There is a lunch celebration on a summer Wednesday in McCort-Ward Hall, complete with pizza and Chinese food. It's a tradition — whenever members of the Bacteriophage T4 Lab publish a paper, they celebrate, and the lead author foots the bill. Today's lunch is on Pan Tao, a postdoctoral fellow from China who has been with the lab for four years.

The paper on next generation plague vaccines has been published in *PLOS (Public Library of Science) Pathogens*. It's the second time in just a few months that Tao has had to treat his colleagues. He was the lead author on a paper published in April in *Proceedings of the National Academy of Sciences*, the journal known as *PNAS*. Both papers present landmark research in the fields of vaccines and virology and are published in two of the most selective scientific peer-reviewed journals.

The *PLOS Pathogens* paper documented the success of a vaccine engineered by the authors that provided 100 percent protection to mice and rats against pneumonic plague. The vaccine might one day provide a means for mass vaccination of humans against bioterrorist threats.

The *PNAS* paper demonstrated the success of a vaccine devised by Rao's lab that delivered both a DNA vaccine and a protein (antigen) vaccine simultaneously into mice. The Catholic University scientists were able to combine two types of vaccines in one shot, a new way to make potentially effective vaccines in the future against complex infectious agents such as HIV-1, malaria, and TB.

Other members of the T4 Lab are listed as authors on these papers, along with collaborators at the University of Texas Medical Branch. The principal investigator on both papers is Venigalla Rao, professor and chair of Catholic University's Department of Biology. He is the founder and the heart and soul of the T4 Lab.

Nearly all of the 15 members of the lab have gathered to celebrate the publication of this groundbreaking research. Before they eat, they look to their leader. With a smile, Rao raises his paper cup of Sprite. "This celebration is well deserved. Of course you know there is always a ‘but’ for me," he says. "We have tested our ideas with success. Now we must advance our concepts to produce a biodefense vaccine that is effective against both plague and anthrax, an HIV/AIDS vaccine, and vaccines that can be effective with just a single dose. These are our challenging and exciting goals and they are very much connected to what we have accomplished so far. So we should celebrate now, keeping in mind that we have a lot to do in the next few years. We will have a bigger celebration maybe three years from now. Who knows, maybe even a year from now."

There is clapping. "Okay Pan, let’s hear from you," says Rao.

Tao simply says that he is happy and grateful, and quickly defers to Marthandan “Marty” Mahalingam, a postdoc from India who has also been with the lab for four years. He is an author on both papers. "Thanks to everybody! Let’s eat," says Mahalingam, with a hearty laugh.

Outside the room where the party is taking place a bulletin board showcases more than 30 papers published by members of the lab in such prestigious scientific journals as *Cell*, *Journal of Molecular Biology*, and *Journal of Virology*. The articles are in plastic sleeves and tacked onto the board in a diagonal pattern, each overlapping the other. They will have to make room for the two latest publications.

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By Ellen N. Woods

CUA’s Bacteriophage T4 Lab has been awarded millions of dollars in grants and has published cutting-edge research. The lab’s team members, led by Venigalla Rao, combine scholarship with passion and dedication. They are on a quest to develop vaccines for some of the world’s deadliest bacteria and viruses.
The virus infects the reputation for cutting-edge science. Rao moved upstairs, and gained an international reputation for cutting-edge science, bringing in millions of grant dollars, secured patents, and built the lab he founded in 1997, which now has about 50 people working in about 20 to 30 minutes. "The reason we get sick very fast by viral infection is the DNA genetic material. The machine that pumps DNA into the cell is the T4 bacteriophage," explains Rao. "When the virus lands on the cell wall and attaches through its tail fibers, it injects its genetic material into the host cell and starts replication. The virus's packaging machine is one of the fastest and strongest biological motors known. The machine pulls the long strand of DNA into a tiny shell called the bacteriophage particle."

"... virus replication is very fast and efficient ..."
After five years, Rao earned his Ph.D. The day after he handed in his dissertation he took his first plane ride ever, heading to Baltimore to begin what would be a nine-year postdoctoral fellowship at the University of Maryland School of Medicine in the lab of Lindsey Black, who was studying bacteriophage T4. “He was an excellent mentor and provided a great training ground. I published two key papers that I still refer to today. One described part of the packaging machine, the whole capsid, and the other described the parts of the motor. These would pave the way to tease out the mechanism of the packaging machine.”

While at the Indian Institute of Science, he had met his future wife, Mangala, a Ph.D. student. She went to the University of Manitoba, Canada, for her postdoc in the field of immunology. But once they decided to marry, she joined him in Baltimore, landing a position at Johns Hopkins University School of Medicine. When the time came for Rao to take the next step in his research career, he had become hooked on unraveling the mysteries of T4. His wife saw an ad for a visiting/assistant professor at Catholic University. He had not heard of the University, but she encouraged him to go on the interview because it would keep them in the area.

“I felt right at home and knew if they offered me the job I would take it,” he said. “I started from scratch. I had one very old minus-70°C Revco freezer and a refrigerator, and that is it. I very scrappily pieced together cheap supplies. I got a Department of Energy grant right away because I was able to tie the T4 work to the human genome, which was an exciting project at the time, but then it would be several years before I got another grant. I was publishing papers, but the grants weren’t coming. Colleagues suggested I change my focus to human viruses, which were more relevant at the time. But I was stubborn.”

