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Editorial

Cancer Prevention Research

Implications of the "Bad Luck" Explanation of Cancer Risk for the Field of Cancer Prevention

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See related article by Rozhok et al., p. 762

In this issue of *Cancer Prevention Research*, the editors have chosen to publish an opinion piece by Rozhok and colleagues ('A critical examination of the "bad luck" explanation of cancer risk'; ref. 1) that comments on the recent publication in *Science* by Tomasetti and Vogelstein (2). This article has already generated a great deal of discussion among the lay public (3, 4) and scientists (5–8) given the somewhat provocative statement that a majority of cancer could be attributed not to specific causes but instead to "bad luck." In particular, the response by the cancer prevention community has been nearly uniformly critical; this response is not surprising, given that a number of researchers and clinicians have invested their careers in the belief that the best approach to cancer is not late-stage treatment but instead prevention. The notion that the majority of cancer is not attributable to defined risk factors or life-style choices but instead to random ("stochastic") events strikes at the very heart of the cancer prevention enterprise. What if this mathematical model were true? That would suggest that there is very little that a cancer prevention specialist, or an individual for that matter, could do to prevent the development of a lethal malignancy.

In many respects, the publication by Tomasetti and Vogelstein (2) has been quite useful in galvanizing the prevention community to reexamine many of their own assumptions and to think more critically about the origins and early development of cancer. While the modeling by Tomasetti and Vogelstein was no doubt rigorously done, it does focus on a select group of tumors and incidence rates from the United States, includes assumptions regarding stem cell numbers that may not stand the test of time, and incorporates them into the very narrow somatic mutation theory of cancer. For those researchers who embrace cancer genetics and deep sequencing of tumors without regard to how the mutations come about, this stochastic model seems quite reasonable. However, for those who study environmental influences on carcinogenesis and have followed closely changes in cancer incidence rates over time and in different countries, the conclusion that cancer rates are primarily determined by baseline stem cell numbers does not seem to fit.

We would agree with the general concept of a link between stem cell behavior and the origins of cancer, although precisely how many stem cells and which class of stem cell ("active" or "quiescent") is first initiated has not been clarified for most cancers. The current opinion piece by Rozhok and colleagues (1) addresses in more detail issues many of the assumptions regarding stem cells that were used in the Tomasetti model, which may have led to an overestimation of the correlation between stem cell divisions and the risk of cancer. In any case, the publication by Tomasetti and Vogelstein was a useful challenge to the prevention community, and only time will prove which view of cancer is correct.

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Note: For a full list of *CaPR* (*Cancer Prevention Research*) Deputy and Senior Editors, please see http://cancerpreventionresearch.aacrjournals.org/site/misc/edboard.xhtml.

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