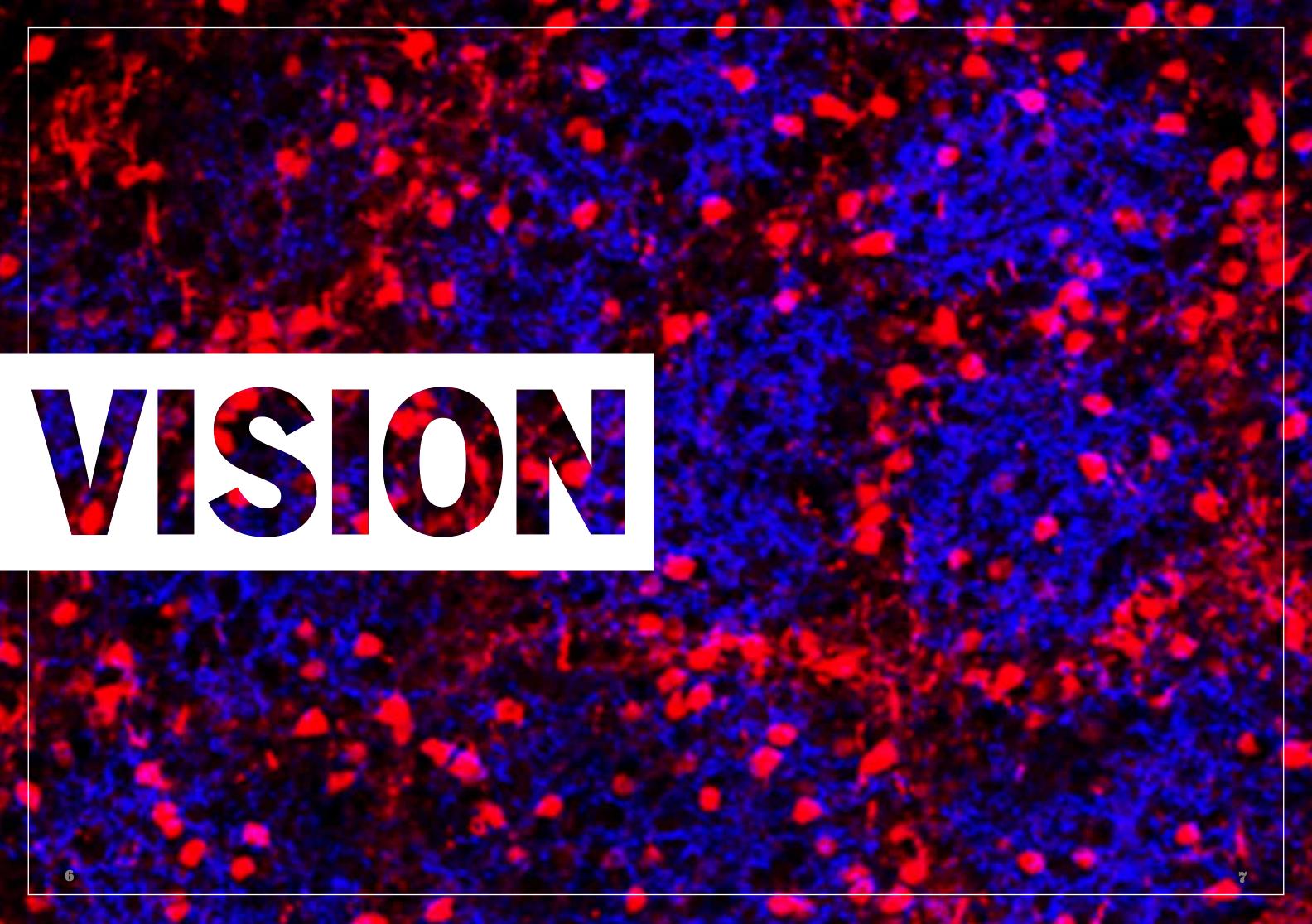
exhibitions, summer institutes, and monthly Science Cafés. Equally, the Center serves as a vibrant hub for the global neuroscience community, continually engaging a worldwide network of collaborators and drawing the field's best minds to Bloomington for the annual Gill Symposium and Awards.

In so many ways, the Gill Center serves as a model for realizing the full promise of a research university. None of these accomplishments would be possible, however, without the unique vision and foresight of Jack and Linda Gill. Their profound commitment to higher education is paired with a virtuosic understanding of how best to create the conditions for scientific breakthroughs. The Gills' trailblazing approach to philanthropy – supporting Centers of Excellence in interdisciplinary science by providing highly flexible research funding – demonstrates that thoughtful investment in teams of world-class researchers can yield tremendous returns in continued growth, widespread influence, and unmistakable impact.

As we celebrate the Gill Center's 20th anniversary, I am delighted to reflect on the Center's tremendous contributions, and to join its faculty and Jack and Linda Gill in heralding an even brighter era ahead.

Lauren Robel

Provost & Executive Vice President Indiana University





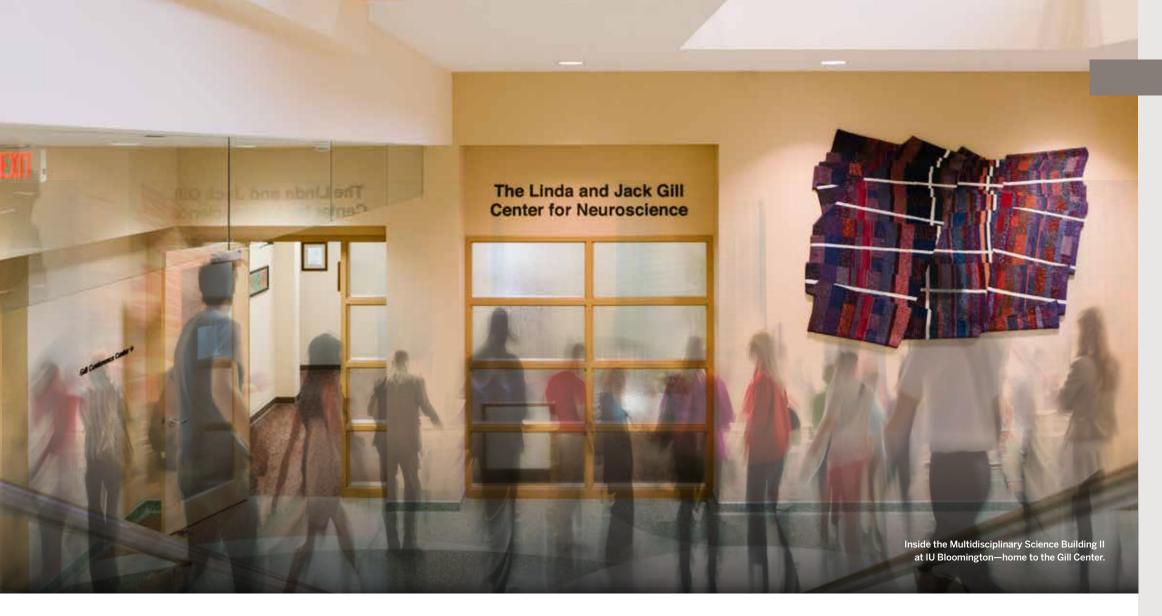
THE GILL VISION

Leveraged Philanthropy in Neuroscience

At the frontiers of science and medicine, the most important explorations involve risk. Probing uncharted questions requires new approaches, pioneering methods, and groundbreaking collaborations. All too often, the limits of traditional funding structures and disciplinary boundaries restrict these advances to slow and incremental steps. It takes a different model – one that embraces boldness and unconventional thinking – to enable giant leaps forward.

The Gill Center for Biomolecular Science at Indiana University provides the field of neuroscience with a unique platform for such innovation. Powered by the extraordinary vision and commitment of Linda and Jack Gill, the Center brings together world-class scientists and state-of-the-art facilities in an atmosphere of unimpeded experimentation. The result is real and rapid progress on understanding issues such as pain, addiction, stress, and dementia.

"Academics are not risk takers by their nature," explains Jack, whose vision for the Center was informed by decades of entrepreneurial experience as one of the founding titans of Silicon Valley. "We see our role as helping researchers create a broader vision and a bolder future. The Gill Center is truly one of the earliest, most pioneering collaborative neuroscience centers, bringing together a concentration of neuroscientists focusing on some of the most pressing issues of our time."



NIMBLE FUNDING STRUCTURE

The Gill Center was founded through a major gift from Jack and Linda's foundation that was matched by IU's College of Arts and Sciences and is supported through the Gills' advisory engagement. The Center aims not only to conduct leading-edge neuroscience research but also to foster a collaborative community, build a worldwide network of neuroscientists, and recruit and train the next generation of researchers. Five Gill Chairs manifest this vision through outstanding research, teaching, and leadership in the field, with expertise ranging from neural circuit development to neurodegenerative disease. Among the unique features of the Center is its ongoing provision of unrestricted research funds to each Gill Chair, allowing for trailblazing experiments that are not constrained by the priorities of traditional funding agencies.

"These funds are like venture capital, allowing us to be brave," says Gill Center Director Hui-Chen Lu, whose research investigates neurological disorders including schizophrenia, epilepsy, and dementia. Gill Chair and former Center director Ken Mackie, whose studies of the endocannabinoid system have implications for processes including memory, anxiety, and obesity, adds, "The usual grant cycle is long, but science moves very quickly. This funding structure allows us to be nimble."

COLLABORATIVE APPROACH

Another unusual feature of the Gill Center is its inherent emphasis on collaboration. Gill Chairs, who must be recruited from outside the university in order to promote the expansion of IU's neuroscience community, are selected not only for their individual records of excellence but also for their ability to contribute to and influence ongoing Center research.

These diverse perspectives have led to integrated approaches that push the field forward by borrowing from multiple streams of research. The Center's dedicated building has also facilitated these collaborations, not only through researchers sharing labs and equipment but also through the informal and interpersonal interactions that result from spending time in close proximity.

"Hanging out with a smart crowd — that's a big part of the success formula," says Jack. He emphasizes the need to attain a "critical mass" of leaders in order to achieve outsize gains in creativity. "The idea is to have a team that is simpatico yet differentiated. The output you get from five people working together like that isn't 5x, it's 10x."

2018 GILL CHAIRS



RICHARD DIMARCHI, PhD RESEARCH INTERESTS: Control of metabolism, structureactivity relationships of macromolecules, chemical biology, bioorganic chemistry, medicinal

chemistry, pharmacology, peptide drug research and development



ANDREA HOHMANN, PhD

RESEARCH INTERESTS: Roles of the brain's own cannabis-like (endocannabinoid) system; pain and analgesia; separating analgesic efficacy and abuse liability; mechanisms of action of drugs of abuse; approaches to block opioid tolerance, reward, and physical dependence; therapeutic disruption of protein-protein interactions



HUI-CHEN LU, PhD

RESEARCH INTERESTS: Understanding the development, plasticity, maintenance, and aging of neural circuitry; gaining molecular insights into how neural activity-dependent mechanisms shape neural wiring; elucidating endogenous neuroprotection mechanisms to direct the development of therapeutic interventions to slow cognitive decline or neuronal loss in neurodegenerative conditions



KEN MACKIE, MD

RESEARCH INTERESTS: Regulation and physiological role of cannabinoid receptor signaling, interactions among phytocannabinoids and terpenes, role of endocannabinoids in synaptic plasticity, novel cannabinoid receptors, neurodevelopmental effects of cannabinoids, cannabis policy



DAN TRACEY, PhD

RESEARCH INTERESTS: Molecular and cellular mechanisms of nociception (pain), molecular and cellular mechanism of touch sensation, development of tools for neuroscience research, high-throughput methods for behavioral analysis, molecular genetics, confocal microscopy, electrophysiology

TRANSLATIONAL FOCUS

The Gill Center also breaks from academic tradition by explicitly encouraging involvement with industry. Several Gill Chairs work directly with commercial partners to ensure that scientific breakthroughs lead to real-world applications.

"Collaboration across the academic disciplines is critical, but that alone is not enough," says Jack. "You can make the greatest innovations and discoveries imaginable – you can write papers, you can get grants – but if you don't bring innovations to the marketplace, you don't benefit the masses."



LEVERAGED PHILANTHROPY

This interconnected and emboldened environment facilitates what Jack and Linda refer to as "leveraged philanthropy"—a model for giving that grows strategically targeted investments into enormously influential programs. From their initial gift of \$5 million, the Gill Center has attracted more than \$40 million in external funding and now houses more than 90 people, including eight research scientists, eight postdoctoral researchers, 10 technicians, 12 graduate students, and more than 40 undergraduates who actively participate in research. The Center also maintains the university's Neuroscience Core Labs, which are utilized by more than two dozen other research teams on campus.

Additionally, through its annual Gill Symposium and Awards Ceremony, the Center attracts the field's top luminaries from around the world, who maintain collaborative and mentoring relationships with the Gill Center's Chairs and students.

"This is an example of a program that started modestly, and from engagement grew big time," says Jack. "With leveraged philanthropy, the donor provides the seed, but the program goes on to become continuous and self-sustaining. Through this Center, IU has truly become a pioneer, both in addressing the major national priority of neurological health and in implementing a powerful new model of philanthropic engagement. This pioneering model has become the most commonly pursued approach by the nation's top research universities."





JACK AND LINDA GILL

Jack and Linda Gill are passionate about supporting higher education because they have personally experienced its transformative power. When Jack was a graduate chemistry student at IU and Linda was pursuing a teaching degree at the University of Kentucky, scholarships helped them overcome challenging circumstances to attain remarkable achievements.

