

Center for Translational Medicine Transforms Data into Real-World Impacts

A focus on outcomes and quantitative innovation are key to the center's success.

BY NALA ROGERS

When the Center for Translational Medicine (CTM) at the University of Maryland School of Pharmacy was created in 2012, children with epilepsy had to wait seven to nine years for access to new medications after approval for use in adults. Today, approval of epilepsy medications by the U.S. Food and Drug Administration (FDA) for pediatric populations takes just one to two additional years, in large part because of CTM's collaborative efforts with the FDA.

By applying its innovative quantitative techniques to data from past clinical trials, CTM showed that any drug that prevents seizures in adults also will work in children, rendering separate pediatric efficacy trials unnecessary.

And it's not just epilepsy medications. The CTM team also partnered with the FDA to inform its regulations for schizophrenia medications, again shortening the delay for pediatric drug approvals by an average of five to seven years. Their work has led to countless other advances, from improved clinical trial designs to new drug dosing regimens that allow heart arrhythmia patients to leave the hospital days sooner.

"We dare to ask these questions. And then we deliver the solutions," says Joga Gobburu, PhD, MBA, director of CTM and a professor in the Department of Practice, Sciences, and Health Outcomes Research (P-SHOR).

PUTTING OUTCOMES FIRST



Joga Gobburu

That solutions mindset is part of what sets CTM apart. Gobburu and his colleagues are experts in pharmacometrics, machine learning, and other statistical approaches for modeling and analyzing vast quantities of complex data. But they never forget that those techniques are means to an end. While other quantitative scientists can sometimes get "lost in a stardust of data points," says Gobburu, the CTM

team puts outcomes front and center, focusing on real decisions that regulators, drug developers, and prescribing physicians must make.

CTM has a reputation as the place to go for quantitative expertise. More than 30 pharmaceutical companies have collaborated with CTM, relying on the center for tasks such as designing adaptive clinical trials, analyzing trial data, and negotiating with regulatory agencies.

CTM also partners with regulators and other academic institutions. For example, it is the statistical powerhouse behind an ambitious collaboration to develop an artificial blood product, which will be stored as a dry powder that medical personnel can carry in a backpack, allowing it to be reconstituted and infused on the battlefield or in other emergency situations.

The artificial blood project is funded by a \$46.4 million grant from the Defense Advanced Research Projects Agency. To fulfill

the requirements of the grant, CTM had to come up with a way to demonstrate that the new product would be equal or superior to stored blood — a problem that traditional statistics were ill-suited for.

"The Center for Translational Medicine and Joga Gobburu were crucial to that proposal," says Allan Doctor, MD, a professor of pediatrics, director of the Center for Blood Oxygen Transport and Hemostasis at the University of Maryland School of Medicine (UMSOM), and principal investigator of the project. "It's one of the reasons we were selected, because we had this particularly robust way to achieve that goal."

In addition to UMSOM and CTM, the artificial blood consortium includes five other universities, three companies, and one nonprofit research institute. All of them funnel their data straight to CTM for analysis. Two years into development, the blood product already is meeting or exceeding its final requirements on several metrics, including the ability to transport oxygen, says Doctor.

He also is working with CTM on two related projects, one to help clinicians decide which patients should receive blood transfusions and another to develop a biomanufacturing pipeline for producing hemoglobin using transgenic yeast. Both projects eventually will be crucial for the success of artificial blood, and they both involve complex machine learning problems, says Doctor.

MASTERING MACHINE LEARNING

CTM has a proven track record of using artificial intelligence and machine learning to solve problems in pharmacology and precision medicine. For example, Rahul Goyal, MS, PhD '24, used machine learning as a student in the School's PhD in Pharmaceutical Sciences (PSC) program to assess why so many medications designed to treat people after a terrorist attack fail when tested on nonhuman primates. Such drugs are known as "medical countermeasures," and they go through a separate approval process because they can't be tested on humans. Goyal's models can be used to project which medical countermeasures will succeed based on early data.

Similarly, one of CTM's faculty members leading the artificial blood project, Mathangi Gopalakrishnan, PhD, MS, an associate professor of P-SHOR, used machine learning to analyze data from

past clinical trials for medications to treat binge eating disorders, which have notoriously high failure rates. Her results can be used to enrich patient populations in future trials by identifying which patients are most likely to respond to a placebo. Placebo non-responders make better study participants because they are more likely to benefit from effective drugs.



