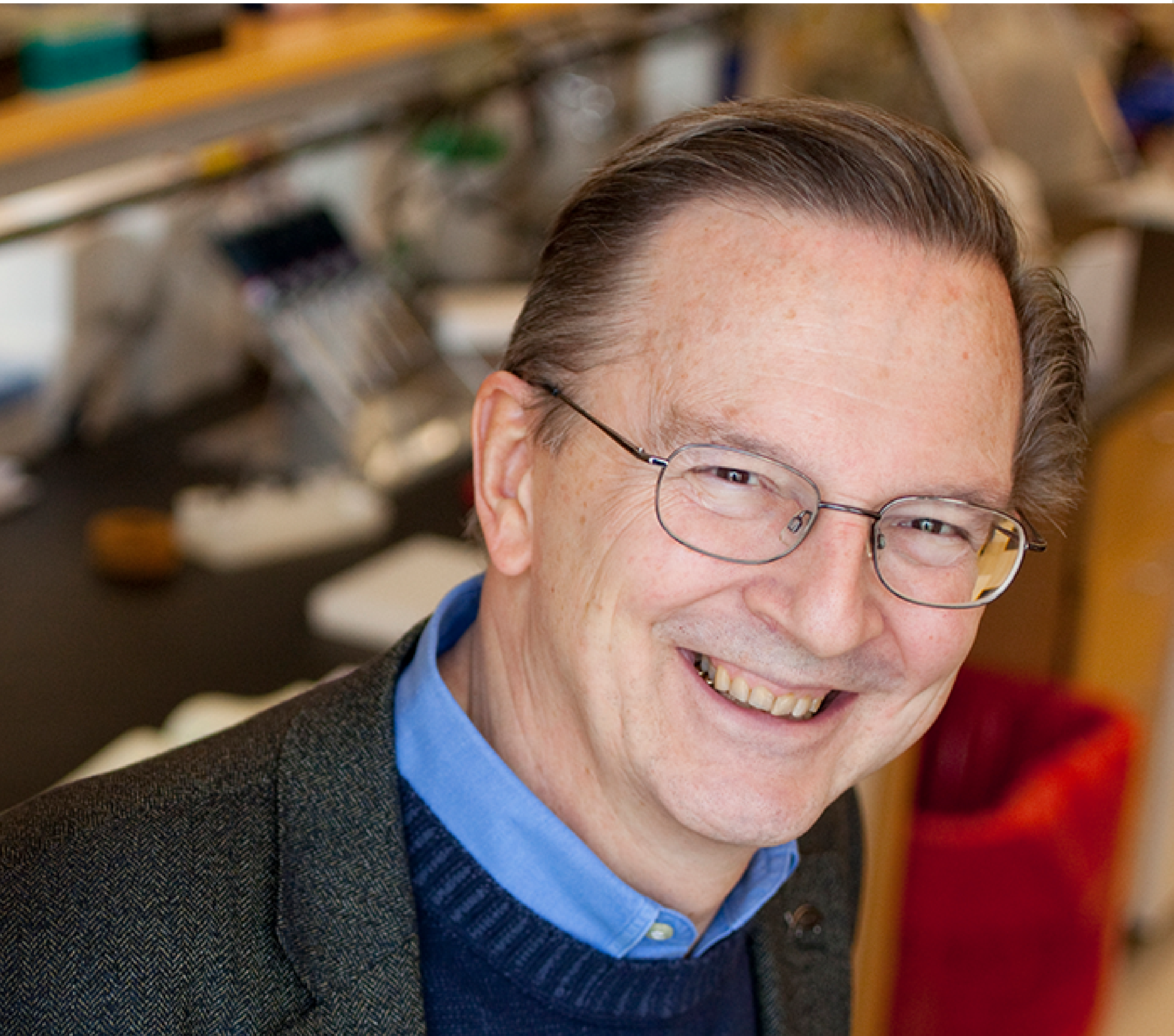
*the* chemists club
Autumn 2022

THE UNIVERSITY OF CHICAGO



# Jack Szostak and the Future of the Origins of Life

# JACK SZOSTAK AND FUTURE OF THE ORIGINS OF LIFE

*Cover Photo by Rose Lincoln, courtesy of Harvard University*

By: Sheila Evans

Professor Jack Szostak joined the Department of Chemistry in September 2022. With contributions in a number of biological fields, including yeast genetics, telomeres, RNA enzymes, and the origins of life, Szostak shared the Nobel Prize in Physiology or Medicine in 2009. Szostak previously served as a Professor of Chemistry and Chemical Biology at Harvard University, Professor in the Department of Genetics at Harvard Medical School, the Alexander Rich Distinguished Investigator at Massachusetts General Hospital and as a Howard Hughes Medical Institute Investigator. He founded the Origins of Life initiative that spans multiple departments. Its aim is to increase our understanding of how the earliest forms of life first emerged on Earth and whether life may exist on other planets. This new Origins of Life research initiative reignites an academic flame sparked initially at the University of Chicago in 1952.

Understanding how complex modern organisms developed involves Szostak and his team returning to the simplicity of the earliest living cells.

Jack Szostak at a welcome dinner with fellow faculty | Photo Courtesy of Raymond Mollering

Their goal is to artificially synthesize simple cells to discover plausible pathways to transition from chemical to Darwinian evolution.

“We think these first simple cells consisted of a self-replicating nucleic acid genome encapsulated within a self-replicating membrane vesicle,” explains Szostak.

Through reaction kinetics, crystallography, sequencing, and other experimental methods, Szostak’s group examines the pathways that first created the nucleic acid compounds essential to life and the assembly of these molecules into the first cells. Experiments on synthesizing self-replicating nucleic acids are fundamental for the origin of life because a living system requires the ability to carry information from generation to generation.

Other departments in the Physical Sciences Division have come together as part of the Origins of Life Initiative to spark collaborations. Fred Ciesla is the Deputy Director of the Origins of Life Initiative and a Professor in the Department of Geophysical Sciences. At this point in planetary sciences, researchers are searching for signs of life using rovers and satellites to examine planets and moons similar to ours. Each researcher adds a different piece to the puzzle. For example, Ciesla studies the recipe for building habitable planets and examines how planets like Earth and Mars formed.