Although they grew up 900 miles from each other – Jack in Texas and Linda in Kentucky – they have similar memories of parents who sacrificed their own education. In order to support struggling households, Jack's father left school after 6th grade and Linda's mother turned down three college scholarships. These decisions left Jack's father working long hours on construction crews, while Linda's mother battled with regret and alcoholism.

Urged by their parents to take a different path, both Jack and Linda committed themselves to scholarly success. For Jack, this meant working full time in a grocery store while pursuing dual undergraduate degrees in chemistry and engineering at Lamar University in Texas. By the time he arrived at IU, he had already distinguished himself as one of very few scientists with the engineering skills to manipulate unwieldy scientific instruments.

His efforts to improve this technology earned him prestigious positions in chemical measurement research. He went on to found a successful laboratory equipment company, later starting one of Silicon Valley's first high-tech venture capital firms, Vanguard Ventures.

Linda was similarly enterprising in pursuing her dreams. Possessed by wanderlust but lacking the financial means to travel, she became a stewardess with American Airlines. In addition to taking her around the world, the company also paid for her graduate studies in counseling at San Francisco State University. This education, combined with her airline experience, gave her the skills for the work she has found most meaningful: volunteering as a hospital liaison between surgical teams and patients' families.

Now approaching their 50th wedding anniversary, the Gills are determined to leave a legacy that extends the reach of higher education. Jack continues to teach at numerous universities, including Stanford, Harvard, MIT, and Rice. Meanwhile, the Gill Foundation has supported scholarships and research, clinical programs, and centers of excellence at the 11 universities attended by the Gills and their four children.







"This is a story about how a compelling theme attracts world-class scientists."

JACK GILL

A History of the Gill Center

The Gill Center's most meaningful work has occurred over the past 15 years, but its origins began in the 1960s, when Jack Gill was earning his PhD in organic chemistry at Indiana University under the direction of Professor Marvin Carmack.

Jack brought to his studies an unusual affinity for instrumentation, having double majored in chemistry and engineering as an undergraduate at Lamar University in Texas. At IU, he found himself tinkering with the instruments in the chemistry laboratories, making adjustments to improve their performance and user-friendliness. This ability to not only operate but also improve lab equipment led to a distinguished and pioneering career in chromatography and lab automation. Jack later parlayed this experience into outstanding success as a Silicon Valley venture capitalist in high-tech entrepreneurship.

Three decades after his departure from Indiana University, Jack and his wife, Linda, had turned their attention to leaving a legacy through philanthropy. In 1997, they established the Gill Foundation of Texas, focused on supporting higher education. The Gills began exploring different ways to maximize their impact, endowing chairs at IU in music and business among other, similar gifts to their respective alma maters. The couple settled on three areas of focus: scholarships for students in the STEM disciplines (science, technology, engineering, and mathematics), centers of excellence in technical fields, and interdisciplinary collaboration.



"The Gill Center is working at the next big frontier, focusing on aspects of neuroscience that can significantly impact people's lives." JACK GILL

RESPONDING TO IU'S 1998 CAPITAL CAMPAIGN

Meanwhile, the dean of the IU College of Arts and Sciences, Morton Lowengrub, was embarking on a capital campaign. As an expert in applied mathematics and computing, Lowengrub was sensitive to the critical importance of obtaining accurate measurements and eager to capitalize on the rapid technological advances of the decade. Recognizing an alignment with Jack's experience, he approached the esteemed alumnus about building a new interdisciplinary center focused on instrumentation and measurement.

"I was impressed with the dean's leadership and his interest in creating new collaborative programs," Jack says. "It was a great approach for reining in an alum who lived two thousand miles away."

The Gills' resulting \$5 million gift was the largest ever to have been designated for science at the College. Through its matching program, the College agreed to make annual contributions equivalent to the revenue from this endowment, immediately doubling the gift's impact.

THE GILL CENTER'S EARLY YEARS

In its original incarnation, the Linda and Jack Gill Center for Instrumentation and Measurement Science focused on bringing together researchers from many fields to improve instrumentation, develop new measurement applications, and train students in measurement science. Its mission statement emphasized "the understanding of complex biological processes" and "the multidisciplinary collaboration of scientists and engineers."

As a collaborative, interdisciplinary center of excellence, the Center embodied the Gills' philanthropic priorities, providing support for five chairs, five graduate fellowships, five undergraduate scholarships, and a biennual symposium to bring scientific luminaries to the Bloomington campus and bestow Gill Awards for their achievements.

Kicking off its activities officially in 1999, the Center held its first Gill Symposium the following year. Inaugural awardee Jonathan Sweedler, a professor of chemistry at the University of Illinois, was recognized for developing new measurement methods in analytical neurochemistry. His contributions have helped shape the study of neurochemical pathways using mass spectrometry-based approaches.

In the ensuing years, many of the College's science departments showed interest in helping to expand the Gill Center, including chemistry, biology, physics, and geological science. However, the Center encountered challenges in recruiting its chairs. The difficulty lay in establishing a sufficiently cohesive identity that would resonate with scientists from different backgrounds.

NEUROSCIENCE: FOCUSING ON THE NEXT FRONTIER

A shift in focus provided the necessary appeal.

During the time that Kumble Subbaswamy was dean of the College, the Center was renamed in 2003 as the Linda and Jack Gill Center for Biomolecular Science, retaining its emphasis on investigating biological processes and facilitating interdisciplinary collaboration but newly prioritizing molecular neuroscience.

The Center's new strategy was to "address fundamental questions of nervous system function in health and disease," stated Professor of Psychological and Brain Sciences George Rebec in the Gill Foundation's 2003 newsletter. "Multiple molecular measurement techniques will probe neuron operations from gene expression to memory circuits. At the core of this effort will be the recruitment of faculty members whose research will define the state of the art in brain science."

The move to neuroscience was a game changer. As Jack explains, this mission placed the Gill Center firmly at the forefront of life sciences, aiming toward discoveries with the potential to increase both lifespan and quality of life.

"If you look at how the most pressing health issues have been addressed through research, as a country we've spent billions on heart disease and cancer Joe Steinmetz with
Michael Walker at the
2006 Gill Symposium.

research. But what happens when we survive heart
disease and cancer? We get neurologic diseases,"
he says. "The Gill Center is working at the next big
frontier, focusing on aspects of neuroscience that can

RECRUITING THE FIRST GILL CHAIRS

significantly impact people's lives."

In its first year under the new arrangement, the Center successfully recruited its first Gill Chair, biochemist Richard DiMarchi. Coming from a position as vice president in the research laboratories of the pharmaceutical giant Eli Lilly and Company, DiMarchi brought two decades of experience in translating biomolecular science into groundbreaking peptide-based therapies.

1963

JACK GILL graduates from IU, with a PhD in organic chemistry



1997

Gills gift **\$5 MILLION** to establish Linda and Jack Gill Center for Instrumentation and Measurement; College pledges to match endowment proceeds

2000

First GILL SYMPOSIUM and GILL AWARD **200**3

Renamed to LINDA AND
JACK GILL CENTER FOR
BIOMOLECULAR SCIENCE,
with neuroscience focus

Gill Chair RICHARD DIMARCHI recruited from Eli Lilly and Company





DiMarchi says of his motivation to leave industry for the Gill Center appointment, "What made it a great opportunity was the spirit of invention. You have to applaud Jack and Linda Gill for their understanding of what could be achieved by focusing on making fundamental discoveries that fuel the advancement of society."

It was also in 2003 that Michael Walker first visited the Gill Center. Serving at the time as the chair of Brown University's psychology department, Walker came to Bloomington as a Gill-sponsored colloquium speaker to share his discoveries regarding the endocannabinoid system's role in regulating pain.

Walker's encounter with the Center convinced him that it would be an excellent environment in which to nurture his pioneering explorations. The following year, he became a Gill Chair and the Center's director. Mackie, who had collaborated extensively with



ABOVE: Andrea Hohmann, John McPartland, Ken Mackie, Michael Walker, and Susan Huang in California, 2002.



Walker and was then at the University of Washington, recalls hearing from Walker upon his arrival at IU.

"He was so excited," Mackie says. "It was at the time that Google Earth was just coming out, and he sent me images of Bloomington in response to my teasing that Indiana was all cornfields."

GROWING THE VISION

In fact, the picturesque limestone campus depicted in Walker's screenshots was already evolving to accommodate the growing Gill Center. A new building was planned, Multidisciplinary Science Building II (MSBII), which would allow the Gill scientists and students who were scattered among several buildings to share a dedicated space within one state-of- the-art facility.

As MSBII took shape, so too did Walker's vision for the Gill Center. In 2006, he hired Misty Theodore

to manage the Center's day-to-day operations and expand the Symposium.

"I knew this was the beginning of something that was destined to grow," recalls Theodore, who served as the Gill Center's program manager for nearly 12 years. "Our objective was clear: to develop a renowned center where great science would happen. Very quickly, it blossomed."

That year's Symposium was a huge success, honoring Gill Awardee Carla Shatz, who was then the chair of the Department of Neurobiology at Harvard Medical School and now heads Stanford's interdisciplinary Bio-X program. Shatz recalls of her visit, "It was just so much fun. There was a big party and reception. Things like that are really important — to get outside the lab and spend time together."



2004

Gill Chair MICHAEL
WALKER recruited from
Brown University

2005

RICHARD DIMARCHI named Central Indiana Corporate Partnership Innovator of the Year 2006

GILL SYMPOSIUM expanded to an annual event

2007

SECOND GILL AWARD created for Young Investigators

Jack Gill appointed IU TRUSTEE by Governor Mitch Daniels

Gill Chair **KEN MACKIE** recruited from University of Washington





SPIRIT OF CAMARADERIE

This spirit of connection and camaraderie came to define the growing Gill Center. Mackie, won over by Walker's enthusiasm, came on board as a new Gill Chair in 2007, bringing his renowned expertise in the endocannabinoid system. That same year, a Young Investigator Award was added to the Symposium to promote early-career scientists. Walker also began the process of recruiting Cary Lai, an expert in nervous system development who was then at The Scripps Research Institute.

"To me it was exciting to join a team of neuroscientists working on a collection of problems that were a little outside the box," Mackie says. "It was also a great draw that because of the funding provided by the Gill endowment and the College I would be able to think more deeply about those problems without the constant grant pressure."

Lai concurs, citing both the funding support and the interdisciplinary nature of the Center as key factors in his recruitment. "Neuroscience is so broad that it's hard to get all the specializations into one lab," he says. "In many cases you really need to collaborate, and the structure at the Gill Center is designed to facilitate that."

Tragically, Walker died unexpectedly of a heart attack in 2008. Mackie stepped into the director position, and the following year MSBII opened its doors.

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"It was exciting to join a team of neuroscientists working on a collection of problems that were a little outside the box." KEN MACKIE

A DEDICATED HOME IN MSBII

Finally in its own purpose-built space for the first time, the Gill Center occupied parts of the first and second floors, including offices for Gill Chairs, research scientists, postdocs, and graduate students and laboratories to accommodate a range of scientific approaches. Crucially, MSBII also featured communal areas for meetings and informal interaction.

Collaboration was "designed into the building," says Lisa Pratt, who served as associate executive dean of the College before joining NASA as its planetary protection officer in 2018. Pratt was instrumental in MSBII's design and construction. "How lucky we were to be able to design for collaboration and creativity" she says.

"The building has a great personality," adds
Theodore. "It's a very open, welcoming type of space.
Everyone has access to each other. When we moved
in, I really felt like we had a home."

As director, in addition to upgrading laboratory facilities through state-of-the-art equipment and infrastructure, Mackie focused on building a scientific collective characterized by synergy and innovation. To strengthen the Center's scientific network and amplify its impact, Mackie devoted himself to establishing connections with leading neuroscientists throughout the nation and abroad. Enhancing the Center's visibility helped to both encourage collaborations with other leading neuroscience programs and spark interest in the Gill Center among potential recruits.

GROWING INTEREST AND COMMITMENT

Gill Chair Andrea Hohmann was the first recruit Mackie brought on board. A former graduate student of Walker, Hohmann came to the Gill Center in 2010 from the University of Georgia. She brought expertise in pain signaling and a great depth of knowledge of the endocannabinoid system, firmly establishing the Gill Center as a leader in endocannabinoid studies.

"Coming to the Gill Center for me was an opportunity to do more vibrant and exciting science and expand the limits of what we would be able to accomplish," Hohmann says. "Because of the focus on collaboration, the laboratory space, and the research funding that was provided, I knew we could work on high-risk/high-impact research."

The arrival on campus of College of Arts and Sciences Dean Larry Singell in 2011 added greater momentum to the Center's growth. Singell took a particular interest in the Center, reaching out to Jack and Linda Gill to discuss the fulfillment of their vision and committing additional College resources for salaries and start-up packages for incoming Chairs.

"It was immediately clear to me how important the Center is for our campus," Singell says. "It's in a unique position, having an interdisciplinary set of faculty members focused on a critical topic. That is a very difficult mission to achieve, and the Gill Center has succeeded in establishing itself as a go-to place for neuroscience research."

