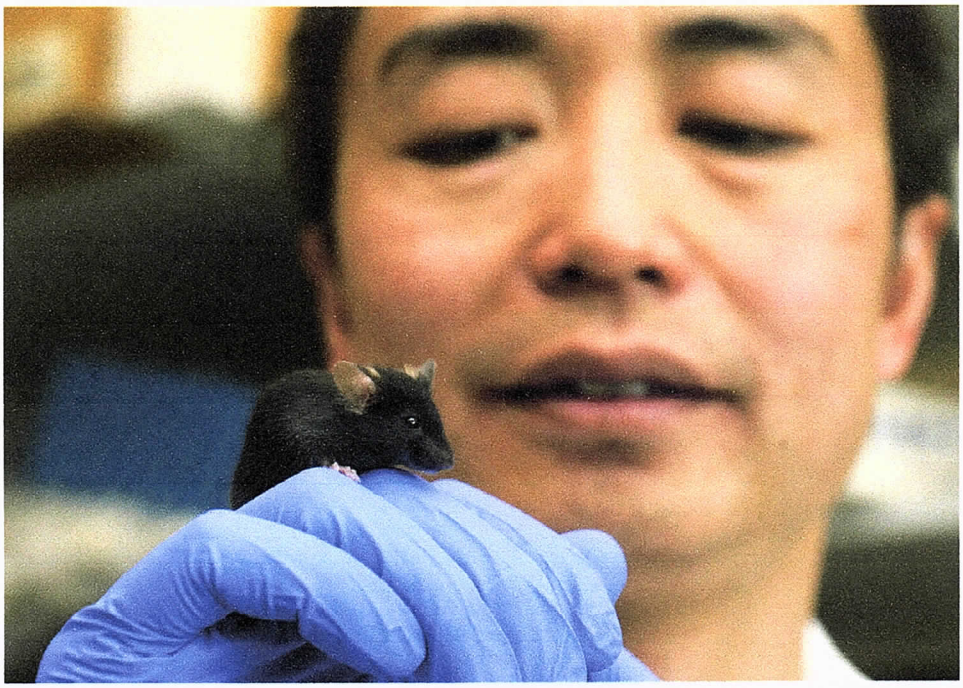
Parasite treatment may help people with brain cancer May 09, 2014|By Meredith Cohn, The Baltimore Sun

Researchers find new uses for old drugs, sometimes by accident



Renyuan Bai, Ph.D., primary researcher, holds one of the mice… (Algerina Perna, Baltimore…)
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At a lab on the edge of the Johns Hopkins University's East Baltimore medical campus, researchers grow tumors on mice so they can try and cure them. But one day, the cancer wouldn't grow.

They tried again and again for months. Figuring there must be something different about this batch of mice, they finally discovered the rodents had been given a drug to prevent pinworm.

Three years later, the common parasite treatment that retails for a few dollars a dose is being given to terminal brain cancer patients in a trial that could lead to more widespread use.

Researchers who toiled for years for such a discovery said they still are investigating how it works.

"We spend a lot of time training and thinking about what causes cancer so we can come up with strategies to make an impact on survival," said Dr. Gregory J. Riggins, a Hopkins professor of neurology and oncology. "Most things we try don't work," he said. "And then we find something completely by accident."

New life-saving and life-improving drugs are most often the result of many years of research and many millions of dollars. But a funding squeeze now has some researchers not only welcoming such accidental discoveries but revisiting old, often forgotten drugs that already have been proved safe.

Pharmaceutical historians note that mold's antibiotic properties had been dismissed for decades before a British bacteriologist was credited with discovering penicillin in his petri dish in 1928.

In more recent years, scientists have embraced unexpected side effects — producing the hair growth remedy Rogaine, initially investigated for hypertension treatment, and the sexual dysfunction treatment Viagra, first tested as a muscle relaxer.

The pinworm drug had shown signs decades ago that it could interfere with cancer, yet no one ever explored why and whether it could be used to treat the disease.

Researchers at Hopkins and elsewhere have become more aggressive in searching approved drugs for new uses, finding promising disease fighters in, for example, a treatment for toenail fungus.

But Stephen Greenberg, a medical historian, said surprising side effects can also be harmful, at least for some patients.

Thalidomide was developed as a morning-sickness drug but caused devastating birth defects, said Greenberg, coordinator of public services for the History of Medicine Division of the National Institutes of Health's National Library of Medicine. Later the drug was brought back to treat and prevent some forms of leprosy and to treat multiple myeloma, a bone marrow cancer.

He also cited the antibiotic erythromycin, which can cause diarrhea and is used now to treat severe constipation. And erythropoietin, known as EPO, was designed to raise the red blood cell count of cancer patients undergoing chemotherapy, but became the illegal performance-enhancing drug of choice for endurance athletes such as cyclist Lance Armstrong.

"How common is this?" Greenberg said about accidental drug discoveries. "I really can't say, but you can be sure that research pharmacologists track every side effect of the new drugs they're developing. … Unexpected things — good and bad — can happen, and they might be held responsible either way."

When the mice at Johns Hopkins wouldn't grow tumors despite repeated efforts, the researchers noticed that this group came with a warning: They had been treated for pinworm with a drug that could interfere with experiments. Reviewing medical literature, they learned the parasite medicine — Fenbendazole — could inhibit cancer growth.

The drug was developed in the 1960s and is used routinely to treat a variety of parasites in animals and people with few negative effects. Riggins and his fellow researchers decided immediately to begin investigating.

By trial and error in the lab, they found another drug in the same family, mebendazole, was the most effective in stalling growth of glioblastoma multiforme, the most common and aggressive type of brain tumor. It's what killed U.S. Sen. Edward M. Kennedy.

The average survival rate is 15 to 20 months. Patients have surgery, if possible, to remove the tumor and then radiation and chemotherapy. There are few therapies, however, because most drugs will circulate through the body but not reach the brain. A new treatment developed in part by Dr. Henry Brem, director of the Hopkins neurosurgery department, uses drug-laden wafers inserted directly into the site of the tumor.

Researchers believe the parasite drug also helps obstruct tumors by inhibiting formation of strands of tubulin, proteins needed by cancer cells to grow.

After lab models showed promise, Riggins and the research associates who identified the drug's properties, Reny Uan Bai and Verena Staedtke, were eager to try it on people. But the manufacturer stopped making the parasite drug, and Hopkins couldn't get enough of the pills produced according to U.S. Food and Drug Administration specifications.

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