> “We know the ingredients necessary for life, such as water and carbon. However, what we don’t know is how life starts, which is why Jack Szostak’s work is so important,” says Ciesla.

Ciesla describes the Origins of Life initiative as trying to build a community on campus of researchers interested in the question. These include “chalk talks” held by PSD that allow individuals to discuss their research interests, tools, and skills and identify collaboration opportunities. While this interest in origins of life study already existed on campus, efforts coalesced with Szostak coming to campus. “Jack has such deep knowledge of the chemistry of the Origins of Life and knows how to connect the pieces. He is the catalyst for all of this happening,” explains Ciesla.

Physicists are also interested in the study of the origins of life. “Physicists like simple problems,” says Arvind Murugan, an Assistant Professor in the Department of Physics, James Franck Institute, and the College. “Biology can be messy, but origin of life problems provide a minimal context to answer fundamental questions about how matter can maintain and process information.” Murugan is especially interested in the constraints on replicating information.

A collaboration with Szostak examines how information in one RNA molecule can be copied onto another. Szostak has recently suggested that genetic information could potentially be encoded collectively across many molecules rather than in one RNA molecule. “Instead of one ‘book’ bound on a bookshelf, imagine there are many copies of different overlapping pages thrown around your house,” explains Murugan. This collaboration is also studying other aspects of copying molecular information.

Murugan and Szostak are exploring the possibility that selecting for copying information faster will lead to copying with fewer mistakes.

Murugan’s group had noticed a counterintuitive “faster is more accurate” phenomenon in present-day DNA polymerases, while Szostak had observed the same in an origin-of-life context. They are now investigating potential consequences for the evolution of error-correcting mechanisms, both at the origin of life and in extant life.

