New T32 Grant – and Abundance of Academic Research-Bound Alumni – Affirm CMSR's Training Approach

Where are tomorrow's biomedical research scientists coming from, and where are they going? It's a question on the minds of everyone in academic biomedical research. Despite a record-high cadre of PhD graduates flooding the field in the U.S. today, most grads skip academic research career paths in favor of industry jobs. The trend is nearly two decades old, and is creating a shortfall in researchers to elucidate the root causes of disease and develop new treatments.

But there are some encouraging exceptions, and reason to hope there's a way to entice talented researchers back to academia. The University of Rochester's Center for Musculoskeletal Research (CMSR) recently restructured its training program to attract and mentor the nation's most promising biomedical researchers with the potential to become independent investigators at major medical centers – and its 2019-2020 class suggests it's on to something: 10 graduates out of a class of 14 chose academic postdoctoral research fellowships. By comparison, the center never had more than two graduates in a given year choose academic destinations. (The 10 academic research graduates: Richard Bell, PhD; Sarah Catheline, PhD; Madison Doolittle, PhD; Christopher Farnsworth, PhD; Margaret Freeberg, PhD; Corey Hoffman, PhD; Alexander Kotelsky, PhD; Jinbo Li, PhD; Xi Lin, PhD; Robert Maynard, PhD; Laura Shum, PhD; and Ryan Trombetta, PhD.)

Like other research centers around the country, two years ago the CMSR lost its NIH T32 training grant that had supported PhD student education and research over the last decade, due to the large proportion of funded trainees who chose industry over an independent research career. In April 2020, CMSR's efforts to restructure its Rochester Musculoskeletal (ROCMSK) Training Program paid off with a new 5-year T32 grant for $2.4 million, which will be directed by Drs. Hani A. Awad, Laura M. Calvi and Danielle S.W. Benoit.

For academic medical centers, the funding is important, but an even bigger concern is ensuring the supply of new scientists to study disease and develop treatments. That's especially true for musculoskeletal research, a field facing staggering demographic trends. The Population Reference Bureau estimates that the number of Americans over age 65 is expected to double from roughly 50 million today to 100 million by 2060.

"As the population ages, there will be a corresponding increase in incidence of age-related musculoskeletal conditions such as arthritis, fragility fractures, and osteoporosis," said Edward M. Schwarz, PhD, Richard and Margaret Burton Distinguished Professor of Orthopaedics and Director of CMSR. "The population of older adults around the world depends on science to discover new treatments and perhaps preventative measures and cures."

Those discoveries will most likely not come from industry, Schwarz said.

"Major pharmaceutical firms downsized during the 2008 recession – eliminating virtually all of their basic scientists in drug discovery – and these companies aren't likely to hire them back. Since their business model centers on acquiring late-stage technologies that have been tested in clinical trials, the burden of new drug development now rests with academic investigators. For diseases like arthritis, osteoporosis, and bone infection, this burden primarily rests with about a dozen NIH-funded academic programs at major U.S. medical centers, including the CMSR."

Defying the National Trend: Bulk of CMSR's Latest Class Heads for Academic Posts

Research shows that dips in NIH funding have a significant impact on PhD grads' career choices. Since the high-water mark of NIH funding (1998-2003) there has been an 11 percent decrease in PhD grads moving into academia; the numbers fell from 50.7 percent in 2003 to 39.7 percent in 2018, and a commensurate 12.5 percent increase in industry employments (from 25 percent to 37.5 percent).

CMSR's graduating class of 2019-2020 is a marked and welcome reversal. These newly graduated scientists have already settled in prestigious academic postdoctoral fellowship positions. And while that could be a one-time boon, there are reasons why CMSR produces scientists who aspire to independent academic research, and reasons to hope future grads will embark on an admittedly challenging career path.

The biggest potential barrier for young researchers to pursue academic careers, Schwarz said, is lack of confidence to compete for limited federal grant dollars.

"The independent NIH grant funding needed for a successful academic career as a Principal Investigator is very competitive, with pay lines of around 10 percent," said Schwarz. "But compared to other medical centers, more of our graduates choose academia because they are confident they can compete for the research support they will need – and win."