2008

KEN MACKIE becomes Gill Center director

Gill Chair CARY LAI recruited from The Scripps Research Institute

2009

Gill Center consolidates into dedicated space in the MULTIDISCIPLINARY SCIENCE BUILDING II



2010

Gill Chair ANDREA HOHMANN recruited from University of Georgia



2015

KEN MACKIE receives IU College of Arts and Sciences Distinguished Faculty Award RICHARD DIMARCHI elected as a member of the National Academy of Medicine



"The Gills have created a research environment so supportive and warm that it makes other scientists envious." DAN TRACEY



A REPUTATION FOR EXCELLENCE

Under Mackie's leadership, the Gill Center's reputation grew expansively. In the five years that followed the move into MSBII, the group obtained grants from federal funding agencies and industry partners totaling more than \$16 million. Collaborations flourished with other national and international institutions, and chairs delivered more than 60 invited talks and lectures to scientific

audiences worldwide.
The Center also housed
an increasing number of
students, with nearly 150
undergraduate, graduate,
and postdoctoral researchers
trained in the five-year
period.

Mackie also focused on strengthening the neuroscience community within and beyond the IU Bloomington campus. The Gill Symposium, in addition to recognizing a Distinguished (senior) and Transformative (junior) annual awardee, added awards for student theses and outstanding images produced as part of

neuroscience research. The Center also partnered with the Program in Neuroscience and several IU College of Arts and Sciences departments to bring in more than 50 neuroscientists from other institutions to deliver seminars.

"Having that type of exposure to the latest and greatest science benefits both the faculty and the students," says Mackie. "Most of our students don't have the means to travel to conferences, but through

these activities they get direct access to leading neuroscientists. It has also been a great conduit for further collaborations and training opportunities."

NEW GILL CHAIRS BRING NEW ENERGY

It was through a Gill Awardee that Mackie was introduced to Dan Tracey, a neurobiologist at Duke University whose work with *Drosophila* fruit flies reveals key insights about pain and the sensation of touch. Recognizing both the Center's alignment with Tracey's pain expertise and the opportunity to expand the group's skill set through his *Drosophila* focus, Mackie brought Tracey on board as a new Gill Chair in 2015.

As with the other Gill recruits, Tracey was drawn in by the Center's unusually collegial atmosphere. "The Gills have created a research environment so supportive and warm that it makes other scientists envious," he says. "This is an anomaly in the world of research. It's the opposite of the typical competitive environment."

This collegiality also enticed Baylor College of Medicine's Hui-Chen Lu, whose expertise in the development and maintenance of neural circuitry prompted Mackie to recruit her as a Gill Chair in the same year as Tracey. While at Baylor, Lu had collaborated with Mackie on several projects investigating the effects of cannabinoids on neuronal development.

"The opportunity to work more closely with Ken and the other Gill Chairs was extremely appealing," she says. "To be at the forefront of neuroscience you have to be multidisciplinary and you have to be collaborative. Not every institution is like that, but here is a group of people that like to share. We truly believe this is the way it should be."

With its full complement of Gill Chairs recruited, the Center's productivity grew exponentially. Singell observes, "We now have a collection of scholars at the Gill Center that any institution would be proud of. They are successful by any measure that you could use for scientific success – publishing in the best outlets, obtaining federal funding, and affecting research outside the Sample Gates by influencing the field through their leadership."

GILL DIRECTOR PASSES THE TORCH

Jack credits Mackie with bringing the Center to its full fruition. "Ken Mackie's focus was squarely on building synergy. All the Chairs he brought in were chosen to balance the others in such a way that each brought expertise in a complementary aspect of brain science. It took great patience, determination, and focus on his objective to get there. The secret sauce is every year getting better speakers, ever more comprehensive collaborators, and greater relevance to the problems of our time."

Linda Gill notes, "For a center of excellence to succeed it has to have champions. After a period of slow growth, having the right people pushing the project made a big difference."

The Center honored Mackie in 2017 for his decade of leadership as Mackie passed the director's torch to Lu. Now guiding the Gill Center into a new era of its history, Lu emphasizes that the Gills' original vision and continuing involvement remain at the Center's heart.

"Jack and Linda always keep in touch with us, and are a huge part of the annual symposium," she says. "They have stayed so invested in our success, which is a great motivation. Jack always wants to push us further, just like I push my students. Ultimately it is his vision that has made all our work possible."

2015

Gill Chair **HUI CHEN LU** recruited from Baylor College of Medicine

2015

Gill Chair **DAN TRACEY** recruited from Duke University

2016

RICHARD DIMARCHI ranked among world's top three translational scientists

KEN MACKIE named a fellow of American Association for the Advancement of Science

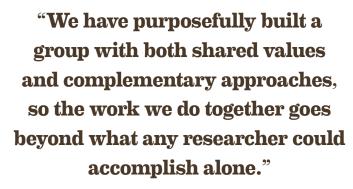


2018

HUI CHEN LU appointed Gill Center director GILL CENTER
CELEBRATES 20TH
ANNIVERSARY







HUI-CHEN LU

The Gill Center Today

Walking into a center for excellence in neuroscience, you might expect a clinical atmosphere, with researchers tucked silently behind locked doors. Instead, entering the Linda and Jack Gill Center for Biomolecular Science, one is enveloped by a sense a warmth, from the smiling portrait of the Gills to the cheerful conversations in halls and doorways. Soft and comfortable seats invite visitors to contemplate the bountiful artwork displayed on the walls, while a colorful design scheme of maroon and melon adds to the ambience of creativity.

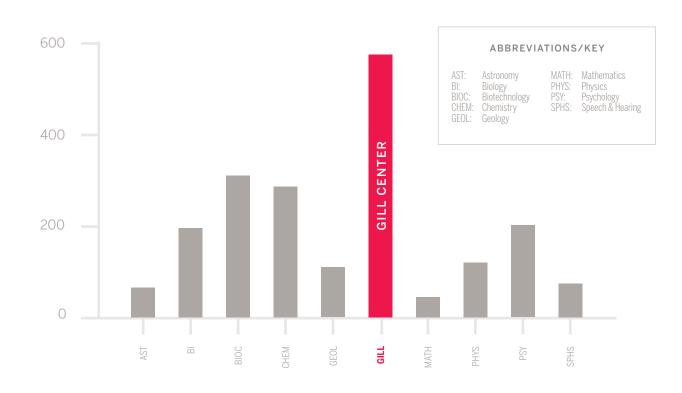
Venture deeper into the Center's web of connected laboratories, and you'll find that this convivial setting supports revolutionary science across a range of approaches, from electrophysiology measuring activity within single neurons to animal behavior studies investigating effects of potential therapies. Through an interdisciplinary mix of expertise in molecular biology, genetic engineering, immunology, endocrinology, neurophysiology, neuroanatomy, and pharmacology, this tight-knit team is pioneering innovations in critical realms of neuroscience including pain, neurodevelopment, and neurodegeneration.

Their research holds promise for better understanding and addressing a wide range of issues including autism, Alzheimer's disease, chronic pain and itch, anxiety, schizophrenia, obesity, and addiction.



Measured in terms of annual grant dollars per tenuretrack faculty member, the Gill Center's funding rate far exceeds that of any other department or center on campus.

GRANT DOLLARS (\$1000) PER TENURE-TRACK FACULTY (2017)



Collaboration, says Gill Center Director and Chair Hui-Chen Lu, is the key to these insights.

"Putting leading neuroscientists with different backgrounds in such close proximity allows for incredible intellectual exchange," she says. "We have purposefully built a group with both shared values and complementary approaches, so the work we do together goes beyond what any researcher could accomplish alone."

These shared values center on a commitment to improving lives by uncovering the core processes of the nervous system. "We're all working for common goals," Lu says. "We don't just want to see what goes wrong in the nervous system. We're committed to understanding at a fundamental level how the system works and how we can support it."

To do so, five Gill Chairs and a growing group of research scientists, technicians, students, and postdoctoral researchers bring together a synergistic set of approaches that collectively yield exciting revelations in our evolving understanding of the brain.

A WEB OF SYNERGIES

All five Gill Chairs use molecular and biochemical approaches to investigate how the brain and behavior are influenced by genetics, physiology, and environmental factors including external chemicals, experience and learning, and stress and injury. Chairs Hui-Chen Lu, Ken Mackie, Andrea Hohmann, and Dan Tracey study neuronal signaling and circuits to better understand how neurons communicate with one another. These networks are vital for learning, memory, and other types of cognitive function, as well as relaying messages such as pain signals from different parts of the body to the brain.



Mackie, Lu, and Hohmann also bring well-established expertise in the endocannabinoid system – a vital internal system involving compounds similar to those found in cannabis – making the Gill Center a global leader in the emerging field of endocannabinoid studies. This system plays key roles in pain response and a wide range of other processes including immune function, metabolism, stress response, and pre- and post-natal brain development.

While Mackie, Hohmann, and Tracey share a focus on pain signaling, they do so through different approaches that allow for validation across multiple avenues of study. Much of Mackie's research takes place at the cellular level, investigating activity within and among neurons in response to specific stimuli. In contrast, Hohmann's research focuses on animal models of pain and validation of novel treatments, complementing Mackie's work by examining how pathological pain states and novel therapies affect the behavior and neural function of rodents (whose nervous systems are very similar to those of humans). Tracey adds the model of Drosophila fruit flies, whose fully sequenced genetic code (most of which is reflected in similar human genes) allows for rich investigations by isolating genes responsible for pain responses. The short life

span of fruit flies also promotes large-scale studies of issues such as traumatic brain injury, a current area of interest for Tracey.

Tracey also investigates other types of somatosensation – the physical sensations associated with touch, pressure, and temperature – an area of inquiry he shares with Hohmann and Lu. Like Hohmann, Lu utilizes mouse models, bringing particular expertise in the formation and maintenance of neural circuitry throughout the life cycle. Her interest in the long-term health and function of neural circuits is shared with Gill Chair Richard DiMarchi, whose biochemistry expertise is contributing to the development of neuroprotective therapies. These therapies show promise in treating diseases like Alzheimer's and Parkinson's as well as traumatic brain injury, a focus DiMarchi shares with Tracey.

Mackie and Hohmann share DiMarchi's dedication to exploring the therapeutic potential of their discoveries through partnerships with biotechnology and pharmaceutical companies. These collaborations enable the development and testing of compounds tailored to treat dysfunctional or degenerative conditions while minimizing unwanted effects from drug treatment. For Mackie and Hohmann, these

"We're not competing with each other for resources, which puts us in a wonderful position to collaborate."

HUI-CHEN LU

efforts center on the endocannabinoid system, particularly its role in pain signaling. In a recent collaboration, Mackie and Hohmann demonstrated that cannabinoids can counteract opioid tolerance in mice, suggesting that patients may be able to continue to receive pain relief from opioids without needing to increase their dosage over time. This research has exciting implications for combating the epidemic of opioid addiction.

Historically, DiMarchi has focused on the endocrine system, which produces and regulates hormones. However, the Gill Chairs' work is revealing interesting overlaps between the researchers' respective areas of focus: Mackie's studies have demonstrated positive effects on metabolism from certain cannabinoids, while DiMarchi's therapies targeting insulin regulation appear to have additional beneficial effects on brain function.

SMALL CENTER, LARGE-SCALE SUCCESS

These synergies result in tremendous productivity and scientific impact. In the past decade, Gill Chairs have published more than 200 studies that have been cited over 6,000 times by other researchers. This highly influential work has attracted extraordinary external funding. More than \$40 million in funding from sources like the National Institutes of Health, National Science Foundation, private foundations, and pharmaceutical partners has been granted to Gill Center researchers since the center's establishment. Measured in terms of grant dollars per tenure-track faculty member, this funding rate far exceeds that of any other department or center on campus.

Lu emphasizes that these successes would not be possible without the extraordinary support given to

Gill Center researchers. In addition to salaries and start-up packages for establishing their labs, provided by the College of Arts and Sciences, revenues from the Center's endowment, which originated with a \$5 million gift from Jack and Linda Gill, are matched by the College to supply Chairs with unrestricted seed funding to pursue new research directions and collaborative opportunities.

"We have a type of freedom you don't usually find among scientists," Lu says. "The support we receive allows us to rapidly explore new ideas and determine their viability before seeking larger grants. This means we're less stressed for survival, so we can be comfortable expanding our horizons and testing out new ideas that push the field forward. It also means we're not competing with each other for resources, which puts us in a wonderful position to collaborate."

COLLABORATIONS ACROSS THE LABS

This open atmosphere envelopes all the Gill Center's members, from the Chairs and senior scientists to the dozens of undergraduates working in their labs. Far from remaining isolated in their respective laboratories, research assistants and students routinely exchange information and ideas across their different areas of specialization.

For example, each month, the Chairs host a Journal Club, at which a student or postdoctoral researcher reads and presents a recently published neuroscience article considered to be groundbreaking. Over a lunch that the Center provides, the Chairs, research scientists, and students discuss the article's implications for their own research directions and the broader neuroscience field.

"The Journal Club is just one way we share ideas and information with everyone else in the Center," says Jim Wager-Miller, a research scientist who manages Mackie's lab and much of the Center's shared equipment. "The interactions I've seen here are different than in other research environments I've been a part of. Science can be very competitive, very secretive. But at the Gill Center, labs with different specialties are more willing to help each other, and this makes it possible confirm observations using multiple techniques that may not be available in any one lab."

