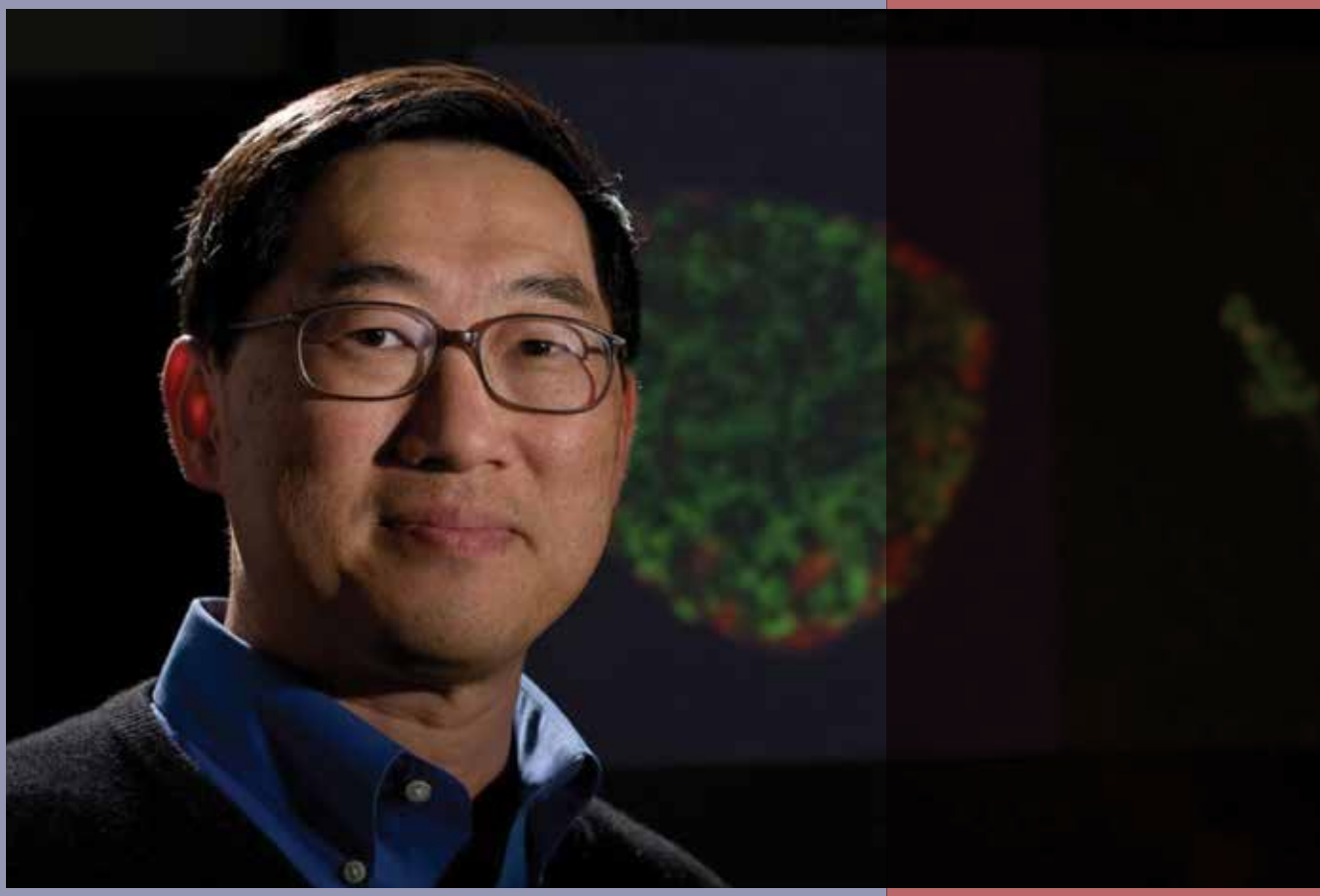


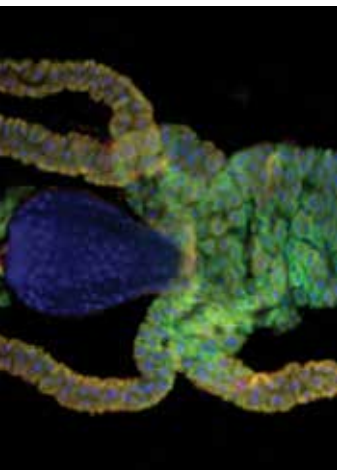
(Above) Dr. Seung Kim '81. (Opposite page) Microscopic image of a fruit fly on G3 journal cover; also below and on following pages.