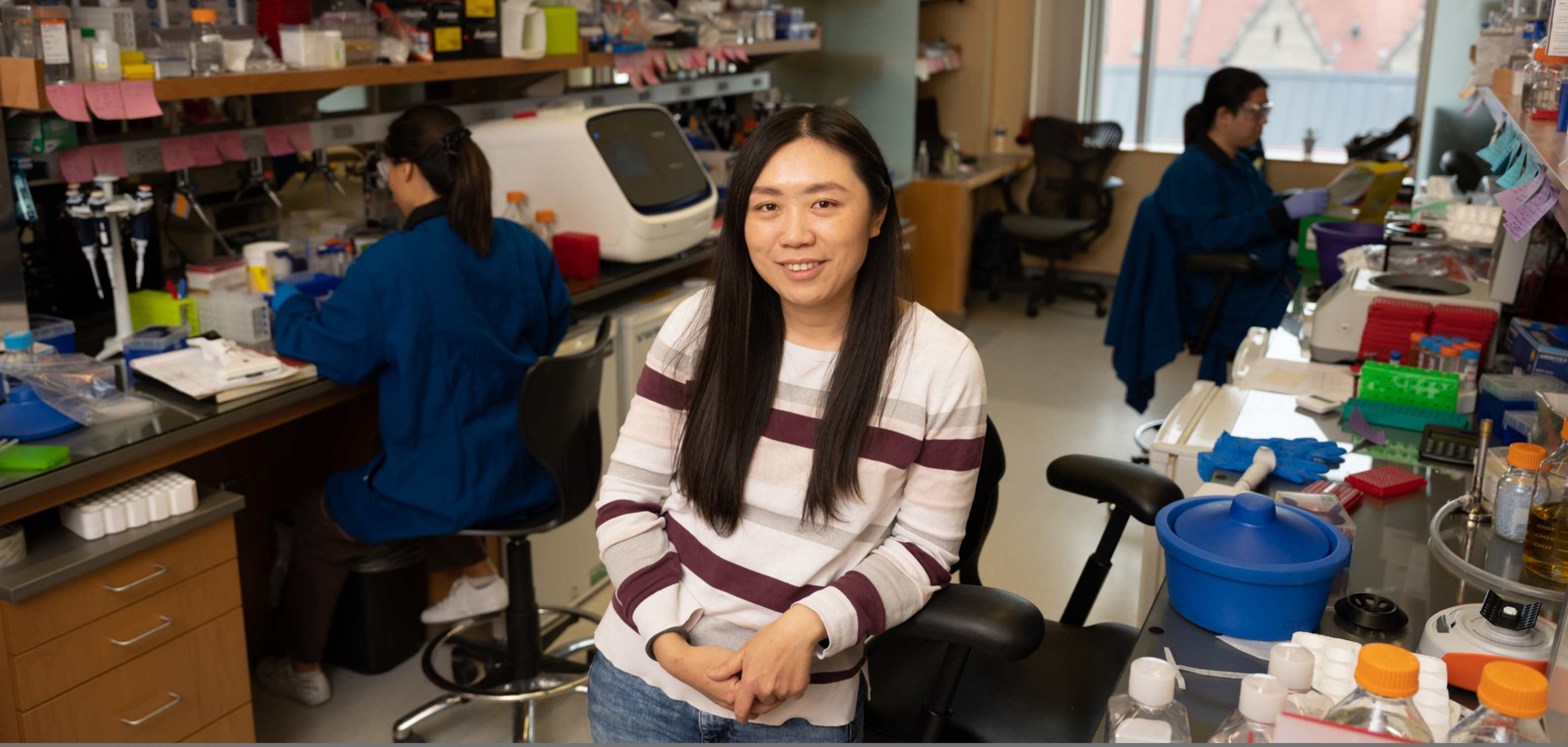
This exploration is conducted in a new research space built up from scratch in Searle, featuring rows of lab benches, chemical fume hoods, and equipment rooms filled with microscopes, mass spectrometers, and other specialized instruments. Cut back to 1952, where a home-built apparatus of glass and metal is being monitored by two chemists: Stanley Miller, a graduate student with Harold Urey, a Nobel laureate in chemistry. Miller injected ammonia, methane, and water vapor into an enclosed glass container to simulate what were then believed to be the conditions of Earth’s early atmosphere. He then passed electrical sparks through the container to simulate lightning. Amino acids, the building blocks of proteins, soon formed. Miller and Urey realized that this process could have paved the way for synthesizing the molecules needed to produce life. After Miller’s death in 2007, scientists recovered sealed vials preserved from the original experiments and reexamined the contents. Well over 20 different amino acids were produced, considerably more than the original amount reported over 50 years previously.