2018 GILL RESEARCH SCIENTISTS



AMEY DHOPESHWARKAR, PhD ASSISTANT SCIENTIST

RESEARCH INTERESTS: Cannabinoid and novel cannabinoid receptors, GPCR signaling, *in vitro* assay development, high-throughput drug screening, drug discovery



JUI-YEN HUANG, PhD ASSISTANT SCIENTIST

RESEARCH INTERESTS: Cortical brain circuitry formation, neurobiology, redox biology, neurodegenerative disease



ANNA KALINOVSKY, PhD ASSISTANT SCIENTIST

RESEARCH INTERESTS: Molecular and cellular mechanisms underlying neural circuit assembly and function, role of cannabinoid signals in cerebellar circuits and their specific behavioral outputs



YVONNE LAI, PhDSENIOR SCIENTIST

RESEARCH INTERESTS: Developing novel therapeutic strategies for the treatment of neurological disorders using disruptors of protein-protein interactions



STEPHANIE MAUTHNER, PhD

ASSOCIATE SCIENTIST

RESEARCH INTERESTS: How sensory neurons detect painful stimuli, mechanosensory transduction machinery, ion channel function, and ion channel trafficking in pain neurons



PIOTR MROZ, PhD ASSISTANT SCIENTIST

RESEARCH INTERESTS: Peptide structure-activity relationships, chemical biotechnology, combinatorial peptide therapeutics, novel treatments for metabolic



ALEX STRAIKER, PhD SENIOR SCIENTIST

RESEARCH INTERESTS: Physiology of cannabinoid receptors in neurons, cannabinoids in synaptic transmission, cannibinoids in ocular health



JIM WAGER-MILLER, MS ASSOCIATE SCIENTIST

RESEARCH INTERESTS: Cellular signaling methods development, best practices for undergraduate lab education



FA ZHANG, PhD SENIOR SCIENTIST

RESEARCH INTERESTS: Peptide structure-activity relationships, chemical biotechnology, combinatorial peptide therapeutics, novel treatments for metabolic disease



COLLABORATIONS ACROSS THE UNIVERSITY

Collaborations become still more interdisciplinary through Gill researchers' partnerships with other Indiana University scholars. In addition to working with colleagues in the department of Psychological and Brain Sciences such as neuroscientists Heather Bradshaw and Jonathan Crystal, Gill Chairs regularly collaborate with faculty members in the College's biology and chemistry departments, and the Center is closely involved in the university-wide push to address addiction as part of IU's Grand Challenges initiative.

Projects with the IU School of Medicine also extend the Gill Center's reach; for example, senior scientist Yvonne Lai launched the startup Anagin with the School of Medicine's Anantha Shekhar. The company builds on Lai's previous research as well as that performed at the Gill Center to develop new therapies, including Lai and Hohmann's collaborative research on protein-protein interactions during pain signaling.

Other IU partnerships use creative approaches to communicate Gill Center findings through visual media. Tracey works with Indiana University -

Purdue University Indianapolis computer scientist Gavriil Tsechpenakis to generate images of the intricate branching patterns of neurons responsible for nociception, the detection of potentially harmful stimuli. Senior scientist Alex Straiker has worked with College Fine Arts faculty members Jawshing Arthur Liou and Betsy Stirratt to create installations interpreting his data on the endocannabinoid system; Liou's video was featured in Hong Kong's Art Basel event and Stirratt's mixed-media exhibit traveled to the Esther Klein Gallery in Philadelphia.

COLLABORATIONS ACROSS THE WORLD

While such projects help to engage new audiences with Gill research, the Center's influence is most strongly felt in the global neuroscience community. In addition to running the annual Gill Symposium, the Gill Chairs collaborate extensively with researchers throughout the United States — notably at Stanford University, the University of California at Berkeley, Northeastern University, and Cold Spring Harbor Laboratory — and in institutions abroad, including neuroscience research centers in Finland, France, Hungary, and China. Chairs frequently deliver

invited talks at national and international science events. Moreover, the Gill Chairs provide scores of neuroscientists with essential and difficult-to-obtain tools for research.

"We are widely known for sharing our unique resources, including protocols, antibodies, and mouse models," says Lu. "Every week, we are Fed-Exing reagents out to other scientists."

Likewise, the Center welcomes visiting scholars eager to learn cutting-edge techniques and methods. Lu has recently hosted researchers from Brazil, Japan, and China, and Mackie has brought several European scholars to Bloomington.

"It's an excellent two-way exchange," Lu says. "In Brazil, for example, the education system is strong and the intellectual capability is high, but they don't have access to our state-of-the-art equipment. Working with us, these international researchers benefit from our technical capabilities, and our students are exposed to different ways of thinking and new connections for their research networks."

A FOUNDATION OF FRIENDSHIP

This pervasive emphasis on strengthening connections has come to define the Gill Center's distinctive character. As collaborations continue to expand at the local, national, and international levels, a focus remains on ensuring that Center researchers have every opportunity to engage with one another.

Mirroring the interconnectivity of the nervous system itself, the Center continually seeks to reinforce ties between its researchers – whether in joint grants and projects or through its frequent potlucks, holiday parties, and birthday celebrations.

"We really are all good friends," says Lu. "And knowing each other so well makes it that much easier to work together. You have less hesitation to bring up new ideas or suggest a change in direction that could lead to a breakthrough."

GILL CHAIR COLLABORATIONS ACROSS THE WORLD





Hui-Chen Lu

Money was scarce in Hui-Chen Lu's household when she was growing up in Taiwan in the 1970s. Toys were rarely purchased, so Lu made her own, crafting figurines from found objects like paper scraps and cherry pits.

Her attention turned to science when, at ten years old, she was tasked with assisting in her grandmother's bookshop. There she discovered a series that captivated her imagination.

"Instead of fairy tales, the books that intrigued me were the ones we called 'curiosity books,'" she recalls. "They had titles like, 'Why Does the Rainbow Have Seven Colors?"

With this interest awakened, Lu was delighted when her middle school biology teacher led her students outside to find specimens.

"We would chase after butterflies and different kinds of insects," she remembers. Examining their wings, eyes, and bodies, she says, "I began to appreciate the diversity of patterns in the natural world."

Although the cultural expectation at the time was for young women to become housewives, Lu was determined to find her own path as a scientist. After completing daily chores of cleaning, laundry, and caring for the family, she would push herself to excel in her academic coursework and prepare for college entrance exams.

Her motivation paid off when she was accepted to pursue a degree in zoology at National Taiwan University. In addition to acquiring a foundation "You can't get
frustrated by critics
or limitations. If you
are motivated and
like what you do,
you will find a way."

in molecular and biochemical science, she gained practical experience in the lab, where she learned the key lessons of "failure, frustration, and how to seek help," she says.

Unexpectedly, Lu also discovered that her years of housework served her exceptionally well. "To succeed as a scientist, you need to have good hands," she explains. "You need accuracy so you don't destroy things. Doing chores from an early age gave me those fine motor skills."

Precision became especially critical when Lu pursued an undergraduate research opportunity to work with fruit flies at the Institute of Molecular Biology at Academia Sinica in Taiwan. Although the institute was an hour and a half away from her university (by scooter, through Taipei traffic), the training she acquired in genetic engineering was so valuable that she decided to stay on as a technician for a year after graduation.

The timing proved fortuitous, as the following year the Baylor College of Medicine in Houston offered its first developmental biology PhD program. Lu joined an initial class of just three students, learning about embryonic development by examining fertilized chicken eggs.

"I would make a little hole at the top of the egg and cover it with Scotch tape," she recalls. "Every couple of hours I would pull back the tape and see what had happened."

During her first year in the PhD program, as a rotation student under Gregor Eichele, Lu investigated how morphogen gradients and Hox genes control the body's front-to-back and head-to-tail axes. While pregnant with her first child, Lu demonstrated the evolutionary conservation of Hox genes by implanting a chicken gene into a fruit fly in collaboration with IU Bloomington College of Arts and Sciences biologist Thomas Kaufman.

Starting a family while in graduate school brought not only practical challenges – there was no nanny budget in her stipend – but also risks related to her career growth. Juggling the demands of work and family required help from friends and colleagues in Houston, yet as Lu explains, "Funding agencies expect you to move to different institutions," she says. "How else can you prove you are gaining new skills and independence?"

Drawing on the resourcefulness that served her in childhood, Lu resolved to advance her career while remaining at Baylor. She diversified her training through a postdoc under neuroscientist Michael Crair. As her two sons began reaching developmental milestones, Lu grew increasingly interested in brain development. When she took on an assistant professorship in the same department, objections from traditional funders led her to a bridge grant from the American Heart Association to produce pilot data. This creative approach succeeded: the resulting data earned Lu her first NIH grant, which enabled her to become a tenure-track independent investigator.

"I had to take a very frugal approach, borrowing equipment from colleagues and collaborating extensively – which in the end made a higher impact," Lu says.

Those studies, which used mouse models to examine synaptic transmission, caught the attention of a private foundation with an interest in neurodegeneration. After speaking with their representatives, "I began to see that aging is just the other end of development," she says.

Approaching neurodegeneration through the lens of neurodevelopment enabled Lu to ask ground-breaking questions, such as how the body maintains the health of its neuronal networks and how "critical windows" of neuroplasticity are opened at specific points in time. In her subsequent posts at Baylor's Neurological Research Institute, and now at the Gill Center, Lu explores neural circuits over the course of the lifespan, from the effects of different inputs on neural circuit formation to the factors that can increase or prevent neurodegeneration. She is also investigating biomarkers of brain health: Lu's mouse studies indicate that elevated microRNA levels appear in the blood prior to symptoms of numerous ailments, including inflammation and Alzheimer's disease.

Summing up her history of defying expectations and turning challenges into advantages, Lu says, "You can't get frustrated by critics or limitations. If you are motivated and like what you do, you will find a way."

Ken Mackie

In neuroscientist Ken Mackie beats the heart of a physician.

His substantial contributions to our current understanding of the endocannabinoid system – which plays significant roles in a wide range of neurological processes, including memory, pain, and metabolism – were influenced by 15 years of clinical experience as an anesthesiologist in a Level-1 trauma center in Seattle.

"Well over half my patients tested positive for THC on their drug screens," he says, referring to the primary psychoactive component of cannabis. "It was clear that many people were using cannabis to try to achieve medical benefits, including managing their pain. For some patients it seemed to be effective, but it wasn't clear how these drugs were working in the body. I wanted to answer this question."

Throughout his time as a clinician, and now in his role as a Gill Chair, Mackie has been a leading force investigating the biological mechanisms and effects of different types of cannabinoids (compounds like those found in cannabis). In addition to uncovering intermediate and long-term effects of exposure to



THC and other cannabis-derived compounds like cannabidiol (CBD), his research has also helped describe the presence and function of cannabinoid molecules produced by the body, known as endogenous cannabinoids or endocannabinoids. His work highlights the promise of new therapeutic applications targeting the endocannabinoid system to address a range of problems, including chronic pain and obesity, while also revealing potential risks associated with THC exposure.

Mackie's first cannabinoid breakthrough came serendipitously. Following his residency, Mackie joined the lab of Bertil Hille at the University of Washington, whose research focused on signaling activity within neurons. Hille was investigating ion channels, gateways in the membranes of cells that allow passage of ions in and out of cells.

"That was right at the time that the first cannabinoid receptor had been cloned," Mackie recalls. "So while it had been cloned, we didn't know what the receptor did."

Working in the Hille lab, Mackie solved this mystery by demonstrating that activation of cannabinoid receptors kept calcium ion channels from opening, thus suppressing neurotransmission and communication between neurons. In effect, cannabinoids serve to "block a message," Mackie explains. For example, a cannabinoid might interrupt a pain signal before it was relayed to the central nervous system.

"Opiates do exactly the same thing to calcium channels and neurotransmission," he adds, "but cannabinoid receptors are expressed on different neurons." Importantly, these receptors are absent from neuronal networks responsible for critical respiratory functions – so, unlike opiates, cannabinoids cannot cause a person to stop breathing. This distinction is one reason cannabinoids may offer an attractive alternative to opiates for pain management.

Mackie's more recent research at the Gill Center reveals another difference between opiates and cannabinoids: while opioid drugs mimic the activity of the body's endogenous opiates (endorphins), the components of

"A lot of people use cannabis; understanding and communicating its effects is an important social issue."

cannabis have a more nuanced relationship to the body's endogenous cannabinoids, either enhancing or blocking their effects. A better understanding of these distinct processes is critical for developing effective therapies; for example, it appears that some negative effects of prenatal THC exposure can be countered with drugs that enhance endocannabinoid signaling.

One of the most important contributions of Mackie's lab is to investigate the separate and combined effects of the cannabinoids THC, which is psychoactive, and CBD, which is not. While some negative effects can be attributed to THC, CBD appears to counteract many of them. In addition, CBD appears to have other health benefits, such as controlling inflammation and reducing epileptic seizures. Moreover, THC may offer its own benefits: Mackie's group has demonstrated that obese mice treated with THC reliably lose weight.

Mackie's overall goal, he says, is for the results of his lab's research to promote informed policies and programs that provide an appropriate response to both the widespread use of cannabis and the potential for cannabinoid-based therapies.

"A lot of people use cannabis; understanding and communicating its effects is an important social issue," he says. "At the same time, we are finding ways to develop new cannabinoid medications that can improve both health and quality of life. It's an exciting time for the field."

Andrea Hohmann

Andrea Hohmann learned early in her career to set aside any squeamishness.

As a graduate student at Brown University, she would regularly visit slaughterhouses to obtain tissue samples, undaunted by the task of saw into cows' skulls to extract their brains and pituitary glands.

"The part that made me most worried was driving home," she remembers. "I was careful not to speed, because if a cop pulled me over, they would find a cooler full of brains packed in ice and bloodied saws and chisels."

The gore was a small price to pay for the chance to study neurotransmitter receptors in the lab of her mentor, Michael Walker (who later became the Gill Center's first director). It was there that Hohmann became interested in the endocannabinoid system, the body's own cannabis-like signaling system. Very little was known about the functions of this system when she first encountered it in the early '90s.