In August, *G3: Genes, Genomes, Genetics*, a journal of the Genetics Society of America, published a peer-reviewed research paper titled "A Drosophila LexA Enhancer-Trap Resource for Developmental Biology and Neuroendocrine Research." This paper was notable for two reasons: Science-wise, it reveals that the authors' work and research have created a collection of new fruit fly lines that can be used flexibly by other science investigators. Perhaps more unusually, its authors include 24 Exeter graduates whose research findings, through an innovative lab and classroom collaboration between the Academy and Stanford University, are the centerpiece of this paper.

Since 2013, this "StanEx" program has introduced Exeter students to hands-on, open-ended biomedical research with which they have been creating and characterizing new strains of fruit flies. This research has taken place partly in the Stanford lab of Dr. Seung Kim '81 during summer internships, and partly in Exeter's classrooms during an 11-week course in which students' work ties directly into Kim's research to identify ways of potentially curing pancreatic cancer and diabetes. The Exeter-student-created strains are now in a public repository in Bloomington, Indiana, accessible to scientists across the globe, and interest in the paper has already generated requests for specific fruit fly lines from the collection from scientists in the U.S., England and Spain.

And it all started with a seminal meeting of like minds between an Exeter student and an Academy alum.

In the summer of 2011, between her prep and lower years at Exeter, Anika Ayyar '14 was participating in Stanford Explore, a lecture series for high schoolers interested in medicine and biomedical research. When she expressed the idea of exploring a research-focused collaboration between Exeter and Stanford to the series director, he introduced her to Kim, a professor of developmental biology at Stanford whose lab works with — among other models — *Drosophila*, aka fruit flies. "I have been



SYNERGY & SCIENCE

HOW AN ONGOING COLLABORATION BETWEEN EXETER BIOLOGY CLASSES AND STANFORD RESEARCHERS IS IMPACTING THE WORLD OF SCIENCE

BY DANEET STEFFENS '82

deeply interested in Biology since elementary school," Ayyar says. "I was intrigued by the work in Dr. Kim's lab at Stanford and found his passion for medicine and research extremely inspiring. I knew that my peers at Exeter would be similarly inspired to hear about his work, and so I requested for him to be invited to talk at an assembly during my sophomore year."

Ayyar's initiative, Kim's subsequent visit as an assembly speaker in February 2012 — Ayyar introduced him — and Kim's informal meeting with Exeter's Biology Club the next day have generated exciting and far-reaching ramifications not just for Exeter students and faculty and Kim's research lab, but for scientists across the world whose research efforts utilize fruit flies. About 75 percent of the human disease-causing genes are also found in the fruit fly, so manipulating a particular gene in fruit flies and then looking at the effects on those flies can help identify which genes are likely to cause diseases in humans. Compared with other animals, such as mice, fruit flies require less space and time to breed, so testing candidate disease genes over multiple generations in flies is comparatively cheaper and more efficient. The outcome of the Exeter students' work, Kim notes, "will allow other scientists to manipulate the flies' genes and cells in a new way that's still compatible with the older, classic way. It increases enormously the combination of ways to manipulate the genes and cells in scientific investigations."

Ultimately, StanEx is the kind of story of connection, collaboration, commitment and determination that epitomizes the best of what the Academy and its alumni can offer.