Beyond building out research capabilities, the Origins of Life Initiative offers the opportunity to train students in interdisciplinary research and learn how to communicate across disciplines. “We a taking the long view with this Initiative. It isn’t something that can be answered in a few years,” says Ciesla, “Our research in laying down answers brick by brick, in the hopes to build a house.”

Figure 4. Left, Harold Urey in examining a series of glass tubing and elements meant to emulate the conditions of early earth. Right, Harold Urey sits near a large paper read out of amino acid data University of Chicago Photographic Archive, [apf digital item number apf1-08423 & apf1-08428], Hanna Holborn Gray Special Collections Research Center, University of Chicago Library.

*"Jack’s gentle demeanor belies his deep passion and determination to solve the OoL puzzle. We are so fortunate to have him on our faculty."*

- Chair Viresh Rawal



# CRISPR-DRIVEN DIRECTED EVOLUTION IN MAMMALIAN CELLS: A NEW APPROACH TO THERAPEUTICS

*Photo by Jason Smith*

By: Sheila Evans

Weixin Tang is a Neubauer Family Assistant Professor who recently received a 2022 Packard Fellowship in Science and Engineering. Tang will receive $875,000 over five years to support her research. Tang's lab uses chemistry-based tools to understand and alter biological processes.

The Packard Fellowship will fund an initiative to create new ways to make therapeutic molecules with directed evolution techniques. Tang's team wants to use mammalian cells rather than the typical bacterial cells used in this research to develop possible therapeutic molecules. Mammalian cells are a closer model to humans, meaning the study of them may better translational potential. However, there is no accessible system to use this approach, so Tang set up to make one. This would mean a platform for any lab to create valuable compounds.

This approach is guided by directed evolution which mimics the process of natural selection to steer development toward useful objectives. The resulting biomolecules have desired biophysical properties such as increased stability or binding affinity, and enzymes with enhanced or reprogrammed catalytic function.

Most of the directed evolution efforts are conducted in test tubes with prokaryotes or lower eukaryotes due to their ease of upkeep and manipulation. However, these results usually cannot translate to humans. The low diversity and potency of the mutant libraries is a major limitation for mammalian-directed evolution.

Tang's platform uses CRISPR-guided technology to precisely customize genes of interest without affecting the rest of the genome. Creating this methodology means that many more labs with general molecular and cellular biology expertise could use directed evolution to develop therapeutics. The efficiency of this approach means that researchers can get valuable information with as few as 10 cells. It is predicted that using these new methods, the size of the mutation library would increase by 5 orders of magnitude from what previously existed.

Tang joined the University of Chicago in 2019. Her previous awards include the Searle Scholar Award, the National Institute of Biomedical Imaging and Bioengineering's Trailblazer Award, and she was an HHMI Fellow of the Jane Coffin Childs Memorial Fund for Medical Research.

