Maine Medical Center Research Institute attracts top scientists, licenses discoveries

BY **LORI VALIGRA**

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PHOTO / TIM GREENWAY

Dr. Clifford Rosen, director of Clinical and Translational Research at **Maine Medical Center Research Institute**, says research labs are like a small business enterprise in vying for money.

When University of Maine, Orono, alumni knocked on Peter Brooks' laboratory door at New York University in 2001 to tell him he'd won the inaugural Maine Alumni Association Spirit of Maine Achievement Award for work reflecting the high standards of the university, the scientist was both surprised and pleased.

That initial contact led to more efforts to try to lure the talented researcher back to his Maine roots. Brooks, who holds a Ph.D. in cellular and developmental biology from the State University of New York at Stony Brook, already had published a couple dozen peer-reviewed scientific papers examining various aspects of cell and cancer growth while at prestigious research institutes like The Scripps Research Institute in La Jolla, Calif., and the Keck School of Medicine of USC. He also had co-founded his first biotech company, Cell-Matrix Inc., which was subsequently acquired.

Maine Medical Center Research Institute

81 Research Drive, Scarborough

Director: Dr. Donald St. Germain

Founded: 1991 (became division of Maine Medical Center)

Activity: Basic biomedical research, clinical trials, fee-for-services

Budget: $22 million (nonprofit)

Employees: 200

Contact: 396-8130

"I always wanted to do research here in Maine," says Brooks, 50, who hails from Pittsfield. "The biomedical research environment here is growing now. Some 10 to 15 years ago I questioned it."

Prompted by the alumni, he visited both the Maine Medical Center Research Institute and The Jackson Laboratory, and decided on Scarborough-based MMCRI, as he likes the southern part of Maine. He also saw great potential in its focus on both basic and translational research, the latter of which applies discoveries from basic science to enhance human health. Now a senior researcher and lab head, he has been at MMCRI since 2007.

MMCRI is an anomaly in Maine. Hospital-affiliated research institutes typically also have a third leg, a university or medical school, such as the Harvard Medical School and Boston's Dana-Farber Cancer Institute, which has both a hospital and research institutes. MMCRI has affiliations with both Tufts University and the University of Maine, Orono.

Brooks is not the only talented researcher MMCRI has attracted. Michaela Reagan, a Harvard Medical School postdoctoral candidate studying multiple myeloma (a blood cancer) at Dana-Farber, will become MMCRI's 13th principal investigator, or PI, when she starts her laboratory there at the end of September. She brings with her some existing grant money.

She says she also is close to signing a collaborative agreement with a small biotechnology company that has offices in Cambridge, Mass., Arizona and Texas, which could bring in more funds. She holds a Ph.D. in biomedical engineering from Tufts University.

"I think it's a great environment," Reagan, 31, a native Vermonter, says of MMCRI, where her title will be faculty scientist. "You don't have to be at Harvard to do good science." In fact, she says one of the major draws of MMCRI is the strength of the PIs.

"They are really world class," she says, adding that too much collaboration and competition, as exists in the Boston area, can inhibit deep thinking and space to do things.

One anomaly of her lab: initially it will be an all-women lab, a rarity in scientific research, though she says she wants to diversify it in the future. She'll initially have two interns from the University of Southern Maine, one technician and eventually will hire postdoctoral researchers.

Ironically, Reagan had never heard of MMCRI and had never visited Portland or Scarborough before meeting Dr. Clifford Rosen, director of the Center for Clinical and Translational Research and a senior scientist at MMCRI. They both spoke at a conference in Brugge, Belgium, in April 2014. He quickly worked to recruit her.

"She's using a silkworm to generate the protein matrix in multiple myeloma," Rosen says. "She's a huge recruit for us, and she's bringing grants with her."

Grant money is critical to MMCRI's PIs, who must raise all of the money to run their labs. Rosen is somewhat of a savant at getting grants, having done so for several decades. He says the applications can take as long as six months to complete. This year, Rosen's lab has a $1.6 million budget, all raised from National Institutes of Health grants, except for $130,000 from Maine Medical Center.

"Our labs are a small business that requires attention and nurturing," he says. "A small research institute like this is really like a small business enterprise. My success depends on my getting funding." His lab, which focuses on bone and fat research, has 11 employees.

