

# From Dartmouth to Honduras

Reducing the Burden of Cancer Through  
Research, Education, and Collaboration



by TIM DEAN

Sunset on the drive from San Pedro Sula to El Rosario during the July 2017 CLARO 1 agricultural project.  
Photo courtesy of Norris Cotton Cancer Center (NCCC).



**One day back in 2011, while riding in a truck on a hot, dusty road in rural Honduras, Linda Kennedy, MEd, associate director of community affairs at Dartmouth's Norris Cotton Cancer Center, turned to colleague Greg Tsongalis, PhD, who'd been unusually quiet, and asked, "So, have you come up with a scientific question yet?"**

**The two were in Honduras to investigate the country's high cancer rates and find out what kinds of research projects could be done to help lessen that burden.**

**"I'd been kind of deep in thought—there were so many questions, I wasn't sure where to begin," recalls Tsongalis, a professor of pathology and laboratory medicine at Dartmouth's Geisel School of Medicine. "I mean, we rarely see individuals who have not taken so much as an aspirin in their lifetime!"**

**T**his wasn't Kennedy's first trip to Central America. For a number of years, while working for Dartmouth College, she'd been helping to lead community-building activities in the mountain village of El Rosario through ACTS (Americans Caring Teaching Sharing) Honduras—a non-profit based in Norwich, VT, which works to foster cross-cultural understanding and promote sustainable programs for health, education, agriculture, and economic development.

"But I didn't know cancer in Honduras at all," says Kennedy, who was still new in her role at the

Cancer Center. "So through the magic of Facebook, we met a young doctor who agreed to take us all over the country. We rode around for about a week and saw cancer from the very poorest conditions, to the most elite clinic, and everything in between."

Many images remain vivid from the trip: public hospital hallways jammed full of patients waiting to see a physician; a large plastic Coke bottle on the windowsill of a pathology lab, used to preserve a tumor; a modern piece of donated pathology equipment sitting on the cracked floor of a facility basement (unusable because of the expense of chemicals



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needed to run it); a medical student working alone as the village doctor in a small remote outpost clinic.

“It was so eye-opening to see what people were going through, and how appreciative they were of anything that you could do for them,” says Tsongalis. “The Honduran people try hard to do as much as they can with the little that they have, which is really impressive.”

While visiting La Liga Contra el Cancer (one of only two hospitals in Honduras offering cancer services) in the city of San Pedro Sula, they met Suyapa Bejarano, MD, who serves as chief of clinical oncology at the facility and would become a key collaborator and close friend. Through Bejarano and her colleagues, Kennedy and Tsongalis began to understand the scope and complexity of the country’s greatest cancer burden, cervical cancer, and the factors that contribute to it.

“In the U.S. and other developed countries, cervical cancer is one of the most treatable and

preventable cancers because of the routine screening programs we’ve implemented, with Pap smears and HPV (human papilloma virus) testing, which allow us to detect things early,” explains Tsongalis. “In low-and middle-income countries (LMICs) like Honduras, this just hasn’t been possible.”

With a population of 8.3 million, Honduras is ranked second lowest (after Haiti) economically in the western hemisphere. About half of its residents live in rural, hard-to-reach areas, and the vast majority of Hondurans are poorly educated. While the country’s cervical cancer rate ranks second highest (to Nicaragua) in Latin America, only 10 percent of women of screening age (20-59) receive Pap smear testing each year.

And without a national cancer registry, it is unknown whether the 10 percent are the same women every year, all new, or a mix. To combat the problem, Bejarano has coordinated a cancer registry in her hospital, and with medical students and volunteers leads a program known as PESCA.

“Working with local leaders, we provide outreach and ‘brigade-style’ Pap smear screenings and education throughout the region about 40 weekends per year, in any location where a community can amass more than 50 women,” she explains. To date, her program has made impressive progress—screening well over 23,000 women in the San Pedro Sula region while reducing the turnaround time of screening results.

With very few trained pathologists available to evaluate Pap smears in Honduras, the typical wait time across the country for women awaiting screening results can be six months or longer. By the time women with cervical cancer seek care, many (about 50 percent at La Liga) are already suffering from advanced metastatic disease.