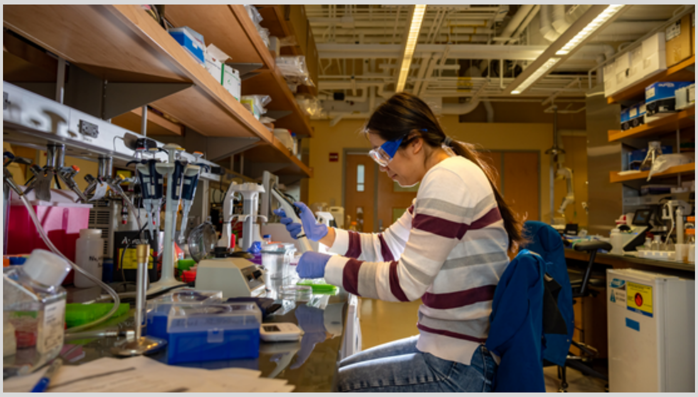
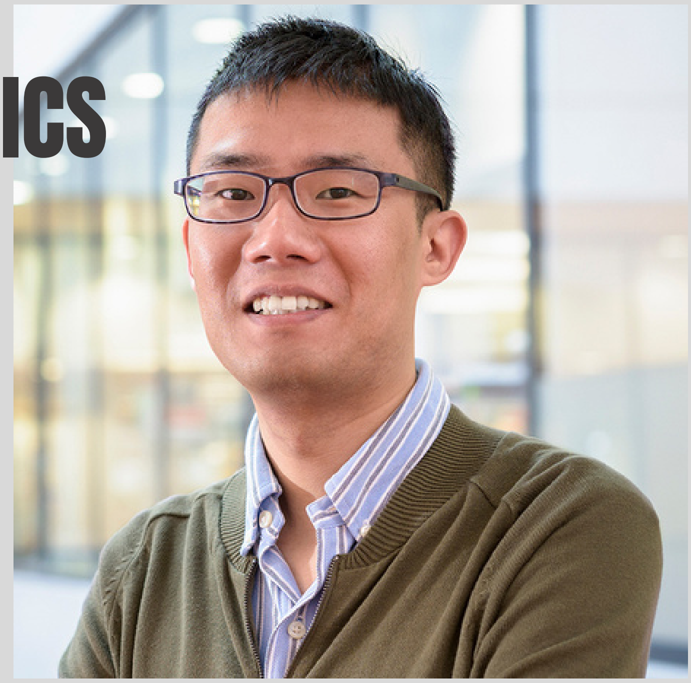


*Photo by Jason Smith*

# UCHICAGO ALUMNUS STARTUP BASE GENOMICS ACQUIRED BY EXACT SCIENCES

By: Sheila Evans



Chunxiao Song, PhD '13

Base Genomics, a biotechnology startup co-founded and built on an invention by a University of Chicago alumnus, was recently acquired by Exact Sciences for $410 million. The startup company sequences genetic and epigenetic data to detect early-stage cancer, which could revolutionize cancer treatment.

“This has the potential to be one of the biggest oncology products,” said Chunxiao Song, a principal investigator and assistant member of the Ludwig Institute for Cancer Research at the University of Oxford. Song, who obtained his PhD in Chemistry from UChicago in 2013, is also the co-founder and chemistry advisor of Base Genomics.

“I mostly focused on the research side of things in the beginning. I kept my head down and worked hard to develop the method,” said Song. “Once the paper on the technology was published by *Nature Biotechnology* in 2019, it started to get a lot of attention, and people outside of academia were interested in collaborating.”

Prior to this publication, Song had met Ollie Waterhouse, an Entrepreneur in Residence at Oxford Sciences Innovation, the world’s largest university-partnered venture firm. Waterhouse was interested in early-stage cancer detection and saw Song’s new technology as a game-changer for the field. Song and Waterhouse then started talking about building a company together. Song reached out to his former advisor at UChicago, Prof. Chuan He, to get his advice.

*“Chuan He encouraged me to build my own company and brand, advising that it would be good for my career in the long term,” explained Song.*

Chuan He, the John T. Wilson Distinguished Service Professor of the Department of Chemistry, is an expert in epigenetics—the study of heritable changes in gene expression that do not involve alterations in the DNA sequence. Song worked as a graduate student researcher in He’s lab and there he was first introduced to the emerging scientific field.

“Chunxiao is an innovator. He invented 5hmC-Seal in my laboratory and has continued to make new innovations that impact biomedicine and health care,” He said. “He is a good example of future academic scholars who generate new knowledge but also impact society with their inventions. I am proud of him.”

“Through Chuan He, I learned that it is possible to maintain academic work while working with entrepreneurs,” said Song. “Base Genomics has turned out to be bigger and have more momentum than I could have dreamed.”

Early detection of cancer could have a huge impact on saving lives and preventing suffering while decreasing treatment costs. For He, the impact of his research has recently developed a personal significance. “A few years ago, my mom was diagnosed with early-stage lung cancer,” said Song. “It was surprising to us because she isn’t a smoker and there is no family history of lung cancer. This kind of story has grown more around us.”