"It was an incredible opportunity to ask some basic questions that had not yet been asked," she says. At the time, Hohmann explains, there was a great deal of skepticism in the scientific community about whether cannabinoid compounds produced any true analgesic effects.

"Although there were animal behavioral studies showing a reduced pain response, the conventional wisdom in the pain field was that cannabis made the animals high so they didn't care about the pain, or it produced motor impairment and because of that they were not able to behaviorally withdraw from stimuli," she says.

Hohmann's persistence in the face of this skepticism was fueled by a determination to uncover processes that could point toward better pain treatments with fewer unwanted side effects.

Having seen both her parents suffer through cancer and chemotherapy and having worked



as a research assistant in alcohol and addiction studies prior to graduate school, she recognized the devastating shortcomings of opioid therapies that lead to tolerance, addiction, and withdrawal.

In order to bypass the criticisms of behavioral cannabinoid studies, Hohmann zeroed in on neurons,

asking whether cannabinoids suppress activity in the neurons that code information about pain and examining the impact of cannabinoids on neurochemical markers associated with pain signaling. This work, which she completed in Walker's lab, was the first to show that cannabinoids suppress the processing of pain information.

Her trailblazing investigations continued as a postdoctoral fellow under Miles Herkenham at the National Institute of Mental Health. Hohmann focused on mapping cannabinoid receptors within pain pathways and identifying the types of cells that contained them. She was part of the team that characterized the impact of genetic deletion of CB1 receptors, verifying that one type of receptor, CB1, is located primarily in the brain, while another type, CB2, is found mainly in the immune system.

At her subsequent post as an assistant professor at the University of Georgia, Hohmann turned her attention to the body's production of endocannabinoid compounds. She began by investigating stress-induced analgesia, the suppression of pain associated with exposure to physical or mental trauma.

"The phenomenon had been known since the 1980s, but it was classified into two types, opioid and non-opioid stress-induced analgesia, and no one had previously identified the transmitter system responsible for the nonopioid type," she says.



"Our approach to pain alleviation targets interactions between proteins that are only associated during a pain state, so it's far less likely to cause unwanted side effects." Hohmann's lab demonstrated that nonopioid stress-induced analgesia was mediated
by the release of endocannabinoids. Building
on this work with her collaborator Daniele
Piomelli at the University of California at Irvine,
she was able to uncover some of the processes
by which endocannabinoids are produced and
mobilized on demand in the body, as well as the
processes involved in their breakdown. These
studies established an enzyme involved in the
breakdown of the endocannabinoid 2-AG as a
previously unrecognized therapeutic target for
treating pain- and stress-related disorders.

Upon joining the Gill Center in 2010, Hohmann further expanded her repertoire of approaches, borrowing from the fields of drug abuse and pharmacology. This research has been critical in suggesting that cannabinoids may provide a valuable alternative to opioid pain medications without the risk of addiction. Additionally, Hohmann has also researched the potential benefits of administering cannabinoids and opioids in combination. In recent research, she has demonstrated that use of a compound targeting the CB2 receptor can prevent opioid tolerance, meaning that in the presence of the cannabinoid, the opioid will continue to block pain at the initial dose rather than requiring increasing dosages to remain effective. The same treatment also reduced symptoms of opioid withdrawal.

Presently, Hohmann is engaged in a new approach to pain alleviation that shifts the focus from neurotransmitters to proteins that interact within the neuronal cell during pain signaling.

"What's exciting about this approach is that it is so specific," she explains. "It targets interactions between proteins that are only associated during a pain state, so it's far less likely to cause unwanted side effects."

As Hohmann's work continues to evolve toward new techniques and directions, she emphasizes that, while she's glad to be done extracting cattle brains, she'll always be open to any scientific approach that will help her find answers to important scientific questions.



Dan Tracey

In the afternoons of the late 1970s, in the Buffalo suburb of Williamsville, New York, a small boy could be found gazing rapturously into the fish tanks of the local pet shop.

Awed and mesmerized, young Dan Tracey was known to spend hours observing and analyzing the fishes' behavior.

"I think I really annoyed the pet store owner with my incessant questions," he recalls.

Fortunately, his inquisitive nature was welcomed by his teachers, particularly his undergraduate mentor at SUNY Buffalo, Carol Berman. Under her guidance, Tracey swapped fish tanks for forests, writing about Berman's work on rhesus macaque monkeys in their natural habitat on the island of Cayo Santiago, Puerto Rico.

As enthralling as he found the monkeys, however, Tracey felt constrained by the limits of field research. "I was dissatisfied with the kinds of experiments you could do studying behavior with the macaques," he explains. "You just didn't have that much control over the environmental variables."

Seeking a more systematic approach to animal behavior, Tracey turned to genetics. During a master's program at Florida International University, he "became enamored with molecular biology," he says. 4

"It's a long road from a basic science discovery to a new clinical treatment, but it has to start with knowing how these systems work."

"I'll never forget the first time I saw DNA. I was hooked," he recalls. "I remember exactly where I was standing in the lab and who was with me. We put our sample through a procedure, and in the last step we added the ethanol and the DNA precipitated. I could actually see the DNA come out of solution. It was so incredible."

The link between DNA and animal characteristics captivated Tracey. His infatuation with gene expression took him to SUNY Stonybrook for a PhD, where he experimented with *Drosophila* fruit flies and *Xenopus* frogs.

Toward the end of his program, two events conspired to determine his future research agenda.

One was a tragedy: His grandfather died of lung cancer after months of terrible pain. It struck Tracey as outrageous that the only palliative offered was morphine.

"I was so surprised that we have made almost no progress in pain treatment," he says. "We're still relying on the opium poppy, as we have for thousands of years."

The second was a happy occurrence. At Stonybrook Tracey met his future wife, a doctoral student in neuroscience who brought him along on her professional retreats. On one such occasion, a professor explained how he measured pain response in rats by placing their tails on metal plates; the plates would be heated until the rats responded by flicking their tails.

"Right away, on our drive back, I started daydreaming about how I could study pain using flies," he says. "As soon as I got home, I conducted an experiment where I touched a fly larva with a

hot probe and, sure enough, it rolled away from the instrument."

It was the first step of a breakthrough. Tracey knew that if he could find mutants that did not respond to the probe, he could isolate fly genes for pain responses. By examining how the gene's expression translated into biological mechanisms, he could uncover new clues to the body's pain pathways.

Tracey tracked down his mutant in the Caltech laboratory of Seymour Benzer, an early genetics pioneer and Tracey's longtime idol. For his postdoctoral research, Tracey worked with his lab mates and a fly mutant they named Painless. The painless gene encoded a new type of ion channel that, when activated, could mediate certain types of pain sensation

Remarkably, an evolutionarily related channel is also found in humans (encoded as a gene known as TRPA1). A similar gene is present in very primitive animals as well – even unicellular organisms – suggesting that this type of pain response has been conserved through billions of years of evolution. In humans, it can be activated by many different types of noxious chemicals, even by chemicals that are structurally unrelated.

"Painless taught us a lot about how pain works," Tracey says. "The channel seems to have evolved in very early life as a way to protect against harmful chemicals."

In Tracey's subsequent studies as a faculty member at Duke University, he continued to follow the Painless trail to determine which cells housed the TRPA1 channels. He describes "really beautiful neurons" whose extensive branches enable nociception, the sensory response to potentially harmful stimuli (see cover image).

Now, as a Gill Chair, Tracey is expanding his *Drosophila* studies to better understand both nociception and mechanotransduction, the processes underlying the sense of touch. By focusing on genes and neurological mechanisms that are also present in humans, his research can both help explain behavior and also pave the way for future innovations in pain treatment.

"It's a long road from a basic science discovery to a new clinical treatment," he cautions, "but it has to start with knowing how these systems work."

THE GILL CHAIRS: PIONEERS IN NEUROSCIENCE

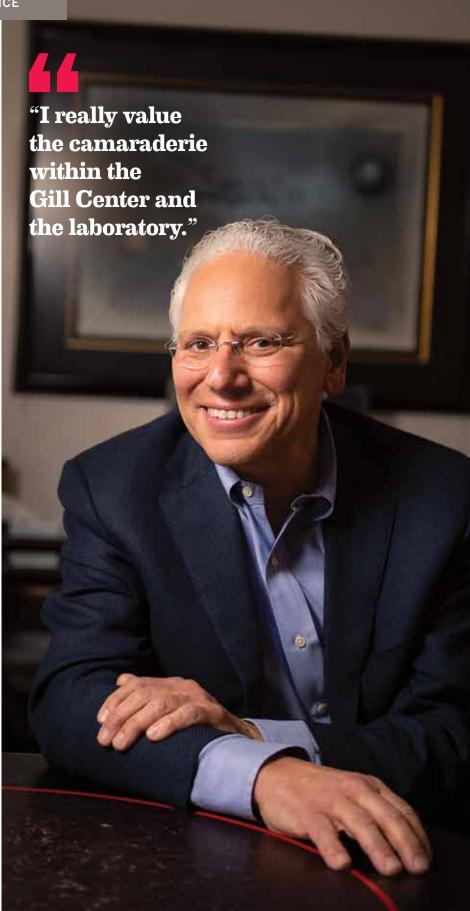
Richard DiMarchi

After four decades of innovation as a biochemist, Richard DiMarchi has amassed more than 100 patents,

co-founded five successful startup companies, and been inducted into the National Inventor's Hall of Fame and the National Academy of Medicine. His accomplishments include serving as vice president of leading-edge pharmaceutical companies such as Novo Nordisk and Eli Lilly, as a former chair of the College's chemistry department, and as an advisor to numerous life science firms. Despite all these titles and accolades, however, the most rewarding acknowledgement DiMarchi receives comes at the most mundane moments.

"Sometimes I'll be sitting next to someone on a plane, and they'll pull out their Humalog," he says, referring to an insulin analog for the treatment of diabetes that he designed at Lilly Research Labs. "Or, just recently, I was waiting in line for a rental car and someone noticed the Lilly logo on my luggage. He told me his wife had broken her hip and was about to start Forteo."

Forteo is another drug DiMarchi had a seminal role in developing while at Lilly; it reverses the effects of early-onset osteoporosis by stimulating new bone growth. Seeing these therapies at work in people's lives is an unexpected thrill for DiMarchi, who thought he gave up the chance to witness individual health gains when he chose to pursue a career as a laboratory scientist.



"I wanted to create the future, not just apply the discoveries of the past," he explains. "I thought that would mostly happen inside the lab. Meeting people whose lives have been changed is an unexpected benefit."

DiMarchi's path has been in many ways unplanned; he didn't grow up dreaming of miracle molecules. As a New York City child of the '50s and '60s, he had one thing on his mind: baseball.

"Anyone who was in New York at that time knew that the Yankees were something special," he says.

DiMarchi was a capable player – he still displays a photo of himself in uniform among the molecular models and professional awards on his office bookshelf – but he was also a pragmatist, recognizing that his abilities were insufficient for a professional athletic career.

"I came to the harsh realization that one needs to make a living," he recalls. "It was clear I had more quantitative skills, rather than linguistic or artistic ones. I found chemistry to be at that interface between academic, theoretical science and that which could be translated to something of commercial worth."

Following an undergraduate chemistry degree from Florida Atlantic University, DiMarchi completed a PhD in protein chemistry at IU. He returned to New York as a postdoctoral fellow at The Rockefeller University to pursue advanced training in peptide chemical synthesis.

His drive to remain at the forefront of innovation propelled DiMarchi to Lilly in the 1980s, when biotechnology was just emerging. In this atmosphere of ingenuity, he pushed the field still further by dismantling the traditional divide between biological and synthetic chemistry.

"With biotechnology, you use organisms to produce compounds; with traditional synthetic technology, laboratory chemists produce the compounds," he explains. "The third alternative is what I call 'chemical biotechnology': we use organisms to produce the synthetic compounds."

This radical marriage of approaches has enabled the sustainable mass production of drugs like Humalog, which now reaches millions of patients worldwide.

After 22 years with Lilly, however, DiMarchi felt excessively constrained.

"There were ideas that I held that didn't immediately fit at the commercial level," he says.

"It's universities that do the basic exploration that allow us to form research hypotheses, which can then be experimentally validated in a biotech company and subsequently developed and eventually commercialized at traditional pharmaceutical companies. My primary interest has always resided at the initial stage of discovery, with a strong desire to see the product of our research translated by others in later stages."

Joining the IU College as a Gill Chair offered DiMarchi the ideal opportunity to shift into this exploratory phase. He focused initially on developing an injectable solution for diabetics that could be used to counter a hypoglycemic attack. This innovation, which has led to a glucagon "pen" analogous to the injection technology used to administer epinephrine, turned out to have unexpected applications.

"Once we had identified a glucagon analog suitable for formulation as a stable solution, we now had the ability to administer the drug consistently over an extended time period," he says. "We found in animal studies that it subtly suppressed appetite, but, more importantly, profoundly stimulated energy utilization to result in significantly lower body weight. We realized we had a molecule that might be appropriate, after further structural refinement, for treating obesity."

The drug candidate, which is now in phase II clinical trials, has demonstrated yet another therapeutic capability: "These drug candidates that were designed to improve metabolism are demonstrating an ability in animal studies to enhance cognitive function," DiMarchi says. "There are indications that it can minimize the adverse effects of Alzheimer's, minimize traumatic brain injuries, and reduce the impact of Parkinson's disease."