“When we met Linda and Greg, we were excited by the opportunity to work in a research collaboration that would allow us to build on our previous efforts and create scalable models focused on prevention and early screening to better cope with our cervical cancer burden,” Bejarano says.

An important part of this work started in the village of El Rosario, where, in partnership with

Photo courtesy of NCCC

Teens from El Rosario in the “Fuerza Arriba” program and Juliana Ortega pose for a picture after volunteering at the May 2017 Men’s Jornada (large screening/education event) in El Rosario, Honduras.



local leaders and ACTS Honduras, Kennedy began teaching teens about how to prevent HPV and other sexually transmitted infections through a program called La Fuerza para el Futuro (The Force for the Future). Its overall purpose is to teach leadership skills, promote the ethic of volunteerism, and create a network of teens among remote villages.

“We’ve had about 40 teens participate each year in a weeklong program to increase their knowledge and help them to become health promoters in their own communities,” Kennedy says. “They’ve produced handwritten educational brochures and distributed them around the region, written and performed skits in remote mountaintop villages, and worked to make condoms available to teens.”

The teens and the existing ACTS Honduras infrastructure, which included a bunkhouse for visiting volunteers, local cooks, and a basic primary care clinic, made El Rosario a logical site for the first major research project between the Cancer Center and La Liga Contra el Cancer. Called La Gran Jornada or “large clinical education event,” it tested the feasibility of bringing a cervical cancer-screening clinic to a rural area, and whether offering things like free transportation (via buses) and screenings would increase participation.

“One of our main ideas was, if we could take cervical swabs and use them to screen for the presence of the HPV virus that is known to cause cervical cancer—it would be an easier, faster, and more sensitive way of testing that would require less training than the traditional method of looking at cells under a microscope (as with Pap smears),” explains Tsongalis.

Since only 14 types of HPV (out of more than 100) are known to cause cancer and are therefore considered high risk, only the women found to have high-risk HPV would need to have their samples go on for Pap testing. “If we could get the test to work in that tough environment, the new system would alleviate a lot of burden on pathologists down there needing to screen cells under a microscope,” he says.

The turnout at the La Gran Jornada greatly exceeded expectations. Over two days, 472 women from 31 villages were screened for cervical (as well as breast) cancer. “One of our Dartmouth-Hitchcock physicians who specializes in breast cancer, Mary Chamberlain, did a great job with Suyapa, teaching the self-breast exam and then doing clinical breast exams on any women who self-identified as having a problem to be checked,” says Kennedy. “Several women were sent to La Liga for breast biopsy or mammogram, and a few breast cancers were found and treated.”



Greg Tsongalis and Linda Kennedy review research data with the portable PCR (polymerase chain reaction) system they used to test the feasibility of offering large-scale cervical cancer screenings in Honduras.

The Pap smears and cervical swabs that were collected from the cervical cancer screening were shipped back to Dartmouth for testing, and the results were sent to Bejarano, who followed up with patients that were positive. As hoped, the HPV screening eliminated a majority of the women from needing any further testing or care.

Buoyed by the success of the 2013 La Gran Jornada, the group, which began to attract additional investigators (offering multidisciplinary expertise) as their work evolved, set their sights on a more ambitious project that could help make large-scale cervical cancer screening sustainable in Honduras.

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The project was made possible by a generous grant from the Munck-Pfefferkorn Education and Research Fund. Named for distinguished Dartmouth Medical School faculty members Elmer Pfefferkorn, PhD, and Allan Munck, PhD, the grants were created to support high-potential research and education initiatives within Geisel.

The project would test the real-world efficacy of a rapid, inexpensive, portable technology that could detect the 14 types of high-risk HPV known to cause cervical cancer, and would also assess the feasibility of implementing workplace cervical cancer screening within a factory setting in the city of San Pedro Sula, Honduras.

“It really required us to rethink how we did everything here in our lab, where we use robotic equipment and state-of-art processes, to come up with a largely manual approach that would work in the field given the challenges of the Honduran environment—which included heat, dust, bumpy roads, uneven electricity, and lack of running water,” Tsongalis explains.

Tsongalis and his team, together with other collaborators, came up with a number of innovations to reach their goals, which included using: a small (car battery-sized) PCR (polymerase chain reaction) instrument sturdy enough to be transported in the back of a truck, lyophilized (dried) chemicals that didn’t require refrigeration to remain stable during storage or transport, and a simple hotplate and pot of boiling water for isolation of DNA. Importantly, the whole process produced test results in two hours, and could conceivably be taught to personnel with minimal or no lab experience.