Mathangi Gopalakrishnan

Much of Gopalakrishnan's research is focused on helping pregnant and nursing women, newborns, and the critically ill — patients who are typically excluded from clinical trials. Such vulnerable populations are a key focus of CTM, she says. While traditional medical research often leaves such patients behind, the CTM team has the skills to make the most of existing data, finding new treatment solutions

without putting patients at further risk.

Gopalakrishnan also directs one of CTM's most unique educational programs: the MS in Pharmacometrics, the first fully online master's program at the School of Pharmacy. Its success has inspired several other online or hybrid MS programs at the School. Most MS in Pharmacometrics students are working professionals at pharmaceutical companies or regulatory agencies, and the virtual format allows them to hone their skills flexibly from anywhere in the world.

A THRIVING NETWORK



Allison Dunn

It also provides unexpected networking opportunities, says Allison Dunn, PharmD '21, MS '21. Dunn completed the School's Doctor of Pharmacy (PharmD) and MS in Pharmacometrics dual-degree program, and she is now a research assistant professor of P-SHOR and a member of CTM with a focus on precision medicine. She recalls working on group projects with students from half a dozen companies, forming a

close-knit group that she is still in contact with today.

"As a student, I learned a lot about the industry itself, what it's like working there," says Dunn.

In addition to the MS program, CTM offers in-person training through the School's PhD in PSC program and a variety of postdoctoral fellowships. One of its newest fellows is Ankit Nagar, PhD, an engineer specializing in artificial intelligence, who recently helped lead a virtual workshop hosted by CTM on artificial intelligence for drug development.



Ankit Nagar

CTM is a dynamic place to learn and work, says Nagar, especially during Monday meetings when faculty, fellows, and graduate students come together to discuss what they're working on. The meetings are never rushed, and everyone stays as long as it takes to work through every problem. Sometimes, the faculty and students analyze published papers. Other times

they hold mock drug approval debates, role-playing as drug sponsors and FDA regulators.

"I've not seen an environment where you would have this level of brainstorming and training," says Nagar. "We walk out like we are a different person."

SPEAKING SAME LANGUAGE

One unusual aspect of CTM's training is its emphasis on communication, says Gobburu. For their work to have value, quantitative scientists must be able to convey their insights clearly and persuasively to decision-makers who don't speak their language. The MS students take a course in strategic negotiations and communications, while PhD students and fellows hone their communication skills on a daily basis. Those skills are part of why collaborators like Allan Doctor come back to CTM again and again.

"They can talk to me in a way that I can understand," says Doctor. "I've worked with dozens of biostatisticians, and they're my favorites."

Students also benefit from CTM's emphasis on pharmaceutical entrepreneurship — part of its larger focus on concrete outcomes. In

its 12 years of existence, CTM has produced five patents, two copyrights, three licenses, and two successful spinoff companies, with many more products in the works.

“If there is an interest in seeing beyond the scope of just pure research, you’re going to find that within CTM, because they have a built-in entrepreneurial spirit,” says Rebecca Bettes, MS, MBA, a senior technology licensing officer in the Office of Technology Transfer at the University of Maryland, Baltimore who works with CTM researchers to protect and license their inventions.

Both of the CTM spinoff companies are based on artificial intelligence (AI) innovations. The first, PumasAI Inc., uses a versatile machine learning algorithm embedded in easy-to-use software, allowing scientists to leverage the power of AI for a wide range of biomedical research projects. The second, Vivpro Corp., is a biointelligence software platform that uses AI to comb through the documents in regulatory databases, helping regulators and drug developers chart the most efficient path to approval. Within five years, each company has grown into a thriving business with dozens

of clients and employees.

“I think their spinoffs are wonderful examples of success,” says Bettes. “Within the time frame that they’ve been able to do it, it’s amazing.”

What is the secret to CTM’s track record of success? Skills and techniques, of course — but also the philosophy and culture. When Gobburu moved to the School of Pharmacy in 2011 after more than a decade at the FDA, he had a vision for a center that would bring together researchers with diverse backgrounds and eliminate traditional hierarchies.

“I wanted to create an organization where everybody is equal, and they have equal voice,” says Gobburu.

Other faculty and students say he succeeded. The egalitarian culture at CTM ensures that ideas flow freely and no one is stuck in silos. On collaborative projects, everyone can see the big picture, and they all pull toward the same goal.

“Nothing is monotonous or unimportant,” says Dunn. “There’s a sense of excitement with everything we do.” ☀