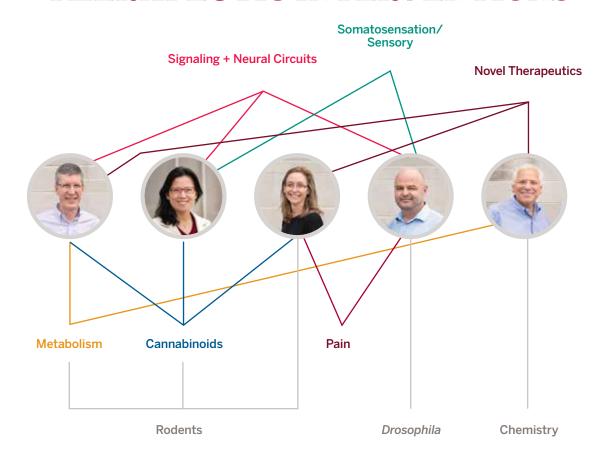
As DiMarchi's research progresses toward greater convergence with that of his neuroscience colleagues in the Gill Center, he has encountered yet another surprising benefit.

"I really value the camaraderie within the Center and the laboratory," he says. "In some ways I've found the sort of team spirit and constructive competiveness I witnessed decades ago in baseball."

The Gill Center supports revolutionary science across a range of approaches, from electrophysiology measuring activity within single neurons to animal behavior studies investigating effects of potential therapies. Five Gill Chairs and a growing group of research scientists, technicians, students, and postdocs bring together a synergistic set of approaches that collectively yield exciting revelations in our evolving understanding of the brain.

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THERAPEUTIC INTERVENTIONS

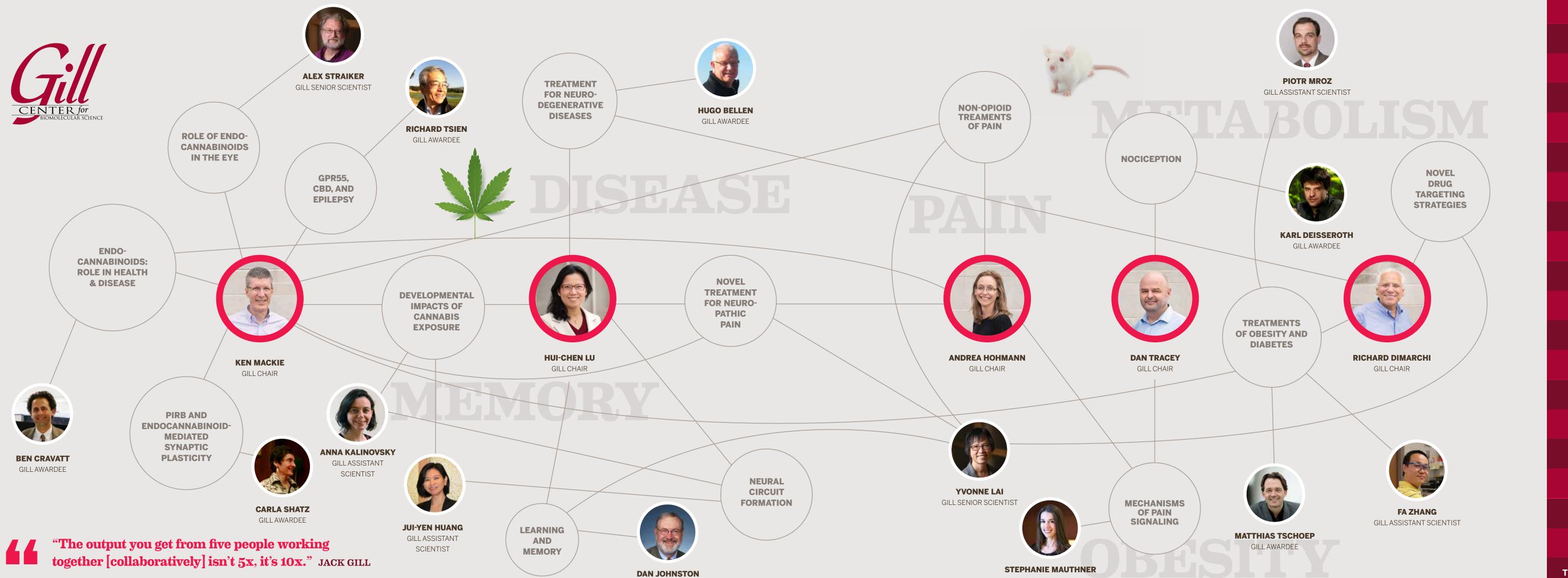


Through an interdisciplinary
mix of expertise, this tightknit team is pioneering
innovations in critical realms
of neuroscience. Their research
holds promise for better
understanding and addressing
a wide range of issues including
autism, Alzheimer's disease,
chronic pain and itch, anxiety,
schizophrenia, obesity, and
addiction.



"The Gill Center
is truly one of the
earliest, most pioneering collaborative
neuroscience centers,
bringing together
a concentration
of neuroscientists
focusing on some of
the most pressing
issues of our time."

JACK GILL



GILL AWARDEE

GILL ASSOCIATE SCIENTIST

ADDICTION

ALS

ALZHEIMER'S

ANXIETY

AUTISM

IMMUNE FUNCTION

INFLAMMATION

ITCH

MEMORY

METABOLISM

NEURODEGENERATION

NEURODEVELOPMENT

OBESITY

PAIN

PARKINSON'S

PTSD

SCHIZOPHRENIA

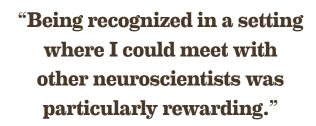
SOMATOSENSATION

STRESS

TRAUMATIC BRAIN INJURY







BEN CRAVATT

Broadening IMPACT

Connecting is at the core of the Linda and Jack Gill Center – not only among Gill Chairs and their collaborators at other institutions, but also with the wider neuroscience community, the broader public that seeks a greater understanding of the brain, and the biotech and pharmaceutical companies that can help to translate Center insights into therapies. Through this continually expanding network, the Center achieves its ultimate goal: ensuring excellence, advancement, and impact in the field of neuroscience.

THE GILL SYMPOSIUM

No effort more clearly embodies this commitment than the annual Gill Symposium and Award Ceremony. Drawing some 300 neuroscientists and students to the IU Bloomington campus, the Symposium is the Gill Center's signature event.

Each year, the Center honors scientists who are making tremendous breakthroughs in cellular and molecular neuroscience. These Gill Awardees share their latest work and insights through keynote lectures. Attendees also hear from other distinguished speakers and from neuroscience students presenting their research posters. A graduate student thesis award and an image award further recognize local excellence in neuroscience. The packed day is characterized by multiple question-and-answer sessions, informal conversations, and











shared meals, providing fertile ground for new connections and collaborations.

The list of Gill Awardees is truly remarkable; it includes several of the world's most innovative and influential neuroscientists. For example, Karl Deisseroth, the 2010 recipient of the Gill Young Investigator Award, pioneered the new technique of optogenetics, which uses light to invoke activity in specific sets of neurons. Scientists now use this strategy to associate particular neural circuits with changes in behavior, such as depression or symptoms of Parkinson's disease. Ben Barres, the 2016 Distinguished Scientist Awardee, upended the field's understanding of glial cells. His work revealed that these brain cells once thought to simply support neurons in fact play a central role in sculpting and maintaining neural circuitry and contribute to

neuroinflammation, which is associated with many neurodegenerative diseases. Carla Shatz, who in 2006 was one of the earliest Gill Awardees, has revolutionized understanding of the processes at work in the developing brain, demonstrating that brain activity in early life influences the wiring of the central nervous system.

A DISTINCTIVE HONOR: THE GILL AWARD

Each of these honorees has a great many awards to his or her name from esteemed organizations like the National Academy of Sciences and the American Association for the Advancement of Science. The Gill Award, however, holds a special significance for its recipients.

"There are awards that you get internally, at your own institution, and there are awards that

you get from agencies like the NIH because of your grants," explains Shatz, who is now the director of Stanford University's interdisciplinary Bio-X Initiative. "But when an external group of distinguished scientists in your field selects you for recognition, that's really meaningful."

Stanford University President Marc
Tessier-Lavigne agrees. The 2010 recipient
of the senior-level Gill Award was the
executive vice president for research and
chief scientific officer for the biotechnology
company Genentech when he was honored
at the Gill Symposium. "Being recognized
for my science by such esteemed peers was
deeply gratifying," he says.

GILL AWARDEES

Jonathan V. Sweedler, PhD

University of Illinois

Eric J. Nestler, MD, PhD

Icahn School of Medicine at Mount Sinai

Carla J. Shatz. PhD

Stanford University

Benjamin F. Cravatt, PhD

Scripps Research Institute

Richard W. Tsien, PhD

New York University

Karel Svoboda, PhD

Howard Hughes Medical Institute – Janelia Research Campus

Robert Sapolsky, PhD

Stanford University

Linda Hsieh-Wilson, PhD

California Institute of Technology

Daniel Johnston, PhD

University of Texas, Austin

Karl Deisseroth, MD, PhD

Stanford University

Marc Tessier-Lavigne, PhD

Stanford University

Leslie B. Vosshall, PhD

The Rockefeller University

Marc G. Caron, PhD

Duke University Medical Center

Guoping Feng, PhD

Massachusetts Institute of Technology

Hugo Bellen, DVM, PhD

Baylor College of Medicine

(continued page 57)

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"There's never been a better time to tackle the debilitating neurological and neurodegenerative diseases that tragically affect so many people." MARC TESSIER-LAVIGNE



The awardee selection process invites participation from the broad neuroscience community; anyone can nominate a candidate by articulating the candidate's contributions to cellular and molecular neuroscience. Previous awardees are a frequent source of nominees, as is the Gill Center's Steering Committee, which comprises the Gill Chairs and other Indiana University neuroscience leaders and ultimately selects the awardees. As a result, the Gill Awards reflect the neuroscience field's own understanding of where the most innovative and promising research is occurring.

Baylor College of Medicine Distinguished Service Professor and 2012 Gill Awardee Hugo Bellen, who was recognized for his groundbreaking work with *Drosophila* (fruit flies) to model human neurodegenerative disorders, explains that this selection process highlights fundamental research that is often overlooked by other agencies.

"The reason I really appreciate the Gill Award is that in my field, most of the awards go to more applied research performed by physicians and not by basic scientists," he says. "That's understandable – their research in attempting to cure patients is recognized. The fact that the Gill Awards have focused on recognizing mostly the basic science research necessary to achieve major advances in medical science is very much appreciated. Receiving an award like the Gill Award invigorates your research and motivates you even more."

LINDA GILL'S TRIBUTE TO DISTINGUISHED AWARDEES

Adding further significance to the award is the unique "tribute" package that Linda Gill assembles for each year's Distinguished Awardee. Through months of research and outreach, she gathers reflections from the awardee's friends, colleagues, students, family members, and mentors, then crafts a narrative of the honoree's accomplishments that blends personal anecdotes with professional achievements. For example, Tessier-Lavigne's tribute noted his propensity to belt out Frank Sinatra's "My Way" at karaoke parties, in addition to his discovery of netrins, proteins that serve as navigators for nervecell connections.

The final bound volume that Linda presents to each Gill Awardee includes all these communications from people whose lives and careers the individual has touched. For example, for Barres, who, before passing away in 2017, distinguished himself not only through his research but also by leveraging his perspective as a transgender man to advocate for gender equality in the sciences, Linda assembled more than 30 testimonials on the impact of his extraordinary contributions. These heartfelt messages range from students writing, "Thank you for showing me the true joy in science," to colleagues declaring, "Ben has been the conscience of us all in pursuit of a 'level playing field' and better society."

"That book Linda prepares is the single biggest surprise and take-home these winners get," says Jack Gill. "When you are presented with those tributes, that makes you go home with a good feeling."

INSPIRATION AND SUPPORT— MEETING THE GILLS

Awardees emphasize that it's not only the tribute book Linda prepares but also the experience of meeting her and Jack that sticks with them.

"The Gills were exceedingly kind, supportive, and in fact inspiring," says 2007 Gill Awardee Richard Tsien, whose research on calcium channels addresses fundamental questions about how neurons communicate. Now the director of New York University's Neuroscience Institute and chair of its Department of Physiology and Neuroscience, Tsien emphasizes, "Jack and Linda are such fine people, and are genuinely interested in understanding what neuroscientific research really means — not only on a practical level, in terms of applications for health, but also from a basic point of view of how the brain operates and makes us who we are."

Diana Bautista, a University of California, Berkeley professor whose research on the molecular mechanisms of touch, pain, and itch earned her the 2017 Gill Transformative Investigator Award, has similar recollections of speaking with the Gills at the symposium. "They were so fun and interested and had amazing scientific questions. It was clear they had really studied the awardees' work – they had looked into what we were doing and our results. And they were such warm, kind people who really care about supporting meaningful research."

GILL AWARDEES

Loren M. Frank, PhD

University of California, San Francisco

Bruce L. McNaughton, PhD

University of California, Irvine

Scott Sternson, PhD

Howard Hughes Medical Institute – Janelia Research Campus

Matthias H. Tschop, MD

Technische Universität München

Garret D. Stuber, PhD

University of North Carolina at Chapel Hill

George F. Koob, PhD

National Institute on Alcohol Abuse and Alcoholism

Beth Stevens, PhD

Harvard Medical School

Ben A. Barres, MD

Stanford University School of Medicine

Diana Bautista, PhD

University of California, Berkley

Clifford J. Woolf, MB, BCh, PhD

Harvard Medical School

Viviana Gradinaru, PhD

California Institute of Technology, CALTECH

Loren Looger, PhD

Howard Hughes Medical Institute – Janelia Research Campus

Ryohei Yasuda, PhD

Max Planck Florida Institute for Neuroscience

Anthony M. Zador, MD, PhD

Cold Spring Harbor Laboratory

Hongkui Zeng, PhD

Allen Institute for Brain Science

A FAMILY AFFAIR

In addition to getting to know the Gills, another highlight for awardees is becoming more familiar with the Gill Center and its researchers. Bautista, who came to campus a day early in order to spend time with the Gill Chairs, observes, "Seeing the way the Gill faculty interact with each other was wonderful. It really felt like a family."

