Max Planck scientist Otto Heinrich Warburg, biochemist, physician and Nobel laureate, would have celebrated his 125th birthday on October 8, 2008. It was he who discovered that industrial and car exhaust gases can cause cancer. And Warburg firmly believed he had discovered even more: the prime cause of cancer. Today, 38 years after his death, the Warburg hypothesis is still as relevant as ever, and always makes a good headline.

“I discovered the quantum chemistry of photosynthesis and, finally, in the field of medicine, the prime cause of cancer.” This is how Warburg himself summed up his greatest scientific achievement. He is considered to be the father of modern biochemistry: biologists have him to thank for enlightening the world about photosynthesis and cellular respiration.

The scientist derived the eponymous hypothesis from his observations in the field of cancer research: healthy cells generate energy by breaking down sugar – using oxygen – the process. Cancer cells, on the other hand, produce energy by fermentation. So they convert nutrients without oxygen, even if oxygen is available. A life without oxygen – this, according to Warburg, is the prime cause of cancer.

This conjecture still keeps scientists busy to this day. In 2006, the Boston-based science magazine Time chose to mark the 80th anniversary of the discovery of the Warburg hypothesis by publishing an account of how he had come to his conclusions. According to the magazine, “Oskar Morgenstern, a New Yorker, received the news that Warburg might have been right.” A team of scientists led by Michael Ristow from the Institute of Nutrition at the University of Bremen confirmed this using the plague as an example: the prime cause of plague was not the plague bacillus from rats to humans. “What the plague bacillus carried this using the plague as an example: the prime cause of cancer was to be found, not outside the body, but inside it – in the chemical reactions within the cells. He speculated that, when cancer cells start to grow uncontrollably, they ought to require more oxygen – just like the sea urchin eggs given added iron. This assumption reflected Warburg’s fundamental research approach, which involved attributing life processes to physical and chemical processes. This notion was frowned upon in those days, with most scientists attempting to explain cancer back in 1924. It now turns out that cells are infected with smaller lesions than did regular cancer cells. Ristow says: “Even possible metabolic causes of cancer are something we couldn’t lose sight of in our research.”

Axe Ulrich, Director at the Max Planck Institute of Biochemistry in Martinsried, sees things differently. Among the research topics that he and his team are exploring are the molecular causes of cancer. The two cancer medications – the breast cancer drug Herceptin and the drug Sutent, which can be used to combat renal cell cancer and have been approved for use on the intestinal tract. In his interpretation, the fact that cancer cells obtain energy from fermentation has more to do with molecular genetics.

"Today, it is generally established that cancer arises as a result of cells that have lost their genetic stability. This, in turn, leads to an accumulation of chromosomal changes and mutations in the cell genome," says Ulrich. “The change in the cellular energy metabolism is a consequence of these genetic changes that is definite, but the reason why malignant tumors develop and grow.”

The fact that Otto Heinrich Warburg’s hypothesis on the origin of cancer was mistaken does nothing to diminish its great service to biochemistry. And he was certainly conscious of his successes: in January 1938, the Times carried an obituary for him – 32 years before. But it wasn’t the fact that they’d mixed him up with a distant relative that annoyed him. They’d mixed him up with a distant relative that annoyed him. They’d mixed him up with a distant relative that annoyed him. They’d mixed him up with a distant relative that annoyed him. They’d mixed him up with a distant relative that annoyed him.

Warburg with the Nobel Prize again: this time for proving the Warburg hypothesis was born. The fact that Otto Heinrich Warburg’s hypothesis on the prime cause of cancer could be a result of cancer is strongly disapproved of, but he would be the first to accept it as a result of cancer. Warburg identified cancer-causing substances, was a vehement opponent of a tobacco ban, and urged people to limit the pollution of the air caused by fumes. But nobody listened. And he took part in the race to find a drug to treat cancer. Late in life, he still believed that the way to treat cancer would be found in the anaerobic metabolism of cancer cells. His idea was that supplements in food, such as the iron found in respiratory enzymes, could sustain – and even reanimate – cell respiration, thus rendering them suitable as a cancer therapy. But he still was in his prime.

Even so, Warburg’s cancer research inspired other scientists and doctors – above all, practitioners of alternative medicine. Methods such as cancer vaccines and gene therapy, as well as certain dietary regimes, were developed following the Warburg hypothesis. However, most orthodox medical practitioners and scientists reject these methods, as they consider their very basis to be erroneous and because there is no convincing proof that they work.

The proponents of these therapies, on the other hand, feel vindicated by a paper published in 2006. They interpret the findings of scientist Michael Ristow from the University of Jena as proof of the Warburg hypothesis. Ristow modified colon cancer cells such that they produced unusually high amounts of fructose – a protein that activates cell respiration to an inordinately high degree. According to the scientist, the cancer cells that were forced to allow cellular respiration to take place did not develop into small, rounder cancer cells but into smaller lesions than did regular cancer cells. Ristow says: “Even possible metabolic causes of cancer are something we couldn’t lose sight of in our research.”

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