Anika Ayyar '14

GIVING AN IDEA LEGS

"That assembly talk was something that I worked on more than just about any other talk that I have ever given," Kim recalls. "Those assemblies were so formative for me when I was at Exeter, so I really wanted to do a good job. But I thought, 'How do I say something that will be meaningful and interesting and perhaps even funny?' " He hit on the exploits and Stonehenge-related achievements of Exeter Physics Instructor Richard Brinkerhoff to capture the sensation, and the savoring, of "Aha!" moments of discovery. But he also highlighted the persistence, endurance and sheer bloody-mindedness that such moments require: "In order to be a scientist you have to have these positive qualities. In my own development as a scientist, I realized sometime in my 20s that I couldn't sleep at night because I was thinking about my experiments; I was really engaged by something, really engrossed in it."

That was part of what Kim wanted to pass on to those future Exeter graduates, "that you're all in search of that thing that will keep you up at night and make you persistent enough to weather all sorts of failure. Because science is really about — in addition to success — a lot of failure."

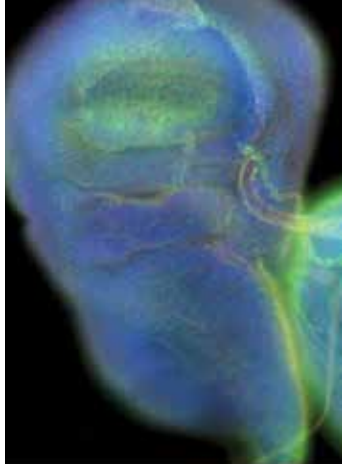
From Brinkerhoff, Kim also learned the importance of writing —"he was an exacting editor," even as a scientist. But one of the problems with science in high school, Kim notes, "is that you already know the answer: You're doing an experiment, but it's a perfunctory exercise where you *already know the answer*. The essence of what's missing is a sense of wonder and discovery, that moment of realizing that you might be the first person ever to think something or connect something or to know something."

"BECAUSE SCIENCE IS REALLY ABOUT — IN ADDITION TO SUCCESS — A LOT OF FAILURE."

When he met with the Biology Club in the Phelps Academy Science Center, Kim was assailed by the familiar odor of formaldehyded fetal pigs, "so I knew that, in terms of teaching science, some things hadn't changed much." He asked Biology Club faculty advisers and Science Instructors Anne Rankin '92 and Townley Chisholm what they felt they were preparing students for.

"Townley said, without hesitation, 'We're preparing them for large college survey courses,'" Kim says. "So I asked, 'Well, is that what you would like to be doing?' and Anne told me that they'd explored possible opportunities to introduce undirected research into their classes, but those efforts hadn't been successful. So *I* said, 'Well, what about working with us?'"

It was a suggestion that proved inspiring to everyone from the Exeter faculty, administration and students to the postdocs in Kim's lab. So what does achieving such levels of professionalism and industriousness at a relatively young age mean to the student participants? Just ask. "By my senior year at PEA I knew that I was passionate about computer science, math and biology," says Lutfi Huq '13, who built the database that makes the strains developed by Exeter students available to scientists and investigators worldwide. "This program was a way to essentially combine all three. The skills I'd learned in my computer science courses at Exeter allowed me to create this database. But that early exposure to real-world science, to research, was very pivotal in determining what I wanted to continue with in my career."