Tsien also recalls that the group of Gill Chairs "resonated really well" with one another. "Everyone was very friendly and open and had clearly developed meaningful synergies among their different laboratories," he says. "They've picked some wonderful people."

Ben Cravatt, the 2007 Young Investigaor Awardee, agrees: "The Gill Center has got a great group of researchers. It's a strong mix of people who are developing new methods of looking at fundamentals of neurophysiology and neurochemistry, as well as those with experience in therapeutic applications." Now chair of the Department of Chemical Physiology at The Scripps Research Institute, Cravatt's research on enzymes is elucidating biochemical pathways of numerous neurological processes, including memory, mood, and pain. He adds, "It's been fun to see the Center build up its capabilities over the past decade, particularly in the area of endocannabinoid research."

THE GILL SYMPOSIUM— INSPIRING PARTNERSHIPS

This ongoing sense of connection to the Center inspires some award recipients to pursue collaborations with the Gill faculty. Shatz recalls that her 2006 visit for the awards ceremony and Symposium "was my introduction to [Gill Chair] Ken Mackie. I got to know him a little at the event and interacted with him over the following years. That relationship has resulted in a very nice collaboration. Recently his generosity with a reagent has helped our lab publish new findings on circuit tuning."

Tsien has similar praise for the resources Gill Chairs provide as collaborators. In addition to reagents, the Gill Center was able to provide his lab with mice that were deficient in a specific receptor relevant to his research on epilepsy and synaptic communication. Cravatt, whose collaborations with Mackie began before Mackie joined the Gill faculty, notes that this partnership was "fortified by the Gill Symposium."

Meeting other awardees is another benefit for Gill Award recipients. Tessier-Lavigne notes that learning about Diesseroth's work at the 2010 Gill Symposium influenced his own research directions. "Getting to know what Karl was working on, even ahead of when it was published, shaped what I went on to do in my own lab," he says. Cravatt, who shared the podium with



Tsien in 2007, concurs: "Being recognized in a setting where I could meet with other neuroscientists was particularly rewarding."

Connecting with awardees and other distinguished Symposium speakers also delivers substantial rewards for the Gill Center. In addition to building and strengthening research collaborations, Gill Awardees have also provided doctoral and postdoctoral research opportunities for Gill Center students and connections to world-class scientists interested in becoming Gill Chairs. Gill Center Director Hui-Chen Lu collaborated with Hugo Bellen at Baylor; Gill Chair Dan Tracey was referred by 2011 Young Investigator Awardee Leslie Vosshall (whose lab at The Rockefeller University studies how sensory stimuli are perceived and processed).

LIFE-CHANGING OPPORTUNITY FOR STUDENTS

Students also benefit tremendously from attending the Symposium, which is the premier neuroscience conference in the state. During the event, students from IU and elsewhere present their research in poster sessions attended by awardees and other leading neuroscientists, an experience that many Gill Center undergraduates describe as the most challenging and rewarding of their college years. Outside the poster sessions, students participate in all aspects of



the Symposium, including the question-and-answer sessions with awardees, informal networking breaks, and meals.

Because these opportunities to engage with leading researchers are so valuable for young neuroscientists, the Center encourages participation by other Indiana neuroscience programs at the IU Medical School and Purdue University, subsidizing the cost of the conference, including free meals. The Gill Center also brings its students to Purdue's annual conference to further promote this intellectual exchange.

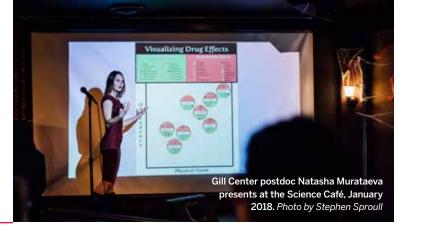
"An hour and a half can be a long way to go for students," says Lu. "We want to remove any barriers that would prevent them from making these connections."

A similar initiative targets young researchers outside the state. The Gill Travel Fellows program provides grants to enable graduate students and postdocs to travel to the Gill Symposium from their home institutions around the country, including Stanford University, Johns Hopkins University, Baylor College of Medicine, Northwestern University, and Penn State College of Medicine. The Symposium also draws participation from industry scientists, such as pharmaceutical researchers from Eli Lilly and Company, and from faculty members from numerous Indiana institutions.



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"There is a real chasm between what scientists do and the public understanding of it. The Science Café is one way to try to close that gap." ALEX STRAIKER



SERVING THE GLOBAL NEUROSCIENCE COMMUNITY

While the annual Symposium is by far the Gill Center's largest event, community building and outreach continue throughout the year. A seminar series in conjunction with the College's Program in Neuroscience brings speakers to campus nearly every week. Gill Chairs are also in high demand as speakers, regularly traveling across the country and world to address audiences of neuroscientists and researchers in other biomolecular and cellular fields.

Service to the academic profession is also an integral part of Gill Chairs' commitment to the neuroscience community. "We all serve at the national level with research journals and organizations," Lu says. "Whether as committee members, reviewers, or editors, we are committed to helping ensure that the highest caliber of neuroscience is supported and published."

ENGAGING THE PUBLIC

Outreach beyond the research community is also important to the Center, exemplified by the monthly Science Café organized by Senior Research Scientist Alex Straiker. Held at Bear's Ale House & Eatery in Bloomington, the event treats members of the public to plain-language explanations of new developments in science.

"The Science Café is motivated by the idea of building bridges," Straiker says. "There is a real chasm between what scientists do and the public understanding of it. This is one way to try to close that gap."

Straiker also strives to engage a general audience through art exhibitions that feature images from different types of microscopy. Venues for these exhibits have included the Ivy Tech John Waldron Arts Center, the WonderLab children's museum, and Finch's Brasserie, a local restaurant. "Seeing the

images encourages people to think about science in different ways," he says. "Often an image can make science seem less intimidating and more approachable."

Lu has used a different non-traditional approach to engaging the broader community: hosting an "Ask Us Anything!" session on the online chat platform Reddit with Gill Center Assistant Scientist Yousuf Ali and Research Assistant Hunter Allen. "It was intense," Lu recalls. "We received more than 200 comments during the session ranging from very basic to very sophisticated questions. It was nice to see how interested people were in the topic, which corresponded to a paper we had recently published on a protein that protects against cognitive decline."

Another target for outreach is local schools. In addition to making presentations in classrooms, Gill scientists are also involved in helping teachers introduce neuroscience to students of different grade levels. For example, Gill Chair Dan Tracey participates in a summer institute that works with local teachers to develop age-appropriate experiments and curricula. He also works directly with high school students through the Department of Biology's Jim Holland Summer Science Research Program, which brings high-achieving students from disadvantaged backgrounds to campus for an immersive week inside a research lab.

TRANSLATING SCIENCE INTO REAL-WORLD THERAPIES

Connecting with industries that translate basic science into real-world applications is the final critical component in ensuring the Gill Center's impact. One channel for this partnership is service on the advisory boards of biotech and pharmaceutical companies – for example, Gill Chair Andrea Hohmann is a scientific advisor for Phytec, an organization promoting preclinical work on therapies involving the

endocannabinoid system; Mackie is on the scientific advisory board of Renew Biopharma, which is using algae to produce cannabinoid-like molecules for therapeutic applications; and Gill Chair Richard DiMarchi sits on the board of directors of Assembly Biosciences, a biotech company that acquired one of the several start-ups he has co-founded.

CONNECTING TO INDUSTRY

DiMarchi's long experience in the pharmaceutical industry – he was the vice president for research at Eli Lilly and Company before becoming a Gill Chair – has also helped the Center orient itself toward translation. "My presence at the Gill Center lends a translatable element, and I'm always prepared to help other researchers key into those opportunities," he says. "The connection between universities, biotechnology, and pharmaceutical companies is vitally important to the translatable knowledge that makes life better for all of us."

Another critical connection to industry comes through Senior Research Scientist Yvonne Lai. In 2013, she co-founded the biotech company Anagin with IU School of Medicine Distinguished Professor Anantha Shekhar. Initially, Anagin focused on developing and testing treatments based on a compound Lai developed prior to her arrival at IU, which she had since been testing in collaboration with Hohmann as a treatment for chronic pain. With the help of two rounds of NIH small-business funding, the company has expanded the compounds under development and investigation, including a treatment for post-traumatic stress disorder. Currently, Lai and Hohmann are working together to explore ways to translate their research on protein-to-protein interactions during pain response into new therapies.

"A startup can't do everything on its own," Lai says. "It needs to partner with academic scientists to perform tests with animal models. The work we do at the Gill Center complements Anagin's work using chemistry to create really novel molecules as therapeutic candidates."

EXPANDING STUDENT HORIZONS

Lai's perspective as a researcher with experience in both academic and commercial settings also enables her to serve as a mentor to scientists interested in translation activities, particularly students at the Gill Center.

"With graduate students and postdocs who want to consider industry options, I can talk with them about what working in companies is like, what those markets are looking for, and how to present themselves and explain how their research can be used in an applied way," she says.

Undergraduates also pursue industry opportunities that arise from their connection with the Gill Center; for example, graduating senior Steve Feldhake is taking on an internship with Renew Biopharma, the company that Mackie assists as a science advisor. He notes that one attractive feature of the position is that it will enable him to continue collaborating with the Gill Center. "At Renew, they are synthesizing cannabinoid derivatives and sending them back to the Mackie Lab for testing," Feldhake explains. "In effect I'm still going to be working with the Center, which I'm very happy about."

These industry connections ultimately serve to fulfill the Gills' original vision for the center. "Half the ball game is doing the fundamental research on how the brain works," Jack says. "Developing the intellectual property is the second half of the job. You need entrepreneurial partners to make sure those discoveries can reach their targets. The translation is what allows us to make real progress on improving brain health."

Ensuring such impact is the shared goal across the Gill Center, its industrial partners, and its awardees. As 2010 Awardee and Stanford President Tessier-Lavigne notes, "There's never been a better time to tackle the debilitating neurological and neurodegenerative diseases that tragically affect so many people. The opportunities for helping people have never been greater. It's a great time to be working with the brain."







"Because IU Bloomington is an undergraduate campus, one of our primary missions is to educate these nextgeneration scientists."

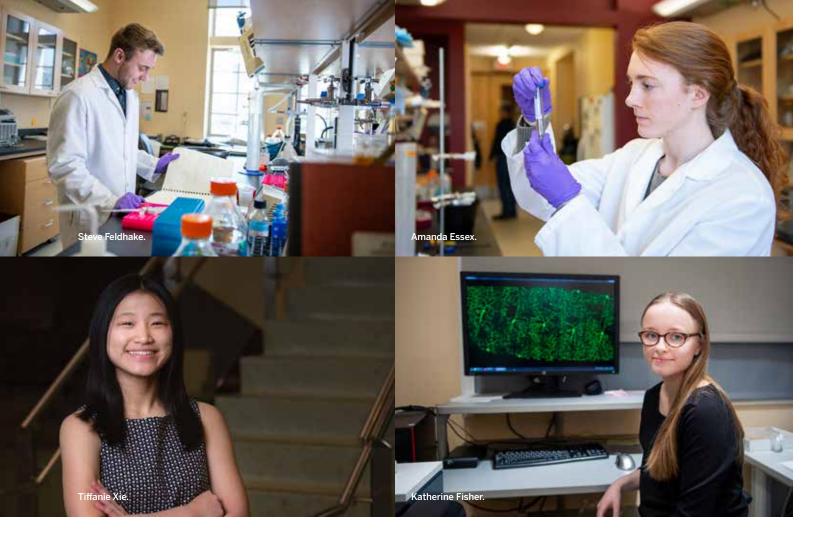
HUI-CHEN LU

Shaping the FUTURE

The Gill Center's dedication to excellence in neuroscience incorporates a commitment to providing the next generation of researchers with outstanding training and hands-on experience. As one would expect of a leading research center, every Gill Chair mentors graduate students and postdoctoral researchers, enabling these young scholars to contribute to cutting-edge research projects that position them to successfully compete for prestigious appointments with academic and other research institutions.

What most distinguishes the Gill Center's approach to preparing future leaders, however, is its exceptional devotion to working with large numbers of undergraduate students. In addition to teaching undergraduate courses, the Gill Chairs and senior scientists involve approximately 40 undergraduates in their research programs, with some labs hosting up to 15 of these students.

"It is very unusual to have such high numbers of undergraduates in a research institute," says Gill Chair and Center Director Hui-Chen Lu. "Ordinarily research scientists depend exclusively on technicians, graduate students, and postdoctoral fellows to assist with their projects. Here, because IU Bloomington serves a large undergraduate population, one of our primary missions is to educate these next-generation neuroscientists. We want to make sure the best and most motivated of these students have an opportunity to succeed."



SOPHISTICATED STUDENT SCIENCE

These opportunities involve tangible, experiential, and often highly advanced responsibilities within the Center's laboratories. Undergraduates can be found patch-clamping individual neurons, coding complex animal behaviors, separating DNA through gel electrophoresis, and visualizing proteins in live brain sections.

