A combination of two medicines long used for treating other illnesses can stop the growth of a deadly childhood cancer, according to a recent study by a Michigan State University College of Human Medicine researcher who has a history of finding new uses for old drugs.

Laboratory tests on cell cultures showed that the drugs DFM0 and sulfasalazine effectively inhibited the growth of neuroblastoma, which causes about 15 percent of all childhood cancer deaths. For years DFM0, or difluoromethaneformitine, has been used for treating African sleeping sickness, and sulfasalazine for bowel disorders and rheumatoid arthritis.

“I think it’s a big advantage when you find an existing, FDA-approved drug that acts on neuroblastoma, because it already has been shown to be safe,” said Andre Bachmann, Ph.D., the study’s senior author. “Re-orienting old drugs for new indications can save lives, time and money.”

Separately, each drug impeded neuroblastoma in laboratory tests, but, when administered together, the two drugs acted synergistically and were more than twice as effective in blocking the cancer’s growth, according to their recent study published in the medical journal BMC Cancer.

“Instead of one plus one equals two, it equals four,” said Bachmann, a professor of pediatrics and associate chair for research in the College of Human Medicine’s Department of Pediatrics and Human Development. “That’s why the synergistic effect is so important. We can use the two drugs in lower doses.”

In this country, most of them age 2 and younger, are diagnosed with neuroblastoma, a highly aggressive tumor, which forms on nerve cells in several areas of the body. With current treatments, neuroblastoma usually goes into remission, but returns in about half of those cases. Only about 10 percent of children with recurring neuroblastoma survive.

Bachmann’s earlier research showed that DFM0 targets a protein called ornithine decarboxylase (ODC), which, when elevated in the cancer, promotes the growth of neuroblastoma cells. He pioneered the idea of re-purposing DFM0 for neuroblastoma which translated from bench to clinic in 8 years and led to phase I and phase II clinical studies.

“In this most recent study, we were interested in finding a second drug that would work even better in combination with DFM0,” Bachmann said.

Through additional research, he identified a second protein in the body called sirtuin reductase (SPR), which interacts with ODC and also promotes the growth of neuroblastoma cells. SFR previously had been identified as a factor in neurological disorders, such as Parkinson’s disease, but never before in cancer.

“That’s when we said, ‘Since SPR and ODC jointly contribute to causing neuroblastoma tumor growth, why don’t we hunt for a second drug that targets SPR,’” Bachmann recalled.

He began the search and learned that other recent studies had shown that the drug sulfasalazine blocked SFL, although it never had been tested against cancer.

Since the 1950s, sulfasalazine had been used in treating inflammatory bowel diseases, Crohn’s disease, and rheumatoid arthritis, but the mode of action had remained unknown.

“That’s what’s very exciting about this drug,” Bachmann said. “I’m very confident about this, because it’s a safe drug that has been taken by humans for many years with little side effects.”

On his latest study, Bachmann collaborated with other researchers, including Lisette Yoo, a graduate student in his Grand Rapids laboratory, and with Drk Geerts, a cancer researcher in the Netherlands, who recently accompanied Dutch King Willem Alexander and Queen Maxima on a visit to Grand Rapids.

Now that DFM0 and sulfasalazine have been shown to preferably stop the neuroblastoma growth in the laboratory, Bachmann anticipates that safe drug combination can be evaluated in clinical trials.

Partnerships between research scientists and physicians are important and prove the value of combining basic research with clinical practice, said B. Keith English, M.D., chair of the Department of Pediatrics and Human Development in the College of Human Medicine.

“Research is a team sport,” he said. “That’s why we have to invest in basic research, as well as in clinical research.”

As for Bachmann, “I think it’s safe to say he’s been a pioneer in finding new uses for old drugs,” English said.

Bachmann recalled the reaction he got at a cancer conference in 2003 when he first proposed repurposing the old drug DFM0 to fight neuroblastoma. “I don’t want to say I got booted off the stage,” he said. “But I couldn’t help noticing some puffed smiles in the audience. Today everybody’s on that wagon, trying to re-discover old drugs like DFM0. It’s somewhat gratifying, I have to admit.”

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**New use for medications fights childhood cancer**

College of Human Medicine researcher Andre Bachmann, left, works with graduate student Lisette Yoo in his laboratory at the MSU College of Human Medicine. (Submitted photo)