In 2016, the team repeated the Jornada concept, this time with a total of 800 women screened using the process—400 at the factory in San Pedro Sula and 400 in the rural village setting of El Rosario (with both thyroid and oral cancer screenings and education being added in El Rosario at the request of Honduran oncologists). Three swabs were collected from each woman: the first for the on-site HPV testing, the second to create a Pap smear to be reviewed by La Liga pathologists if necessary, and the third shipped back to Dartmouth for repeat HPV testing to see how the results matched up.

“Both events were very successful, and we



Medical students Charlene Dunaway and Tom Flynn prepare high-concentration Tinopal solutions for use in the July 2017 CLARO 1 agricultural project.



Tracer dye shows contamination on a farmer’s hand during the July 2017 CLARO 1 agricultural project in El Rosario.

achieved an excellent concordance rate with the results, nearly 90 percent,” says Tsongalis, “Only 15 percent of our two Honduran cohorts had high-risk HPV, so just their samples were forwarded to pathology for traditional Pap smear review, reducing their workload by 85 percent. Dr. Bejarano then followed up with the women who needed further testing or treatment.”

Fortunately for women who are identified by a positive Pap test, their pre- or even invasive cervical cancer can often be cured with an office treatment.

“For us, it was like a jump to the moon in terms of showing us what was possible and how we could continue to improve and expand on our screening and prevention efforts in the future,” says Bejarano.

One of the most important aspects of the study was that it allowed the team to compare the frequency and types of high-risk HPV virus seen in one region of the country versus another, and to what is seen in the U.S.

“We were surprised by the results; the most prevalent types of high-risk HPV differ significantly

when you compare Honduras to the U.S. and other developed countries, where most vaccine development has taken place,” says Tsongalis. “This has significant implications—it likely means that different vaccines need to be developed to target the specific high-risk HPV types seen in Honduras and other LMICs to better protect those women from cervical cancer.”

A second, scale-up project funded by MuncK-Pfefferkorn and launched this fall, is screening 2,000 women (for high-risk HPV) in a larger factory setting in San Pedro Sula. “Honduras only has about a dozen pathologists, there is no in-country training program, and they still have a large backlog of specimens that need to be processed,” he explains. “We’ll be using some innovations in DNA extraction, low-cost digital imaging, and telepathology to see if we can increase the capacity of their pathology services.”

The outcomes and momentum generated by the partnership’s research activities over its first five years has led to three other projects that were started in 2017. Funded by grants from the Cancer Center, the projects together comprise the Community Led Action Research in Oncology (CLARO) program.

“CLARO uses a participatory research approach that includes not just scientists but community members who identify needs, help generate research questions, and are most likely to be affected by the study findings,” says Kennedy. “Several Geisel and Thayer students are playing key roles in these projects, which will continue into next year.”

The first CLARO project is aimed at assessing and reducing farmers’ exposure to carcinogens that are contained in the agricultural chemicals they use to spray their crops. Using a variety of educational techniques to teach safe use (including skits put on in villages by the teen health promoters), fluorescent tracer dyes, and a shower facility (built by ACTS) for workers, the project team is tracking improvements over time.

Team members Tom Flynn and Charlene Dunaway, both third-year medical students at Geisel, went down to El Rosario for 10 days last summer for phase one, using a space in the ACTS clinic to set up testing stations.

“Basically it involved having the farmers add the tracer dye—that we tested and prepared in Dr. Mark Spaller’s lab at Geisel last spring—to the pesticide in the backpack sprayers they use,” says Flynn. “And then when they returned from the field, we used some handheld black light flashlights to have them (and family members) see, and to allow us to record, where they’d gotten contaminated on their clothing and different parts of their bodies.”

Ethan LaRochelle, a graduate student in the Optics in Medicine group at Dartmouth’s Thayer

School of Engineering, came up with a technique to capture digital images as part of the study. “I built a box out of PVC and some vinyl essentially, with UV lights inside it, and then put a special filter on a SLR camera that I positioned above it on a tripod,” explains LaRochelle. “We’re going to be analyzing those images to look at the amount of exposure farmers get on their hands.”

