“Precision Pediatrics connects ‘the new biology’ to individual children.”

The College of Human Medicine offers medical scientists the opportunity to collaborate not only with each other in the new Grand Rapids Research Center, but with researchers and physicians in East Lansing, Flint and throughout the state, English said.

“I do feel like there’s a tremendous opportunity here,” he said. “The opportunity to build a department that really has a statewide footprint is really exciting.”
In his Grand Rapids laboratory, André Bachmann seeks old drugs and naturally occurring substances that can be adapted to fight childhood diseases, including cancer.

Thanks to Bachmann's research and his collaboration with Giselle Sholler, MD, associate professor of pediatrics and director of Pediatric Oncology Research at Helen DeVos Children's Hospital, a drug called DFMO, originally developed to treat African sleeping sickness, is in a Phase II clinical trial as a treatment for neuroblastoma, a childhood cancer that often is fatal.

He also is studying a compound based on a chemical produced by a bacterium that infects bean plants that appears to kill cancer cells, including multiple myeloma and neuroblastoma, by interrupting their ability to digest proteins.

Through Spartan Innovations, a Michigan State University Division established to turn MSU research into businesses, Bachmann and a University of California colleague are forming a biotechnology firm to produce the compound called TIR-199. While TIR-199 shows promise in fighting some kinds of cancer, it will undergo many years of research and modifications before it can be tested in human clinical trials, Bachmann said.

He joined the College of Human Medicine, Bachmann said, because it offered the opportunity to collaborate with physicians and other researchers, allowing them to quickly turn discoveries in the lab into treatments for patients.

One such area of study is into polyamines, an organic compound essential for the function of all living cells. Too much polyamine can promote the growth of cancer cells; too little might be connected to multiple organ dysfunction and other disorders, such as progeria, a genetic disease characterized by premature aging in children.

“Even though autism and cancer are different disorders, the genes underlying them often are the same.”

Bachmann has ongoing projects with other physicians, including with Elna Saah, MD, a Flint-based pediatric hematologist-oncologist, in a study of sickle cell anemia.

“For me, it’s important to have daily interactions with clinicians,” Bachmann said. “It’s very gratifying and keeps you close to the clinical challenges they face daily. It is wonderful to go to work every day and try to make a difference in the world.”
A study by Daniel Campbell published in 2014 was the first to show that an interaction between a gene called MET and exposure to high levels of air pollution increased the risk of developing autism spectrum disorder.

“My next step always is, how do we use this information to help people with autism?” said Campbell, senior author of the study published in the journal *Environmental Health Perspectives*. “All it takes is talking to a few parents to realize how difficult this is for the entire family, not just the child.”

After eight years with the University of Southern California, Campbell recently joined the College of Human Medicine’s growing autism research program. The third trimester of pregnancy and the first year of life appear to be the critical periods for the onset of autism, he said.

About half the population has a variant in the MET gene that causes a predisposition to autism, he said, but only a small percentage develop the disorder. His 2014 study found that those infants who had the variant and were exposed to high levels of air pollution, such as by living close to a major highway, were three times more likely to develop autism.

Campbell has published other studies about the genetic origin of autism, such as one published in *Science Translational Medicine* showing that overexpression of what is called the “long noncoding RNA” in a gene called MSNP1AS increased the risk of developing the disorder.

“This is new and exciting stuff for brain science,” he said. “What drives me is to try to figure out what’s going on in the biology of these kids and how to reverse that. We’re really excited about the potential for finding some sort of evidence-based molecular therapy to help kids with autism.”
In recent years, Giselle Sholler has observed a welcomed trend among many of the children she treats for cancer.

“It’s been great to see patients graduating from hospice,” she said.

The reason is that some children previously believed to be terminally ill are responding well to new cancer treatments under her precision medicine study. In another strategy to prevent kids from relapsing, she is studying a drug called DFMO now in multiple clinical trials overseen by Sholler. In collaboration with André Bachmann, PhD, associate chair for research in the College of Human Medicine’s Department of Pediatrics and Human Development, Sholler studied DFMO, originally developed to treat African sleeping sickness, as a possible therapy for neuroblastoma, a highly aggressive tumor that forms on the nerve cells of young children.

In the past, few patients survived neuroblastoma if it returned after going into remission. So far, 87 percent of the children treated with DFMO in clinical trials have remained in remission, dramatically increasing their chances for long-term survival, said Sholler, who also is director of Pediatric Oncology Research at Helen DeVos Children’s Hospital and chair of the Beat Childhood Cancer international consortium.

The drug also is being tested with patients diagnosed with medulloblastoma, the most common malignant brain tumor of childhood.

From every cancer patient at DeVos, Sholler and her colleagues take blood samples and tumor biopsies for genetic testing to personalize their treatments, an approach known as precision medicine. She and Richard Neubig, MD, PhD, chair of the college’s Department of Pharmacology and Toxicology, are studying “high through-put screening,” a process that allows them to test hundreds of drugs in the laboratory to find the best one for treating each patient’s tumor. In the near future, they hope to bring this work into the clinical care.

“...we want to fully understand the biology of their tumor to make better treatment decisions.”

That is likely to be a vast improvement over the traditional approach of prescribing the same treatment for patients diagnosed with same type of cancer, regardless of genetic differences.

“For every child diagnosed here, we want to fully understand the biology of their tumor to make better treatment decisions,” Sholler said. “I believe this is how we will treat patients in the future.”
Some of the genes linked to cancer and other diseases, including neurofibromatosis and tuberous sclerosis, both characterized by benign tumors throughout the body, also are associated with autism, although that does not mean that a person with autism is more likely to develop those diseases.

“Even though autism and cancer are different disorders, the genes underlying them often are the same,” Daniel Vogt said. “The main idea is there have been a lot of genes identified as underlying autism, but we really don’t understand the functions of those genes.”

He hopes to change that. Once the function is understood, the next step will be to develop treatments to prevent or at least mitigate the effects of autism.

In cancer, genetic mutations often stop the normal functioning of protein in cells, Vogt said. In autism, the protein is still functioning, but not very well.

“Our goal is to try to figure out how to help the protein function better,” Vogt said, likely through a form of genetic engineering.

That will not be easy, as autism is believed to result not from a single mutation, but from a cascade of mutations combined with an external stressor, such as exposure to something in the environment.

Vogt previously did graduate work at Case Western Reserve University and Cleveland Clinic, and he conducted neuroscience research at the University of California San Francisco. He was drawn to the College of Human Medicine because of its translational approach to research, which emphasizes pursuing studies that can quickly benefit patients.

“That was a big selling point,” Vogt said. “At the end of the day, I want to know that what I’m doing actually is helping people.”