First there was panic. In early 1961, an outbreak of liver cancer among middle-aged rainbow trout raised in fisheries began to spread, bordering rapidly on epidemic proportions. In the rush to finger a culprit, alarmed fish farm owners pointed at everything from pesticides to water sources. Only later did they suspect the food.

Aspergillus molds, an extensive family of various fungi, thrive on grain—corn, peanuts, rice, and, in the case of the fish farms, rotten wheat ground into trout feed. Both humans and rainbow trout are susceptible to a byproduct of aspergillus molds, aflatoxin, a potent carcinogen and the root of the liver cancer outbreak. The grains were hastily removed. The epidemic ended. Problem solved.

Slowly, scientists realized the potential of this accidental discovery. Previously, it was thought that the causes of liver cancer were confined to lifestyle consequences, the result of years of alcoholism or Hepatitis infection. Studies on the mechanisms that caused liver cancer proved to be difficult. Researchers had to wait for enough subjects to enroll in liver cancer studies and then survive long enough to yield meaningful results. But—if liver cancer could be consistently induced in rainbow trout using an environmental carcinogen known to affect humans, and if rainbow trout exposed to aflatoxin could effectively make liver cancer subjects more available, then scientists could study a perfect disease model, one that capitalized on the unlikely parallel between trout and man. Best of all, rainbow trout were inexpensive when compared to other disease models. The relatively inexpensive trout allowed study sizes to be increased a thousand-fold. For the first time, the rainbow trout gave researchers a license to dream big, to examine the otherwise unnoticed trends and subtle discrepancies that could lead to a cure or treatment.

As of today, there is only one real “cure” per se for liver cancer patients once symptoms arise — a liver transplant. However, with the length of the waiting list for liver transplants, as well as the risks of the procedures, better treatments are necessary. Similar surgeries designed to remove part of the liver are risky at best, especially for patients teetering on the brink of already unstable conditions, and as with any cancer, there is always the possibility that tumors could reappear. Ironically, the largest problem lies in the nature of the liver itself. The primary role of the liver, to detoxify, means cell-destroying chemotherapy targeted towards the liver is largely rendered ineffective.

After the rainbow trout scare, aflatoxin no longer poses so much of a risk in the United States or any country wealthy enough to afford testing. The procedure is a pricey one and requires shipping millions of periodically chosen samples of grain supplies to approved laboratories where technicians grind the grains and check for aflatoxin.

Like other known carcinogens shared by humans and rainbow trout, aflatoxin requires metabolic action to induce cancer. In other words, in its raw form, the toxin itself is not to blame. Instead, aflatoxin wreaks havoc only when metabolized and absorbed, and the true cancer-causing agents are by-products of the toxin, produced when the body attempts to digest, process, and break it down.

Therefore, scientists hypothesized it makes sense that liver cancer induced by ingestion can also be treated to some degree by ingestion. In the most promising studies, variations in diet and treatments fed directly to rainbow trout played a role in inhibiting the spread and development of liver cancer.

Embracing the rainbow trout as an ideal liver cancer animal model initiated a search for both the more traditional chemotherapy — a drug to actively kill existing liver cancer cells — and a chemopreventive, a blocking agent that would not treat cancer after the fact, but rather prevent it from ever appearing. In the rainbow trout studies, scientists look for a dietary supplement
or treatment to change the actual metabolic process that breaks down aflatoxin and other carcinogens, stopping the creation of toxic byproducts before they start. Rainbow trout are perfect for the studies because, although vastly different from humans in many ways, trout share key similarities in both patterns of gene expression and mutations that precede cancer and metabolic systems. Trout carry the same enzymes that transform aflatoxin into a deadly carcinogen as humans. Scientists have learned to tread carefully around the word “treatment,” and even more so around the word “cure.”

Despite this caution, similarities between trout and humans make it quite likely that promising chemopreventives or chemotherapies discovered as a result of trout research will hold the same potential for a human cure.

From the rainbow trout studies, a single standout substance has begun to emerge: chlorophyllin, a stable derivative of chlorophyll, known to elementary students worldwide as the green pigment that colors plant leaves. The allure of chlorophyllin is that it is not only anti-cancer, but anti-carcinogenic, meaning it can render the carcinogen itself impotent. The first hints of these properties were demonstrated originally in the rainbow trout model in extensive studies conducted at the Linus Pauling Institute at Oregon State University, a leading center for rainbow trout research.

The effects of chlorophyllin were both discovered and verified in enormous trout studies, a testament to the benefits of the trout animal model, before chlorophyllin was moved into equally promising human studies centered in China. Chlorophyllin works simply. When taken shortly after ingesting suspect grains, it binds to aflatoxin, so that metabolic enzymes, unable to break down the toxin, cannot process it for absorption. Although further research is necessary, chlorophyllin stands poised to become one of the most effective prevention methods against aflatoxin-induced liver cancer, and all for just pennies a dose. Better yet, as of now chlorophyllin has no known side effects. If successfully distributed in aflatoxin-heavy areas, it could potentially spare liver cancer patients the side effects of chemotherapy, radiation and transplantation.

Despite all that rainbow trout has to offer, some note its limitations. Obvious differences between trout and humans mean it cannot be expanded to study disease beyond the liver; even non-cancerous liver disorders which do not deal with metabolic carcinogens. With the liver cancer field however, rainbow trout excel in versatility — so far both environmental carcinogen as well as chemopreventives have shown remarkably similar effects in both humans and fish. Beyond aflatoxin, the original source of this accidental animal model, rainbow trout offer an excellent mirror of human responses to carcinogens and dietary treatments. Ambitious scientists have already moved into a wider range of carcinogens including PFCs, a class of polyfluorinated chemicals found in everything from food packaging to paper.

Science has come a long way since 1961, transforming the disaster of an epidemic deftly into the promise of a cure. In effect, the beauty of the trout model is that it gives scientists invaluable insights in the search for a cure for liver cancer patients.

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