“While we were in El Rosario, the community was also building a facility for the farmers, so they will have a place to shower and essentially decontaminate after work, change into clean clothes, and have a space to store their pesticides,” says Dunaway. “We’ll be going back later this fall to work with the same group of farmers, to compare exposure levels and see if the interventions are working, and then with a new group, as well.”

Since building a facility in every village isn’t possible, Kennedy and her ACTS Honduras partners—including the Dartmouth College undergraduates who volunteer in El Rosario each year—are planning more outreach and educational activities to teach

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Photo courtesy of NCCC



Suyapa Bejarano, MD (maroon scrubs) stands with local volunteers to dedicate a memorial to a woman who was diagnosed with breast cancer during the 2013 Jornada and passed away the following year.

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Photo courtesy of NCCC



A PESCA volunteer takes the blood pressure of one of the Jornada participants while his grandson watches during the May 2017 Men's Jornada in El Rosario, Honduras.

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farmers who live farther away how to safely store the chemicals at home, and how they can protect themselves and their families from contamination.

One conversation with a forward-thinking village leader and collaborator was especially memorable for Flynn. “He told me what he wants to do is create a culture of safety,” Flynn says, “and that he recognizes that no intervention will be sustainable without buy-in at the group level.”

“He also said the project wasn’t about him or his village. He was adamant that the new facility they’re building is open to anyone who wants to come and learn from its example. He dreams that someday the lessons learned from this study in El Rosario can be shared far and wide to improve and protect the health of all his countrymen.”

Dunaway, who is Honduran, understands this sentiment intimately. “One of the most enjoyable aspects of this project has been to see how enthusiastic and motivated the villagers are to work with us,” she says. “They can see how much their community has improved over the years, and they greatly appreciate all of the opportunities that their children are having now that they didn’t have growing up.”

LaRochelle, who is also lending his technical skills to several other partnership projects, wholeheartedly agrees. “The Hondurans are just great to work with,” he says. “They are eager to do any project that we want to do with them, and they’re very resourceful when it comes to problem-solving. It’s also been rewarding to work with people from across our organization—from the hospital and the Cancer Center to Geisel and the College—who are so motivated to help.”

The success of the women’s Jornadas in El Rosario prompted male village elders to ask if the research teams could provide a similar screening program for men. And so the second CLARO project, called the Men’s Jornada, was born. Held in May, the project used simple but effective tools to educate men and screen them for five common types of cancer—testicular, prostate, colon, skin, and oral. Men who were found to be high-risk received follow-up testing and care as needed at La Liga.

The third CLARO project, focused on implementing evidence-based palliative care for patients undergoing chemotherapy, was driven by Bejarano and her desire to have more continued follow up with patients and to help them with their symptom burden.

“Common symptoms include nausea and vomiting, anxiety and depression, fatigue, pain, and constipation, which not only can cause suffering but interfere with their ability to tolerate treatments,” explains Bejarano. The main barriers to providing good symptom management, she says, include geography (distances patients have to travel), limited access to appointments (hospital hours are reserved for treatment delivery), and provider knowledge.

To address these challenges, the project team is testing the feasibility of having trained nurses make prospective telephone calls to patients undergoing chemotherapy twice a week for 12 weeks.

“We worked closely with the Honduran team to adapt a module from a palliative care intervention we did here in the States. The idea is to proactively help patients manage their symptoms before things get to a crisis point,” explains Kathy Lyons, ScD, a psycho-oncology researcher at the Cancer Center and a project team leader. “We developed a training manual and also a mechanism for tracking results, which includes collecting the study data and interviewing the Honduran clinicians at La Liga to get their feedback.”

A key part of the study’s successful launch over the summer, says Lyons, was the dedicated

involvement of second-year Geisel student Meghan Bullock, a former oncology nurse who had lived in San Pedro Sula (doing medical mission work) for a year, and is fluent in Spanish.

“My role was to work with the co-investigators to train the nurses in the use of the manual and scripts that we designed, adapting them to their cultural context, and also in the format of the telephone calls,” says Bullock, who was there for six weeks. “It included running them through simulation calls and different scenarios, and then troubleshooting and making adjustments for any issues that came up. Dr. Bejarano also asked me to create a standard operating procedure for important decisions such as how physicians would respond to urgent patient needs after hours.