To expand the work of Base Genomics, Exact Sciences will be building out their primary team at Oxford. “I hope to remain involved and advise the chemistry,” expressed Song. “It’s still in its early days but there is momentum to make the early detection of cancer accessible.”

Song encourages others to dream big: “You can still do research you love while forming partnerships in business. Once you develop good chemistry, people will come to you.”


# UCHICAGO RECEIVES $10 MILLION FOR NEW PRITZKER PLANT BIOLOGY CENTER

By: Louise Lerner

*Postdoctoral researchers Guanqun Wang and Haoxuan Li compare a rice plant with gene modification (left) against one that has not been modified at the Biological Services Learning Center's greenhouse. | Photo by Natalie Lund*

A gift of $10 million to the University of Chicago from the Margot and Tom Pritzker Foundation will establish the Pritzker Plant Biology Center on the University's Hyde Park campus.

The research hub, a first of its kind for the University, will focus its efforts on investigating new ways to promote plant growth and increase crop yield. This research has the potential to address and solve one of the most significant global challenges today: climate change's pressure on food production.

"The collaborative nature of our work will be a great asset in advancing new breakthroughs in increasing crop yield and promoting plant growth," said Chuan He, the John T. Wilson Distinguished Service Professor in Chemistry, Howard Hughes Medical Institute investigator, and the first director of the Center. "I greatly look forward to assembling and managing an elite team of researchers who will work together to make the Center a world leader in mechanistic plant biology research."

More than a decade ago, He pioneered a new field of research by discovering a previously unknown mechanism for gene expression regulation.

*"The collaborative nature of our work will be a great asset in advancing new breakthroughs in increasing crop yield and promoting plant growth."*
*- Prof. Chuan He*

He discovered that in most animals and plants, RNA does not just blindly carry out DNA's blueprint but instead actively regulates which part of the blueprint is expressed. Cells place and remove chemical markers on RNA that change the outcome of gene expression. Since that discovery, He and his team have been trying to understand the effect of this process on plants, animals and human diseases.

Recently, He and collaborators added a gene encoding for a protein called FTO–a gene that erases chemical marks on RNA–to rice plants. The experiment increased the plants' mass by 50% and produced 50% more rice. The plants also grew longer root systems, which help plants be more drought tolerant.

The team repeated the experiment with potato plants. Though the plants are part of a completely different family, the results were the same, indicating that there's a degree of universality to the process. These findings have important implications for food supply issues, possibly allowing farmers to produce more food for an increasing population, despite a warming climate.

*Above, the potato yield from unmodified plants. Below, the yield from plants with the RNA modification. Image courtesy of Yu et al.*

*On the left, rice plants without the RNA modification. On the right, a rice plant with the RNA modification that boosts yield. Image courtesy of Yu et al.*

The Pritzker Plant Biology Center will allow He and his team to continue with this research and explore new avenues of inquiry. The Center will prioritize research on plant biology and agriculture, but their findings may have impact beyond plant biology and food security. Production of stock materials, like wood, rubber, and grass for cattle, may also benefit from this work.

“Our primary goal is to understand underlying pathways and mechanisms that regulate plant growth,” He said. “Technologies that allow dramatic yield increase of different crops will obviously have major social impacts on food security but also other materials we typically get from plants. Another important aspect of the Center is developing plant species more tolerant to drought and climate change.”

“Through the decades we come back to science as an opportunity to have a meaningful impact on society,” said Tom Pritzker. “We tend to look to support gifted leaders, and Chuan He clearly fits that description. Chuan explained the opportunity and the desire to move quickly. Margot and I developed conviction in Chuan and are pleased with the outcome.”

As part of the Physical Sciences Division, the Center will support an interdisciplinary team that includes plant biologists and plant RNA biologists, genomic scientists, bioinformaticians, biochemists and other staff. Experimental plants will be grown at the University of Chicago greenhouse on the roof of the Biological Services Learning Center.

“This new Center will dramatically bolster our efforts in investigating pathways promoting plant growth and crop yields to combat some of the most pressing problems we face on a global scale,” said Angela V. Olinto, dean of the Physical Sciences Division at UChicago. “The work of Professor Chuan He and his team is transformative at many levels, and I am grateful for the Margot and Tom Pritzker Foundation’s partnership in supporting their groundbreaking research.”