Some of his funds come from grants shared with other collaborator institutions, like Harvard, Yale and the University of Michigan medical schools. He also works with Boston hospital researchers, including at Dana-Farber, Brigham and Women's Hospital and Beth Israel Deaconess.

And, like Brooks, some of Rosen's research was licensed by a new company. Called New Paradigm Therapeutics Inc., the Chapel Hill, N.C., company was spun out of the University of North Carolina by Rosen's collaborator at that school, Dr. David Clemmons. It is developing therapeutics for patients with severe osteoporosis, or brittle and weak bones. Rosen says he is not involved with the company, though it is based on collaborative research by Clemmons and himself.

Some of the MMCRI researchers have additional appointments, for example, Rosen also is an adjunct staff scientist at The Jackson Laboratory

Rosen notes that another attempt to start a similar institute for basic research at Eastern Maine Medical Center in the mid-2000s worked only for about three years, then folded. He was involved with the board of directors of that effort in the beginning, but said EMMC didn't have the resources or infrastructure to keep it going.

“They weren't able to attract NIH or federal funding,” he says. EMMC did, however, establish a Clinical Research Center in 2006 where it tests new drugs and develops best practices for patient care.

“This [research lab] is like any small business in Maine,” he says. “We are competing for money like businesses compete for money. I've been doing this for 25 years. The currency in research is funding and how much you publish.”

Adds Robert Friesel, director of the Center for Molecular Medicine: “Each PI has to support all of their research and staff with grants.” Each of the current 18 labs has a PI and from two to seven researchers on staff. Friesel holds a Ph.D. in biochemistry and molecular biology from the George Washington University School of Medicine

Most of the research funding for MMCRI comes from NIH or the Department of Defense, though foundations like the American Heart Association, American Cancer Institute, Maine Cancer Foundation and philanthropies also contribute, as does Maine Medical Center, says Dr. Donald St. Germain, director of MMCRI and vice president for research at Maine Medical Center. MMCRI's budget is $22 million. It is a division of Maine Medical Center, whose budget tops $1 billion.

About 5% to 10% of MMCRI's budget comes from services provided to other research institutes, such as mass spectrometry, magnetic resonance imaging scanning and use of its confocal microscope.

“We are also very open to collaborations with the business community,” St. Germain says. “We can provide services to biotech companies, and we can have intellectual collaborations in the basic and clinical research and the commercial arenas.”

He expects funding to rise 5% to 10% next year, even in the face of tight federal budgets for science, as the center's researchers have had success in getting NIH and other grants.

The research center itself was built up using funds from two NIH Center of Biomedical Research Excellence, or COBRE, awards, which are given to individual institutions in states like Maine that lie in the lower half of the NIH funding range. The money goes to building labs, buying the laboratory equipment and to research projects.

MMCRI received two such grants, which give $2 million per year for five years, and then are renewable twice. The annual amounts decrease over time. Friesel says one grant focuses on vascular biology and the other on stem cells and regenerative medicine. The total for both COBREs is $44 million. Since one of the grants is set to expire in nine months, MMCRI is readying a new grant with a different theme, bone and fat metabolism.

COBRE support comes in three sequential, five-year phases. Phase I focuses on developing research infrastructure and providing junior investigators with formal mentoring, as well as research project funding to acquire preliminary data and compete for independent research grants. Phase II is used to further improve the research infrastructure and continue developing a critical mass of investigators. After 10 years of COBRE support, centers are expected to be able to compete successfully for other sources of research funding. Phase III money aims to sustain a collaborative, multidisciplinary research environment with pilot project programs and mentoring and training components.

Friesel says MMCRI looks for funding everywhere, but the hospital's development office does fill funding gaps when needed, such as for operating costs.

Maine Medical Center also conducts about 350 clinical trials involving about 100 physicians. Companies pay the center to test their drugs on patients. St. Germain says it's still a small amount of income.

MMCRI initially was located near the Maine Mall, but St. Germain says the current facility in Scarborough, built in 2001 and added onto in 2008, occupies 77,000 square feet. There are 16 PIs, each with lab staff, to total 166 employees. St. Germain says another 40 people conduct research across the hospital's clinical and ambulatory facilities as well as its health services research group.