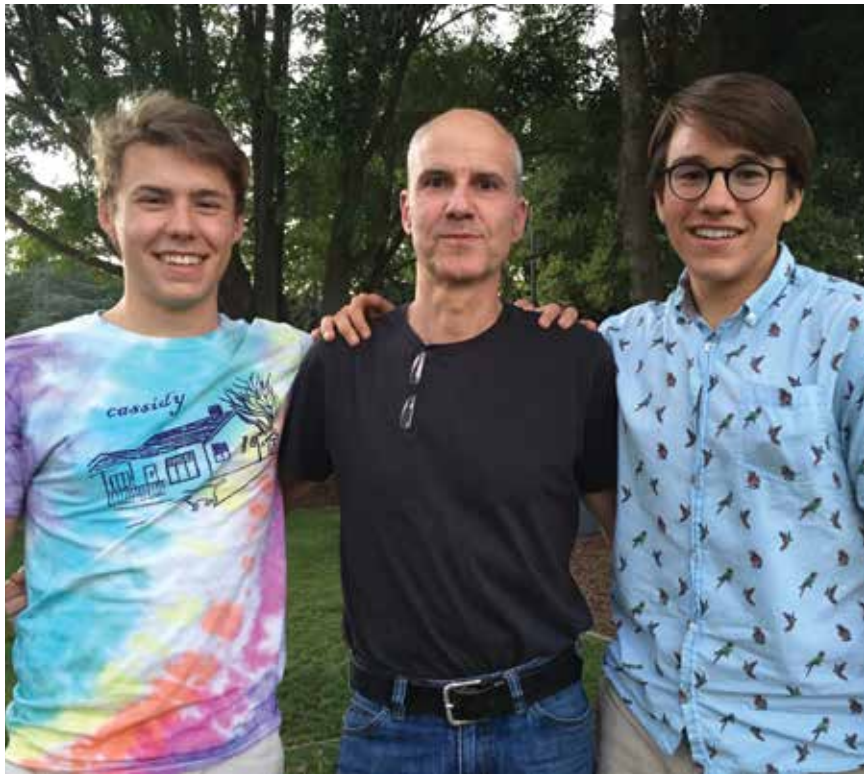


Huq, a senior at Cornell who leveraged his StanEx experience into internships with the Mayo Clinic and the National Institutes of Health, is utilizing computer science and math as tools for his biology research and has a strong interest in microbiology: He plans to mix medicine and research as a physician scientist. "Scientific research is, at its heart, collaboration with other scientists," he says. "That was alive and present in the course. Just by coming to Exeter, you're already amidst kids who have very strong work ethics, strong moral and core work values; it was even more so in this context.

"My peers were driven and extremely collaborative. We discussed all the work we were doing with each other, and it imitated the exact sort of environment that you would see if you were doing, for example, a Ph.D. or running a lab. ... We had very strong mentorship, but lots of the work was also conducted independently. Having that amount of trust and that opportunity to conduct basic science research with the availability of good mentorship, that's what makes the program so wonderful."

LEARNING THROUGH TRIAL AND ERROR

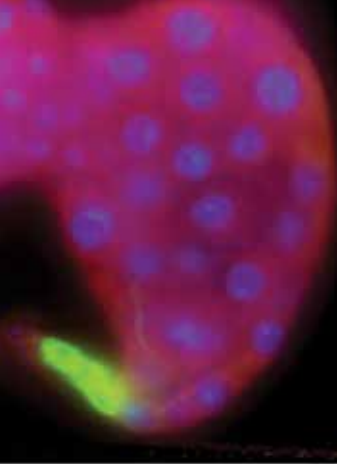
"I don't think I ever expected to have published a paper at 19," says Madeline Logan '15, now a pre-med sophomore at Yale majoring in biology and English. "It's really, *really* cool." The opportunity to work in Kim's lab over a summer, she says, was eye-opening in unexpected ways. Logan discovered that real-life work, such as dissecting fruit fly larvae — "which is really hard because they are so small. You have to dissect them under a microscope with very thin devices" — isn't just about the successes, but about the failures and how you use those failures to advance. "Specifically in the scientific process, but also in general, you can have a tough time of it," she says. "I messed up a bunch of my initial dissections; there were some bumps along the way. But I learned from the scientists who mentored us that that's OK, that that's part of the process. It's *normal*. Learning that you can mess up like that and that it will ultimately end up being OK, that failure is something you can work through — that was important for me to learn."



Ethan Gould '16, Dr. Lutz Kockel and Rex Tercek '16 at an end-of-summer celebration.

New lessons weren't relegated just to students, however. Chisholm and Rankin, for their revised classroom roles, literally, and gamely, went back to grad school. "I did my master's in '88," Chisholm says, "measuring neural output, the responses of orbitofrontal neurons to different olfactory, gustatory and sound stimuli, from the brain in an alert macaque monkey. This work with Seung and the students, though ... I've never done genetics work like this, and the chance to *get* to do it and to go to Stanford for weeklong stints to be trained by the postdocs ... in terms of professional development, it's like, well, my year of graduate school was like letting a kid loose in a candy store. This has been a return to the candy store. It's just been so much fun."

