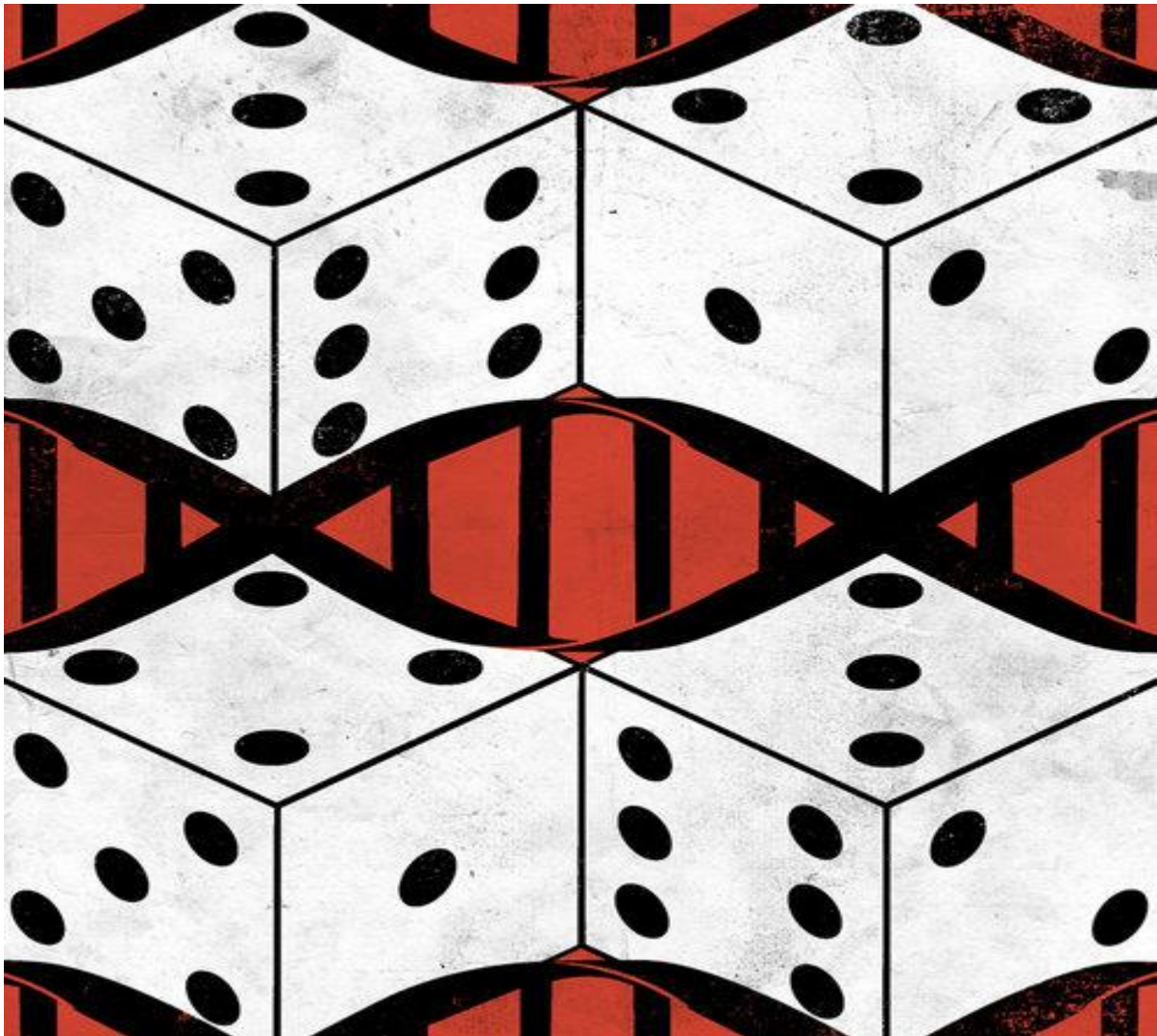


# Cancer's Random Assault

<http://www.nytimes.com/2015/01/06/health/cancers-random-assault.html? r=0>

By [DENISE GRADY](#) JAN. 5, 2015



Credit Tim Robinson

It may sound flippant to say that many cases of [cancer](#) are caused by bad luck, but that is what two scientists suggested in an [article published last week in the journal Science](#). The bad luck comes in the form of random genetic mistakes, or mutations, that happen when healthy cells divide.

Random mutations may account for two-thirds of the risk of getting many types of cancer, leaving the usual suspects — heredity and environmental factors — to account for only one-third, say the authors, Cristian Tomasetti and Dr. Bert Vogelstein, of Johns Hopkins University School of Medicine. “We do think this is a fundamental mechanism, and this is the first time there’s been a measure of it,” said Dr. Tomasetti, an applied mathematician.