MMCRI still isn't highly productive when it comes to patents and licensing intellectual property, St. Germain says. “Our primary goal isn't so much intellectual property, but top-notch, state-of-the-art medical research. We have a research and patient impact in Maine.” But he does like that intellectual property and potentially product development can result from the research.

Todd Keiller, director of the Office of Technology Transfer at MMCRI, has spent 25 years working to transfer technology from various institutions, including Worcester Polytechnic Institute in Massachusetts, to industry or other researchers. He holds an MBA from the Tuck School of Business at Dartmouth College, and works part-time for MMCRI, commuting from Massachusetts and working via the Internet.

“Most hospitals have a technology transfer office, but what is unusual for Maine Medical Center is that it doesn't have a medical school, although it does have an affiliation with Tufts University School of Medicine,” says Keiller. His office has a budget of $100,000 per year. The aim is to have four to five new invention disclosures or ideas a year.

He scours MMCRI, and Maine Medical Center in general, for even the smallest bit of intellectual property. One example is a nurse who developed a staffing model algorithm that makes more efficient use of time, placing staff where they are most acutely needed. “We are copyrighting that,” Keiller says. “They are doing a trial on her floor, and then will consider using it on other floors.” The hospital also trademarked its “Let's Go!” childhood obesity prevention program.

He also looks at very early stage research, such as a new device a hospital neurosurgeon is building. “We'll help him patent and license it,” Keiller says. The hospital pays for the patents. A provisional patent application for a mechanical device can average $2,500 to $3,000 to prepare and file.

What really excites him is work like Rosen's and Brooks', where discoveries can be licensed out and even turned into new companies.

Unlike Rosen, Brooks is involved as the scientific founder of CryptoMedix LLC, which is registered in Harpswell but still doesn't have a physical location. Brooks describes the cancer therapeutic company as very early stage, but it already has three sets of granted patents from his former lab at the University of Southern California and at Maine Medical Center.

Brooks became interested in understanding the so-called microenvironment around a tumor, also known as the extracellular matrix.

Typically, cancer treatments target only the cancer tumor cells, aiming to kill them. But Brooks believes treatments can be more effective by also targeting the microenvironment surrounding the tumor, which acts almost as soil would in protecting and feeding a planted seed.

One of the main structures he is studying is collagen, which comprises about 90% of the total protein in the extracellular matrix. Collagen looks like a braid. Hidden within it are structures known as cryptic epitopes. If a normal cell changes into a cancer cell, it can break the braids of collagen, in turn releasing the cryptic epitopes, which act like fertilizer to make the cancer cells grow.

His approach is to use the antibodies that can recognize the harmful epitopes and block their activity, in this case, starving the tumor cells.

“I am very excited about CryptoMedix' emerging science,” says Dr. Bernd Seizinger, executive chairman of the company. He adds that based on Brooks' most recent work, there is a new link between cryptic epitopes of collagen — the major target of CryptoMedix' anti-cancer drug candidates — and immuno-oncology, which focuses on fighting cancer cells by activating the cancer patients' own immune system.

“Immuno-oncology is currently the 'hottest' area of cancer research and anti-cancer drug development, and is thought to represent a quantum leap in future cancer therapies, promising longer-lasting, anti-tumor effects,” Seizinger adds.

Brooks says that the first approach of the company is to move one of the antibodies from its current tests in mice and convert it into an antibody for humans that can work as a therapy. He says that could take nine months to a year, and then he'll have to conduct tests in preclinical models for another six to eight months to get enough data to apply to the U.S. Food and Drug Administration for an Investigational New Drug application to conduct a Phase I clinical trial, which would tell whether or not the drug candidate is toxic. It takes an average of 10 years to get a new drug to market if all goes well.

Seizinger says the company is already entertaining potential seed funding for that work, and once the ongoing scientific studies are concluded and more patents are filed, he expects later in the fall to start a broader fundraising campaign with leading biotech venture capital funds.

Though his approach is unconventional, Brooks credits his father and his Maine upbringing for sticking to his theory. “People said I couldn't do it, so I guess that's my Maine roots,” he says. “And my father taught me to step back and look around the edges.”