"The independence I've had has been incredible," says junior Katie Fisher, whose project under Gill Chair Dan Tracey aims to characterize changes in neuron morphology in the *Drosophila* nervous system by applying the "brainbow" technique used to highlight neurons in different colors. "When I started in the lab as a freshman, I had plenty of monitoring and mentoring, but quickly there was a lot of trust put in me in a way I hadn't expected."

Research scientist Jim Wager-Miller explains, "With each student, we come up with an independent research project. I try to tailor their responsibilities so they each have a slice of the lab's research that's all their own."

INVESTING IN UNDERGRADUATES

Naturally, the challenge of working with undergraduates is that they tend to arrive without laboratory experience. Extensive training is necessary in order to enable these students to contribute meaningfully to the Center's work.

"The techniques we use are very difficult to master," says senior scientist Alex Straiker. "The learning curve for electrophysiology, for instance, is pretty legendary."

"We try to get students in their freshman or sophomore years, so they have time to make a real contribution," adds Wager-Miller.

Sophomore Tiffany Xie explains that her training as a freshman in the Lu Lab included basic technical skills such as keeping equipment clean and using pipettes to dispense precise quantities of solutions. Once she mastered these bench skills, however, she was soon involved in investigating how the absence of a key glutamate receptor in the cortical neurons of mice affected gene expression.



"The support we receive at the Gill Center lets us be more flexible in our approach and engage people who are new to research, which is a priority for all of us."

HUI-CHEN LU

Undergraduates are also trained to train other students, with more experienced student researchers mentoring newer recruits. Senior Amanda Essex, who has worked with research scientist Anna Kalinovsky in Gill Chair Ken Mackie's lab since her sophomore year, explains, "I was initially trained by an undergrad, and as I moved up I started supervising other students. It's one of the ways that the Gill Center introduces us to the responsibilities of working in a research environment."

Lu points out that it would not be possible to make these long-term investments in student researchers without the extraordinary unrestricted funding provided through the Gill Center's endowment and matched by IU's College of Arts and Sciences.

"Because of our Gill stipends, we have the freedom to direct resources toward undergraduate training," she explains. "With federal funding grants, we have to account for every penny and specify precisely who is doing what. The additional support we receive at the Gill Center lets us be more flexible in our approach and engage people who are new to research, which is a priority for all of us."

DEVELOPING LIFE SKILLS

Technical training is only one component of what the Center provides for its youngest researchers; Lu emphasizes that "life skills" are equally vital in preparing these students to succeed. "I start by teaching them about timelines," she says. "We set out milestones for each week that they need to meet in order to continue. We also work on boring, routine tasks in the beginning, so they learn that even these can be difficult to do well."

Senior Steve Feldhake, who has worked in the Mackie Lab since he was in high school, says this focus on planning has been the most helpful feature of his time at the Gill Center. "My time management skills have been just about perfected," he says. "Juggling eighteen hours of classes with research in the lab meant I had to improve my ability to balance everything at once. That's honestly the biggest thing I'll take with me."

BECOMING RESILIENT

Another key lesson the Gill Chairs impart is how to handle failure. "I have been surprised by how many undergraduates have never dealt with failure," Lu says. "All scientists will fail, sometimes very badly, and they need to know how to recover. One thing we make sure our students learn is how to find help."

Feldhake offers an example from his first independent project in the Mackie Lab. "For the entire summer after my sophomore year, I was trying to synthesize a piece of DNA, and I failed. There was a lot of second guessing myself, but everyone was very reassuring. In the end I had to stop working on that project and it took Jim [Wager-Miller] another month and a half to figure it out, so at least I knew that particular piece of DNA really was difficult to synthesize."

Mackie highlights a related competency: coping with uncertainty. "It's very easy to be interested in science in your classes, but what you learn from books is very different from how science is actually done," he says. "Working in a lab on the edges of what's known brings a lot more uncertainty, which can be hard to confront. You need to be able to work with multiple and sometimes conflicting inputs to sort out what's important."

Xie notes that she enjoyed discovering how this uncertainty can open up new and unanticipated lines of inquiry. "I thought that after I completed a project, that door would close, but instead I was glad to see that I was left with more questions than answers."

Fisher agrees, saying, "I was always very curious, but my curiosity has peaked here."





GREAT RESEARCH, GREAT CONVERSATION

This curiosity is further served by interaction among the different labs through shared weekly meetings, and by dozens of speakers who visit the Center each year from many areas of neuroscience. Says Xie, "One thing I appreciated about the Gill Center from the start was that there is not only a lot of great research but also a lot of great conversation."

Students are also pushed to lead such conversations by mastering presentation skills, an essential proficiency for careers in research. In addition to presenting their findings to their undergraduate peers in the Gill Center, students prepare poster presentations for the annual Gill Symposium that brings leading national and international neuroscientists as speakers in addition to attracting student and faculty attendees from around the state.

"We train students not just in how to put together their poster but also how to lead a discussion – the whole package," Lu says.

Essex describes her poster presentation sessions at the Gill Symposium as "a great experience." She explains, "It's always stressful presenting to very well-established researchers like the speakers and attendees at the Gill Symposium, but you get really great feedback from people who are quick and sharp and know their stuff."

PREPARING AND PROMOTING THE NEXT GENERATION

The rewards for students are tremendous: in addition to acquiring experience that makes them highly attractive candidates for PhD programs and medical schools, many students graduate with publications already on their CVs. Ensuring that student researchers are publicly recognized is such a high priority that undergraduates are prominently featured on several Chairs' websites, and Gill Chair Andrea Hohmann includes photographs of individual student contributors in all her research presentations, effectively introducing these young scientists to organizations like the National Institutes of Health and the Society for Neuroscience.

"My job is to promote the students," Hohmann explains. "It's because of the formative experiences that I had as an undergraduate in a laboratory that I became a scientist. I want to make sure I can open up the same kinds of opportunities for them."

These opportunities range from pursuing PhD programs (as Fisher plans to do) or medical school (which Essex will start in the fall) to working in emerging fields that are translating neuroscience into new therapies. Feldhake is taking this latter path, embarking on an internship in intellectual property development for the biotechnology company Renew, for which Mackie is a scientific advisor.

"I never pictured this plan when I started college, but through my time here I came to understand that there are many different perspectives contributing to effective neuroscience," he says. "I'm certain that what I've gained at the Gill Center is going to carry forward into any career. I could not have asked for a better experience."

Gill Center Alumni Profiles



"What I learned at the Gill Center gave me so many tools that I was able to jump right into a PhD program."

MEGAN HUIBREGTSE



Jill Farnsworth

As a young girl, Jill Farnsworth wondered, "What makes me, me?" To pursue this question, she contacted a number of science faculty members when she entered IU as a freshman, including Gill Chair Ken Mackie.

"As soon as I met Dr. Mackie I knew I'd found the right lab," she says. "He asked me a lot of questions that other people overlooked, like what motivated me to pursue science and what insights I wanted to achieve. Ken and Jim [Wager-Miller] are two really great examples of problem solvers. They taught me how to optimize my problem-solving through cost-benefit analysis, by constantly asking questions in this interactive way."

Farnsworth's Gill Center research on endocannabinoids led to publications in scientific journals, which helped her secure a position as a PhD candidate in the Center for Structural and Functional Neuroscience at the University of Montana.

"As a scientist, your publications are almost who you are," she says.
"The fact that I had done a huge amount of research before applying to graduate school helped me immensely."

Now at Montana investigating molecular and biophysical mechanisms involved with learning and memory, Farnsworth credits her early start in the Mackie lab with preparing her for the rigors of graduate school.

Jose Mitjavila

"I feel like I stumbled into one of the greatest gems of IU Bloomington," says Jose Mitjavila, who became a Gill Center student researcher after taking Gill Chair Ken Mackie's course on the history of neuroscience.

Mitjavila worked in the lab of senior scientist Alex Straiker, investigating how different chemical compounds affected neurons' electrical activity. This hands-on experience was excellent preparation for medical school, which Mitjavila now attends at the IU School of Medicine.

"After three years at the Gill Center, I had done everything from formulating a project, collecting data, and analyzing the data, to writing an abstract and making a poster," he says. "When I arrived in medical school, it was clear that there was a major focus on research, and I was very glad to have already learned those skills."

Now in his final year, Mitjavila says he is continually struck by how well the Gill faculty continue to support him as he pursues his professional goals.

"I had no idea when I went in how much of a resource and support network these professors would be for me," he says. "All of the Gill Chairs and scientists have led such interesting lives and careers and they've been incredibly willing to share their insights with their students."





Megan Huibregtse

By the time she was a sophomore, Megan Huibregtse had experienced four concussions. These injuries, which resulted from sports and an aggressive encounter with a cabinet door, prompted the biochemistry major to turn her attention to the brain and its resilience.

"I made a list of all the professors whose research interested me, and Dr. Hohmann's work on pain was very compelling," she recalls.

Huibregtse's work contributed to investigating interactions between different proteins during pain signaling. She also helped to code mouse behavior for potential indications of cannabinoid withdrawal.

"I was actually able to craft a couple of behavior-coding protocols that the lab still uses," she says.

In her senior year, Huibregtse met with a professor at IU's School of Public Health-Bloomington, hoping to learn more about his research on concussions.

Unexpectedly, he offered her the opportunity to become his PhD student – bypassing the usual master's degree requirement.

"I thought I was behind schedule because I didn't start studying neuroscience until my junior year," Huibregtse says. "It turned out that what I learned at the Gill Center gave me so many tools that I was able to jump right into a PhD program."

Song Kim

"What I found interesting was how big of a role the brain plays in shaping how we perceive and respond to the world around us," says Song Kim, a Cox Research Scholar who credits the Gill Center with exposing her to a wide range of neuroscience.

"The Center has such a strong interdisciplinary spirit," she says. "One of my favorite memories is the Gill Symposium, where I got to hear from incredible scientists presenting their current research."

Kim also presented her own research through a poster at the Gill Symposium, an experience she credits with preparing her for the challenges of medical school, which she now attends at the University of Pittsburgh.

"The skills you need to present information can be really hard to develop," she says. "I learned in the Mackie Lab how to ask well-informed questions and craft a very clear narrative."

Kim emphasizes that this grounding is critical not only for excelling in the medical school environment but also for performing effectively in the health care field.

Her experience at the Gill Center has also given her a head start in her medical field of interest: Kim is currently pursuing a career in brain health.





Diana Salas

Diana Salas became interested in neuroscience as a teenager, after a family member suffered a stroke at the age of 18.

"It made me wonder about the vulnerability of the brain," she says.

At IU, Salas earned a place in the prestigious McNair Scholars Program, a national initiative to support students from disadvantaged backgrounds who are interested in attending graduate school.

"I was interested in how the triggers that cause our brains to change affect behavior and memory," she says. "That's what led me to the Lu Lab. Being there meant being pushed. We were like mini grad students, conducting and then presenting our research. It was nerve-racking but a great opportunity to learn how to communicate about science."

Salas' experience in the lab enabled her to take on a challenging neurophysiology position after graduation, working with a team of neurosurgeons to minimize the risk of nerve damage to patients during surgery. She is now pursuing a master's degree in cellular and integrated physiology at Indiana University—Purdue University Indianapolis and plans to attend medical school.

"My time in the Gill Center led to all these amazing opportunities," she says. "I'm a better scientist because of it."

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AFTERWORD



Indiana University was founded in 1820 on the promise to the people of the newly established state of Indiana that the life of the state and its citizens would be greatly enriched by an exceptional

institution of higher education. For nearly 200 years, Indiana University has kept that promise through the outstanding achievements of generations of faculty members in numerous fields of inquiry.

Today, as we prepare for IU's third century of service—and as we prepare to reflect on and celebrate all that IU has achieved in the previous 200 years—the Linda and Jack Gill Center for Biomolecular Science stands among the most bold and fruitful enterprises in the university's recent history. Its collaborative character, captured in the stories and images within this volume, exemplifies the interdisciplinary temperament and pioneering spirit that make IU a powerhouse for scientific discovery, particularly in the life sciences and health-related fields.

From its beginnings as an idea forged in 1998 between alumnus Jack Gill and then-dean of the College of Arts and Sciences, Morton Lowengrub, the Gill Center has grown to become not only the most influential concentration of neuroscientists in the state, but also a global resource for materials, methods, and partnerships critical to advancing the field. Its impact is felt across the many academic disciplines that interface with neuroscience—from chemistry and biology to psychology and medicine—and, crucially, within the applied realms of biotechnology and pharmaceutical development. The breakthroughs achieved by the Gill Chairs, research

scientists, and student researchers are inspiring new therapies with enormous potential to address a range of problems from obesity, stress, and chronic pain to addiction and neurodegenerative disorders.

While the past two decades have seen the Gill Center grow into a widely recognized and acclaimed center for excellence in neuroscience, the years ahead hold still more promise. The Center continues to grow, both by measures of productivity and in the numbers of talented scientists and students it cultivates. Thanks to the vision and foresight of Jack and Linda Gill, the Center's endowment is now capable of providing research support for a sixth Gill Chair who, when recruited, will add to and strengthen the extensive research synergies already in place that make the Gill Center so distinctive and effective.

It is immensely gratifying to observe the farreaching accomplishments in research, teaching, and translation that this chronicle records. All of us at Indiana University look forward to witnessing the Gill Center's future advances. IU is truly fortunate to have such an exceptional team of world-class scientists committed to research that can improve lives—and to be the beneficiary of the Gills' far-sighted vision that continues to guide the center toward still greater excellence.

Michael A. McRobbie
President



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