A Strategy to Recruit the Best, and Train Them for Success in Academics

CMSR's 2018 strategic plan focused on building a center that would recruit the nation's most talented musculoskeletal researchers, and prepare them for careers at leading research centers around the world.

"We refocused and implemented new programs to create a center that attracts scientists who are geared to academic research and marshals them competently through their graduate and post-graduate training" said Hani Awad, PhD, Professor of Orthopaedics and Biomedical Engineering and Director of CMSR's ROCMSK Training Program. "We emphasized Individual Development Plans (IDP) to tailor the training program to each trainee's strengths and values and to ensure that the training equips them with the tools they need to pursue independent research careers. As we restructured the program, we also appreciated that the ability to compete for federal funding is a significant barrier to independence for

young scientists, and we posited that this can be overcome if the trainees are able to win mentored NIH fellowships such as the Ruth Kirschstein National Research Service Awards (F31/F32) or Pathway to Independence (K99/R00) grants during their training.

“To enable that, we built in the requirement for the T32 trainees to compete for these awards with the ambitious goal of achieving a 50% success rate with these awards, which exceeds the national average. If that goal is achieved, the grant writing process will be demystified, and our trainees will be poised for successful independent academic careers.”

ROCMSK is a unique training program, Awad adds. “Inclusivity has always been in the DNA of the training program. Every trainee has access to every faculty member and fellow student – to ask questions, to troubleshoot lab problems, to partner on research. Trainees select their areas of focus but have the opportunity to learn from everyone else here. And everyone – faculty and trainees – is expected to help others. It creates a culture where everyone learns from each other and everyone supports each other.”

“We are excited to continue our highly effective training of the next generation of musculoskeletal scientists and innovators” adds Danielle Benoit, PhD, Professor of Biomedical Engineering and Co-Director of the ROCMSK Training Program. “Our training plan includes a dynamic, contemporary curriculum, intensive interdisciplinary state-of-the-art pre-doctorate and post-doctorate research experiences, highly effective mentorship, and networking opportunities.”

Weekly Presentations Hone Trainees’ Presentation Skills

In addition to the training curriculum, the CMSR hosts weekly seminars so trainees get practice presenting and defending their work to peers, faculty, and CMSR technicians. The discussions also give trainees valuable feedback on research challenges they’ve encountered. Trainees present their research progress twice each semester.

“Our work-in -progress Wednesday seminars are the heart of our program, with the participation of faculty and students from different departments and areas of expertise,” said Laura Calvi, MD, Professor of Medicine and Co-Director of the ROCMSK Training Program. “We all share the interest in musculoskeletal biology, but come from very different disciplines, including medicine, biomedical engineering, and orthopaedics. Our focus may be stem cell biology, or metabolism, autoimmunity, development or infectious disease, so we each contribute our know-how and our tools to each other. This is a uniquely rich environment for the students that strengthens their training and prepares them to work in diverse research teams. This experience also makes our students versatile in terms of future research directions.”

One of the center’s most recent graduates, Richard Bell, earned a coveted research spot at the Hospital for Special Surgery in New York City.

“When you talk about orthopaedics and musculoskeletal research, there are really only five or six names, and CMSR is one of them,” said Richard Bell, Ph.D., a 2019 graduate who is now a post-doctoral

fellow at the Hospital for Special Surgery in New York City. “It’s well known and when you look at the numbers, Rochester is one of the largest recipients of orthopaedic research funding from NIH.”

As an undergrad, Bell worked at a research lab at Duke University.

“I had applied to other schools but when I got to Rochester, the overall interest and excitement in CMSR about musculoskeletal research, helping students – the whole community and how welcoming it was – pushed me over the top. It was clear everything was in place – mentorship, equipment, space, and expertise of the faculty – to be as successful as you wanted to be.”

Collaborative Environment, Results-Driven Research Pace

CMSR’s efforts to build a supportive culture are embedded in the details – even in the way the meetings kick off: every student who is presenting gets a formal introduction by a fellow student. It builds collegiality and respect for colleagues’ work.

