

New information on cancer causation

Editorial

On March 24, 2017 Johns Hopkins researchers Cristian Tomasetti and Bert Vogel published a paper in *Science*¹ which forcefully argues that a majority of cancers result from transcription errors in process of cell division, which they identify as "Replicative Mutations. This finding further explicates the earlier findings of the authors, also published in *Science*² 2015 in which they postulated that variation in cancer risk could be explained by the numbers of stem cell divisions, essentially arguing that the more cell divisions the more opportunity for Replicative Mutations to occur. It is worth noting that this finding was initially met with a high degree of skepticism among cancer researchers. Some argued that the claim of a major role for what are essentially random mutations, rather than genetic mutations (such as BR-2) or DNA damage resulting from environmental factors such as smoking, exposure to asbestos etc., would hamper efforts at cancer prevention and detection.

Vogelstein addressed that concern head-on at a news conference at the time of publication: "We all agree that 40 percent of cancers are preventable," he said at a news conference. "The question is, what about the other cancers that aren't known to be preventable?" The mechanism of action in Replicative Mutations was described by Vogelstein. He notes that every time a perfectly normal cell divides, it makes several mistakes when it copies its DNA. These are naturally occurring mutations.

Most of the time, those mutations are in unimportant bits of DNA. That's good luck. "But occasionally they occur in a cancer driver gene. That's bad luck," Vogelstein says. After two or three of these driver genes get mutated in the same cell, they can transform that healthy cell into a cancer cell.

Basing their analysis on several very large international cancer registries the authors used mathematical modeling to determine the distribution of causation based for cancers caused by genetic defects, environmental exposures and replicative mutations.

The answer: 66 percent of the total mutations are random, about 29 percent are due to the environment and the remaining five percent are due to heredity. These numbers vary depending on the type of cancer, they found. Lung cancer is largely the result of environmental causes, while the vast majority of childhood cancer is a result of these bad-luck mutations, they found.

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Michael Sharp S

Regulatory Consulting, Inc, USA

Correspondence: Michael Sharp S, Regulatory Consulting, Inc., 5005 Clayton Ct. St Augustine, USA, Tel 2177879, Email drssharp@aol.com

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Both critics and the authors agree that cancer causation is a complex matter, which involves an interaction between a variety of factors. It may be that damage from environmental factors can increase the likelihood of transcription errors, hormones may play a role in how cells react to mutations.

Finally, the finding that two-thirds of cancers of a random biologic process can lead to research efforts to better understand, predict and identify these cancers using increasingly sophisticated screening tests. The knowledge that almost 30 percent of cancers are due to the environment should be taken as motivation to continue to increase cancer prevention and screening efforts.

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Conflict of interest

The author declares no conflict of interest.

References

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