*A view of the greenhouses on the roof of the Biological Sciences Learning Center (Robert Kozloff/The University of Chicago)*

# Congratulations
## DEGREES AWARDED

### PhDs
***Autumn Quarter 2022***
Philipp Gemmel (Snyder)
Jerald Hertzog (Rowan)
Christopher Melnychuk (Guyot-Sionnest)
Julia Murphy (Sibener)
Thais Scott (Gagliardi)
Lukas Whaley-Mayda (Tokmakoff)
Yibin Xue (Dong)
Hannah Yi (Scherer)
Norman Zhao (Anderson)

### MS in Chemistry
***Autumn Quarter 2022***
Ricardo Almada Monter
Mahdi Assari
Irma Avdic
Pratyasha Chakraborty
Shu Ting Rachel Chan
Zhijie Chen
Seth Freedman
Kuntal Ghosh
Jose Luis Guerra
Matthew Hennefarth
Alvin Huang
Ahhyun Jeong
Kwanghoon Jeong
Sheila Keating
Saehyun Kim
Spela Kunstelj
Kexin Li
Wen Li
Justin Ngai
Kinga Pajdzik
Tamsuk Paul
Zihan Pengmei
Anuchit Rupanya
Victoria Sauve
Oleksandr Sikalov
Michael Van Duinen
Shreya Verma
Zitong Wang
Ping-Jui Wu
Junjie Xia
Yibin Xue
Zining Zhang
Norman Zhao

### BA in Chemistry
***Autumn Quarter 2022***
Clinton Wolfe BA

## NOTABLE AWARDS

**Bryan Dickinson** wins the 2022 ACS Chemical Biology Young Investigator Award

**Guangbin Dong** has been named the first Weldon G. Brown Professor

**Chuan He**, **Wenbin Lin**, and **Jiwoong Park** recognized as Clarivate 2022 Highly Cited Researchers

**Giulia Galli** receives the ISSNAF Lifetime Achievement Award 2022

**Yamuna Krishnan** Wins NIH Director's Pioneer Award for High-Risk, High-Reward Research

**David Mazziotti** & **Jiwoong Park** Elected APS Fellows

**Weixin Tang** named Packard Fellow

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# *the* chemists club

## Autumn 2022

## *Dear friends,*

We are pleased to share our success stories from the first quarter of the academic year. The members of our Department continue to produce outstanding research and publish award-winning work of the highest quality. Recently, Weixin Tang received the David and Lucile Packard Foundation Fellowship, which is awarded to only twenty early-career scientists in all fields nationwide. In addition, Yamuna Krishnan won the NIH Director's Pioneer Award for High-Risk, High-Reward Research, an extraordinary honor given to investigators who use highly creative approaches in their work.

We are delighted to report that Nobel Laureate Jack W. Szostak, who joined our faculty last year after many years at Harvard, has settled into his new position in our Department. Jack is a pioneering scholar of genetics who for many years has been examining the biochemical origins of life. He leads a new interdisciplinary program called the Origins of Life Initiative that examines the earliest processes governing the origin of life on Earth and elsewhere in the universe. We are thrilled to have him with us and are proud to be moving forward together to address fundamental questions about the origin of life.

The interdisciplinary skills of our talented chemists continue to be rewarded through expanded initiatives. This autumn, Professor Chuan He was selected to serve as the founding Director of the new Pritzker Plant Biology Center, which was established with a gift of $10 million from the Margot and Tom Pritzker Foundation.

Of course, none of the work done by our faculty would be possible without the talent and dedication of our caring teaching faculty and our support staff. Every day, our faculty and students benefit from their consistent, reliable, and highly professional work.

Our alumni continue to thrive in academia, industry, and business. We acknowledge and celebrate the success of our outstanding alumnus Chunxiao Song, the co-founder of Base Genomics, a biotechnology startup that was acquired by Exact Sciences for $410 million. Base Genomics sequences genetic and epigenetic data to detect early-stage cancer, a process that could revolutionize the diagnosis and treatment of cancer.

We send our warmest wishes for the new season.

Best regards,

Viresh Rawal
Professor and Chair