The program, he says, has an enormously positive impact on the students, as well as on the ways in which he and Rankin work together: "The other dimension of doing this course with a team teacher whom I've grown to know and admire even more than I did before is just wonderful, and, with two classes of six students each, you really get to know these students as individuals. You're engaged in a discovery process that is about discovery for the students but also discovery



for the teachers. This is just one small area of genetics research that we cover," he adds, "but it's directly pertinent to human medical research, and hosting this joint enterprise, in our little lab here at Exeter, is fantastic."

Chisholm has also noticed that program participation gives his students newfound confidence; it's a real pleasure, he says, to watch that develop. "Students get to experience firsthand the power of modern genetics, they get to work with the latest techniques and tools, they get to ponder open-ended questions — it's just great. They spend a good seven weeks not only developing these molecular biology techniques, they become very proficient in them and they are also thinking hard about what their data mean and how this fits into the rest of what Dr. Kim's lab is doing. It's incredibly exciting for the students to see what can be done."

ENGAGING IN MEANINGFUL RESEARCH

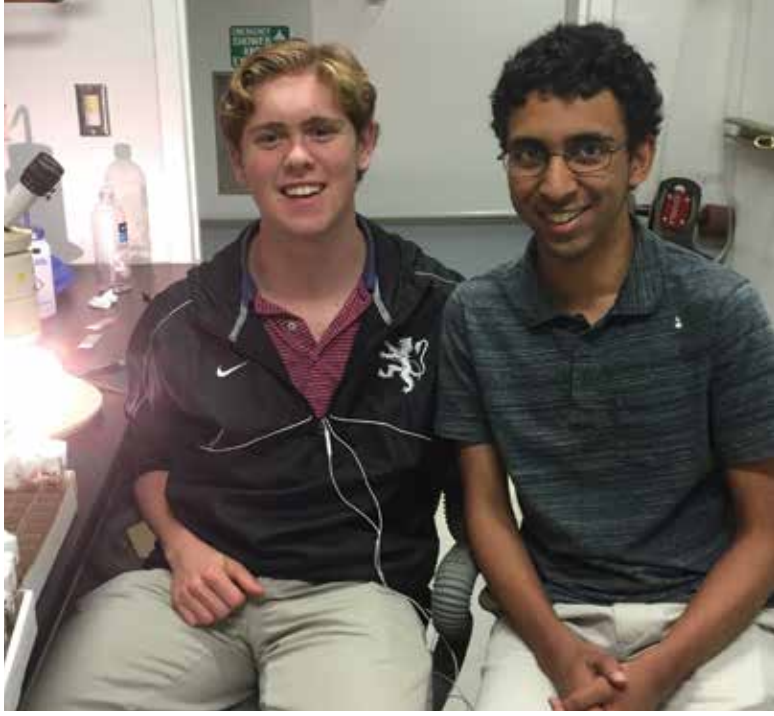
Ayyar's experience with the program affirms Chisholm's words. Her participation sparked something in her, instilling a desire to be part of medicine and biology, she says, "because when you're working on a problem related to diabetes or cancer, diseases that are very real and impact so many people globally, to think that you could contribute even in a small way to move that research forward in finding solutions and cures for those diseases, is highly motivating for a young high school student. That possibility alone is enough to make you passionate about working in this field for a long time." Ayyar, a junior at Duke, completed an engineering internship with Google this summer and is studying biomedical engineering and computer science. "I'm interested in the intersection of technology and biology," she says. "I want to learn more about how to make an impact in medicine through combining those two fields."

Gathering of *Bio470* interns with their Stanford mentors at the Kims' home in 2015: Dr. Ronald W. Alfa, Kathleen Rose Skelly, Emma Herold '13, Rex Tercek '16, Elle MacAlpine '14 and Dr. Sangbin Park.