“The Wednesday seminars are meaningful because they motivate students to keep their research moving at a good pace,” said Calvin Cole, PhD, Research Assistant Professor of Orthopaedics and Surgery. “They are not only presenting their science but also that of their mentor and the lab. Knowing that they will be critiqued by the other faculty in the center is great incentive to do their best work and stay on track throughout the year.”

Students also get plenty of support and practice with writing grant applications and publishing research papers.
“As an example of successful trainees, Ryan Trombetta authored nine publications during his matriculation through a CMSR graduate program,” Cole said. “That shows how productive you can be with the right encouragement and structure.” Trombetta’s research in Hani Awad’s lab within the CMSR focused on designing and fabricating 3D-printed calcium phosphate bone graft substitutes laden with antimicrobials to treat orthopaedic implant-associated chronic osteomyelitis (OM). In his research, Trombetta developed a preclinical complete hardware exchange model, which was a more faithful recapitulation of the clinical scenarios. He then recognized that the standard antimicrobials we use are not effective against biofilm or antibiotic resistant phenotypes (small colony variants or SCVs). He had the freedom to define the directions and scope of the proposed work and to reach out to other labs to diversify his training and expand his repertoire of research skills.

To gain experience in microbiology, he identified Dr. Paul Dunman of the Microbiology Department, who specializes in high throughput screening of drug and compound libraries, as a potential collaborator and recruited him to his committee. Trombetta then spent several months in Dr. Dunman’s lab and performed a high throughput screen of a large drug and compound library, which led him to identify four promising compounds that were effective against both biofilm and SCVs. He then incorporated the most promising candidate of his drug-screening, Sitafloxacin, into 3D-printed calcium phosphate scaffolds (CaPS) functioning as a local drug vehicle and biocompatible spacer. His work demonstrated that his approach is effective in the management of the infection and showed the induction of significant bone formation in his novel preclinical model.

Trombetta's journey in his PhD underscores the flexibility of the training environment in the CMSR, and the findings from his PhD studies are translationally significant and clinically transformative. Upon graduation, Trombetta joined the United States Army Institute of Surgical Research (USAISR) as a post-doctoral fellow within the Extremity Trauma and Regenerative Medicine Task Area, where he continues to study orthopaedic infections with Dr. Josh Wenke, a preeminent scientist in this area.

Another graduate, Sarah Catheline, published two papers at CMSR and is working on her third, which will publish in Nature Communications. Catheline, now doing post-doctoral training at Children's Hospital in Philadelphia, chose CMSR "definitely for the environment – it's incredible. Very collaborative. Even though the lab I joined was small, there are so many trainees at CMSR and it's a very trainee-friendly environment."

Catheline studied the role of NF-kappaB in age-related osteoarthritis development. She will be first author on the Nature Communications paper; senior author will be her thesis advisor, Jennifer Jonason, Ph.D., Research Assistant Professor of Orthopaedics & Rehabilitation at CMSR.

Jonason cited the culture at CMSR as fertile training ground for promising scientists. "It's important that research involves continuous learning, and that trainees have fun. Students I see coming through the center are driven and motivated, but also really invested in learning. It's that perfect combination that helps them move on to successful fellowships afterward."

She saw that progression in Catheline, who got opportunities to present her work outside of CMSR throughout her training. The experiences were valuable to Catheline's training and career development, Jonason said.

"She ended up winning several awards during her time here; these opportunities built her confidence and provided networking time with leading scientists in our field from around the world."

Late in her training, when Catheline had built a body of work to present, she submitted an abstract to the Gordon Conference in Italy; based on the strength of her work, she was invited to speak, and met her current post-doctoral mentor there.

A few months away from CMSR, Catheline said she chose her career path because "I realized how much I like the freedom to pursue different ideas and what the data is telling you as opposed to being very narrow in what you might be asked to do in industry. In academia you can diversify and you don't have to be a specialist in one technique – you can employ a wide array of techniques to pursue the questions you want to ask."

"That's how the best discoveries are made," Jonason said. "It's important for academic scientists to remember that sometimes the benefits of their research aren't going to be tangible or immediate, but adding to what the field knows or understands is really important."