Though the researchers suspected that chance had a role, they were surprised at how big it turned out to be.

“This was definitely beyond my expectations,” Dr. Tomasetti said. “It’s about double what I would have thought.”

The finding may be good news to some people, bad news to others, he added.

Smoking greatly increases the risk of lung cancer, but for other cancers, the causes are not clear. And yet many patients wonder if they did something to bring the disease on themselves, or if they could have done something to prevent it.

“For the average cancer patient, I think this is good news,” Dr. Tomasetti said. “Knowing that over all, a lot of it is just bad luck, I think in a sense it’s comforting.”

Among people who do not have cancer, Dr. Tomasetti said he expected there to be two camps.

“There are those who would like to control every single thing happening in their lives, and for those, this may be very scary,” he said. “ ‘There is a big component of cancer I can just do nothing about.’

“For the other part of the population, it’s actually good news. ‘I’m happy. I can of course do all I know that’s important to not increase my risk of cancer, like a good diet, exercise, avoiding smoking, but on the other side, I don’t want to stress out about every single thing or every action I take in my life, or everything I touch or eat.’ ” Dr. Vogelstein said the question of causation had haunted him for decades, since he was an intern and his first patient was a 4-year-old girl with leukemia. Her parents were distraught and wanted to know what had caused the disease.

He had no answer, but time and time again heard the same question from patients and their families, particularly parents of children with cancer.

“They think they passed on a bad gene or gave them the wrong foods or exposed them to paint in the garage,” he said. “And it’s just wrong. It gave them a lot of guilt.”

Dr. Tomasetti and Dr. Vogelstein said the finding that so many cases of cancer occur from random genetic accidents means that it may not be possible to prevent them, and that there should be more of an emphasis on developing better tests to find cancers early enough to cure them.

“Cancer leaves signals of its presence, so we just have to basically get smarter about how to find them,” Dr. Tomasetti said.

Their conclusion comes from a statistical model they developed using data in the medical literature on rates of cell division in 31 types of tissue. They looked specifically at [stem cells](#), which are a small, specialized population in each organ or tissue that divide to provide replacements for cells that wear out.

Dividing cells must make copies of their DNA, and errors in the process can set off the uncontrolled growth that leads to cancer.

The researchers wondered if higher rates of stem-cell division might increase the risk of cancer simply by providing more chances for mistakes.

Dr. Vogelstein said research of this type became possible only in recent years, because of advances in the understanding of stem-cell biology.

So why does a blue whale containing the largest number of cells of any organism on the planet not have a correspondingly high cancer rate?

The analysis did not include breast or prostate cancers, because there was not enough data on rates of stem-cell division in those tissues.

A starting point for their research was an observation made more than 100 years ago but never really explained: Some tissues are far more cancer-prone than others. In the large intestine, for instance, the lifetime cancer risk is 4.8 percent — 24 times higher than in the small intestine, where it is 0.2 percent.

The scientists found that the large intestine has many more stem cells than the small intestine, and that they divide more often: 73 times a year, compared with 24 times. In many other tissues, rates of stem cell division also correlated strongly with cancer risk.

Some cancers, including certain lung and skin cancers, are more common than would be expected just from their rates of stem-cell division — which matches up with the known importance of environmental factors like smoking and sun exposure in those diseases. Others more common than expected were linked to cancer-causing genes. To help explain the findings, Dr. Tomasetti cited the risks of a car accident. In general, the longer the trip, the higher the odds of a crash. Environmental factors like bad weather can add to the basic risk, and so can defects in the car.

“This is a good picture of how I see cancer,” he said. “It’s really the combination of inherited factors, environment and chance. At the base, there is the chance of mutations, to which we add, either because of things we inherited or the environment, our lifestyle.”

Dr. Kenneth Offit, chief of the clinical [genetics](#) service at Memorial Sloan Kettering Cancer Center in Manhattan, called the article “an elegant biological explanation of the complex pattern of cancers observed in different human tissues.”

He said the hypothesis “appears to be correct,” but added that it is “just a first approximation,” and he noted that certain types of cancer did not fit the model. One form of [thyroid cancer](#), for instance, has a much bigger hereditary component than the model would suggest, he said.

Although the article focused on factors in cancer beyond people’s control, Dr. Offit said that about half of cancer deaths could be avoided.

“So one would not want to dilute the important public health message that although most cancer is likely due to random events (affecting DNA replication) at the cellular level, at the population level, the most powerful interventions to decrease the burden of cancer are to stop smoking, know your family history and aim for ideal weight,” he said.