Rao says he was rejected at least three times by NSF and twice by NIH. “I kept submissions. I was doing an experiment at my bench in the lab when the NSF program director, Dr. Chitnis Parag, personally called me ‘the professor’ because I seemed to know an answer for everything. I didn’t care if he was right or wrong, I just wanted to keep my focus on the project.”

Great Minds Think Alike

The T4 Lab works in partnership with scientists at the U.S. Military HIV Research Program at Walter Reed Army Institute of Research; the National Cancer Institute at NIH; the National Institutes of Allergy and Infectious Diseases at NIH; the Department of Physics at the University of California, San Diego; University of Texas Medical Branch; the Department of Biological Sciences at Purdue University; and the Department of Physics at the University of Illinois.

“Research done in a vacuum can be very slow and ineffective. Scientists need to accept they are not experts in all areas. They have to be willing to learn from each other,” says Sriram Subramaniam, the head of the Biophysics Section in the Laboratory of Cell Biology at the National Cancer Institute. “In collaboration with Dr. Rao we are close to important advances in HIV structural biology. Exciting things are on the way. What he is accomplishing at CUA is extraordinary by any standards, even among the largest, most sophisticated research institutions.”

Subramaniam is known for his work in the field of high-resolution cryoelectron microscopy. His lab has the most sophisticated instrumentation and technology to solve structures of proteins to near atomic resolution. In a complementary relationship, Rao’s T4 Lab is expert at engineering the proteins and biochemical analyses, for instance the HIV virus envelope protein.
The 83-year-old Rossman has solved the structures of many viruses and proteins using X-ray crystallography. He and Rao have collaborated for nearly 14 years on bacteriophage T4 structure, assembly, and DNA packaging.

“Anything in life requires expertise. So for the best science, we collaborate. We bring what we know best together with what others know best,” says Rossman. “Rao and I have long discussions. The science is interesting and productive, and the friendship is what I treasure most.”

For nearly 15 years, Rao has collaborated with the U.S. Military HIV Research Program at Walter Reed Army Institute of Research. One of the labs is led by Carl R. Alving, who Rao says is “one of the world’s experts on antigens and vaccines.” Walter Reed was a key player in orchestrating a successful human clinical trial of an HIV vaccine. The trial, conducted in Thailand, showed positive results with 33.2 percent efficiency. Not enough for FDA approval, but enough to give hope to researchers around the world.

The collaborator with whom Rao spends the most time is his wife, Mangala Rao, section chief, Antigens and Immunology, at Walter Reed. They collaborate on research by day and enjoy talking shop at the dinner table.

“Marty, can you open the door for us?” The brilliant scientist asks how much time he spends with the students. “I stop at the cell culture room. ‘Marty, can you open the door for us?’ The brilliant scientist seems to remember the code.

Finally he arrives at the meeting room to take in the packed room. Many team members have made dishes from their native countries: Chinese shrimp and noodles, curry chicken, Middle Eastern fried rice, sushi, and masala fried fish are among the items on the menu.

“Room is a place where we store samples. Here are freezers, incubators. The crystallization oven. All designed to work efficiently.” He stops at the cell culture room. “Marty, can you open the door for us?” The brilliant scientist seems to remember the code.

As the discussion winds down, Rao is asked how much time he spends with the students. “I am always here for students; to mentor, to give advice. That’s my most important priority. We help and support each other. We are not afraid to make mistakes. That’s sometimes how we learn the most. At the end of the day, though, each student is the owner and driver of his or her own project.”

It has been a busy fall for Rao — he submitted two grant proposals in November alone. In two days, he will leave for India where he will stay for four weeks writing his parents and siblings. It has been more than five years since he’s gone home, so he decided to make it an extended trip. He will take his research works with him and teleconference and Skype with his lab members and collaborators daily.

Subramaniam’s lab has prepared a postdoc Thanksgiving lunch to bid him farewell and they wait with food set up in their meeting room.

They’ll have to wait a bit longer. Rao is giving the Ph.D. students a tour of the third-floor facilities that he helped design based on a desire for collaborative space and efficiency.

Goli Yamini has been a Ph.D. student in the T4 Lab for a year. She says it’s size and Rao’s reputation led her to CUA. “I love that this lab is intimate and at the same time cutting edge. I knew I could grow here. Sometimes at larger programs you can get lost and the professor may not be accessible.”

“As a larger research institution someone of Dr. Rao’s caliber would spend 80 percent or more of his time doing only research. He might not even teach a full course, but a few classes here and there,” says James Greene, dean of graduate studies and a professor in the Department of Biology. “At CUA, he teaches courses and runs his department and mentors young faculty and students, from high school to doctoral. They have amazing opportunities to work with him.”

On the Tuesday before Thanksgiving, Rao is providing an orientation to his lab to first-year graduate students. “This is a room where we store samples. Here are freezers, incubators. The crystallization oven. All designed to work efficiently.” He stops at the cell culture room. “Marty, can you open the door for us?” The brilliant scientist seems to remember the code.

“T o be a scientist, you have to love what you are doing, to feel connected to the problem you are solving. For me, answering scientific questions is very satisfying. It makes me feel connected to humanity. If I can make even the tiniest contribution to stopping the virus that causes such a horrible disease, that sparks a light in me — it fuels my curiosity and my passion,” says Ph.D. student Goli Yamini.

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