“The nurses were really engaged, especially given that this was during their normal working hours and they had to incorporate the training into their already busy schedules,” Bullock says. “I could see a change from the first phone calls they made to the calls they were making before I left—they were really connecting with the patients and feeling more comfortable with the project.”

The study recently met its enrollment goal of 25 patients. “So far, things are going well—the nurses are excited to be able to use new skills and contribute to a project so important to our patients,” says Bejarano. “And as with all of our collaborative efforts, we’re very enthusiastic about the opportunity this provides to increase our research programs and improve the health of our people. The best is yet to come.”

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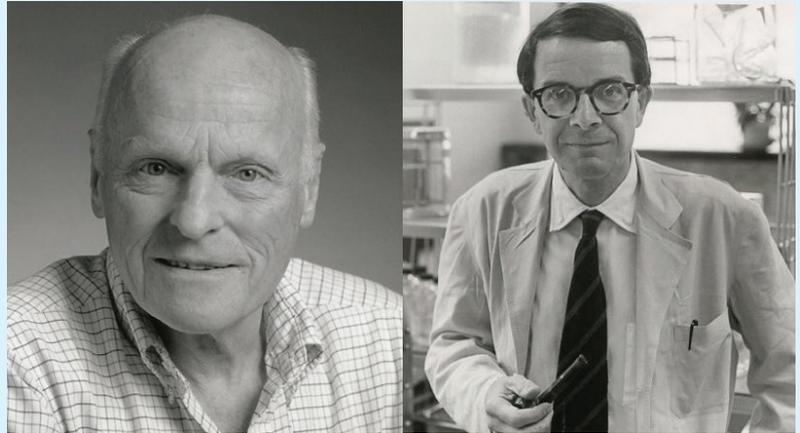
TIM DEAN IS A SENIOR WRITER FOR *DARTMOUTH MEDICINE*.

Charlene Dunaway, a third-year medical student at Geisel, in clinic with Suyapa Bejarano, MD, chief of clinical oncology at La Liga Contra el Cancer.



Photo courtesy of NCCC

## MUNCK-PFEFFERKORN GRANTS BRING RESEARCH CLOSER TO THE MARKETPLACE AND HELPING PATIENTS



The endowment is named after two luminaries from Dartmouth’s medical school: Elmer Pfefferkorn, PhD (R), and the late Allan Munck, PhD (L).

In 1987, three Dartmouth Medical School scientists co-founded a successful biotech company, Medarex, based on their discoveries in the lab. Medarex went on to produce two of today’s leading antibody-based cancer therapies. Now, profits from that endeavor are supporting the annual Munck-Pfefferkorn Awards, which fund new biomedical research projects at the Geisel School of Medicine that have high potential to benefit patients and to generate future revenue through grants or entrepreneurial endeavors.

**Distribution from the Munck-Pfefferkorn endowment has allowed Geisel to invest almost \$2.1 million into 17 different programs over two annual funding cycles.**

“The Munck-Pfefferkorn endowment fund was born in a spirit of supporting investigators to try new and innovative lines of investigation,” said Duane Compton, PhD, dean of Geisel. “I’m excited to see the variety of scientific projects that this endowment can help launch. It’s an invaluable tool for the school and its faculty.”

The endowment is named in honor of two luminaries from Dartmouth’s medical school: Elmer Pfefferkorn, PhD, emeritus professor of microbiology and immunology, and Allan Munck, PhD, emeritus professor of physiology and neurobiology.

“The impact that Elmer and Allan had on Dartmouth, on science, and on all of us cannot be overstated,” said Michael Fanger, PhD, Emeritus Professor of Microbiology and Immunology at Geisel and a co-founder of Medarex. “To see that impact extend to the next generations of researchers, clinicians, and patients is consistent with their legacies and all of our shared goals.”

Another Medarex co-founder Paul Guyre, PhD, Professor of Physiology and Neurobiology and of Microbiology and Immunology at Geisel, agrees and added, “It is tremendously gratifying that these grants can accelerate some of our colleagues’ most creative ideas toward positive effects on both people’s lives and Dartmouth’s future.”

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JENNIFER DURGIN