From the start, Ayyar spent extra time in Kim's lab helping to lay the groundwork for the program. "Over spring break, right after Dr. Kim came to Exeter for his talk, I was invited to join Mr. Chisholm and Ms. Rankin at Dr. Kim's lab in Stanford, and listened as Dr. Kim and his team brainstormed what aspects of his research could be brought to Exeter," she says. "At that point, I remember feeling like this was all kind of over my head: How were we, high school students, going to grasp and conduct sophisticated, real-world research? The genetics and scientific concepts involved in the course were very advanced — you wouldn't go into that much depth even in an AP biology class. So it was a little daunting at first, but the novelty and challenge was also incredibly exciting: Fly stocks are going to be shipped from Stanford to Exeter and students were going to be working on a real project with wide-reaching implications! The fact that they trusted us with that kind of responsibility was mind boggling but really cool."

As part of the initial 12-strong cohort, Ayyar also enjoyed new leadership responsibility during the program's second year, sharing the knowledge she'd absorbed: "My senior year, there was a new batch of 12 students taking the class, and that was when I helped teach, and shared my experience with fly dissections and other lab work. Guiding my peers to discovering exciting aspects of research and learning will always rank as one of my most rewarding experiences, and I learned so much through the process myself."

She's happy, too, that both initial cohorts of students were able to produce something so tangible — a published paper in a scientific journal as well as the newly accessible fruit fly strains — out of their work: "We were just really fortunate that our work resulted in a publication, that too in a



Myles Hagney '17 and Arjun Rajan '17 at the fly station in Kim's Stanford lab during the 2016 internship program.

prestigious, professional journal. That just reinforces how impactful the work is." But, like Logan, she also appreciates some of the more surprising lessons she gained through the program. "A continuously influential concept for me is the realization that things don't work a lot of the time and that research requires a lot of perseverance," she says. "You're not going to start work on a research problem and then get the results you expect and be done — that's not how any scientist has ever achieved anything. Success in science requires determination and is the culmination of a whole cascade of failures and learning from them each time; it's about making your failures useful, adapting to what you learn when things don't work, and continuing to move forward. Because eventually you do reach a point of exciting discovery and success in your research, but it might just be very different from your initial assumptions!

"When I went back to the lab the second time, there were points where it seemed like we were doing the same process over and over again, like every day, for five days straight, and we were making the same mistakes. And it was at that point where I realized how useless it is to keep trying and hoping for a different result every time instead of analyzing the failures and the process and moving forward constructively from that."

Ayyar says it was "incredibly empowering" to have a group of professionals place such faith in her and her fellow students in terms of their capability and potential — like Huq and Logan, Ayyar is palpably appreciative of the generous mentoring they received while at Kim's lab and from Chisholm and Rankin. And she is delighted that the students' work has produced results that can be shared with others in the field: They've made a meaningful, professional contribution to science. "You can see, in the paper, the fly lines that produced relevant results that are actually useful to the scientific community," she exclaims. "We named our lines with our initials, all of us students, when we created them, so these lines that are going out into professional fly repositories in the biological community have high school students' names as their markers! Out there! In the world!"

> "STUDENTS GET TO EXPERIENCE FIRSTHAND THE POWER OF MODERN GENETICS … ."

For Kim, giving students that revelatory experience is what this program has always been about, and he's already pursuing expansions, scaling up with a collaboration between his lab and Commack High School on Long Island. Chisholm and Rankin shared their experience and offered encouragement to teachers there, and Kim shared an early draft of the now-published paper to show the practical impact that was possible. With the input of Exeter leadership, Kim is also investigating the possibilities of implementing a similar program in a high-needs school.

"My hope is that there is a reservoir of students who are not exposed to the most interesting, engaging aspects of STEM [science, technology, engineering, math], and that we will unleash that latent population to find those compelling aspects at an earlier stage and then ideally become addicted to it," Kim says. "I don't want to force anything on them, it's just a new way of engaging people: People are exposed very early on to poetry, music, drama, writing, reading well-written things; I don't think that they're exposed soon enough or in an authentic enough way to science. Math is an exception perhaps. I think things are slowly changing, but I think that the most direct way to teach science or other fields is to give people the opportunity to engage *without any distance* between the material and their interests. That, in the end, is what we're trying to do." E