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2009 : October 2009 - Emerging Research Fronts : Michael B. Kastan Discusses Cell-cycle Checkpoints and Cancer

EMERGING RESEARCH FRONTS - 2009

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Michael B. Kastan talks with *ScienceWatch.com* and answers a few questions about this month's Emerging Research Front Paper in the field of Molecular Biology & Genetics.



Article: Cell-cycle checkpoints and cancer

Authors: Kastan, MB; Bartek, J

Journal: NATURE, 432 (7015): 316-323 NOV 18 2004

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SW: Why do you think your paper is highly cited?

The control of cell cycle progression after DNA damage and other cellular stresses is an important determinant of cellular and organismal outcome following stress exposure. DNA damage contributes to cancer development, is a major mechanism by which we try to kill tumor cells, and contributes to the side effects of cancer therapies on normal tissues. Thus, it is of great interest in the cancer biology field.

These signal transduction pathways that control cellular responses to DNA damage and other stresses are also proving increasingly important in many other fields of study, including neurosciences, metabolism, aging, and environmental links to human disease. This paper was a review article in a prominent journal. This visibility, in combination with the importance of the field, probably both contributed to the paper's citation frequency.

SW: How did you become involved in this research and were any particular problems encountered along the way?

As a clinical oncologist, I have been interested in the molecular basis of DNA damage responses from both cancer development and cancer therapeutic perspectives. Since my initial report in 1991 that the p53 tumor suppressor protein is a cell cycle checkpoint determinant after DNA damage, a significant fraction of the efforts in my laboratory have focused on signal transduction pathways that are initiated by DNA damage and other cellular stresses.

Work in my lab over the past decade has also contributed to the expanding insights on the ATM protein kinase as a central mediator of cellular stress responses. Dr. Jiri

"Since these pathways are also important in many other disease processes, it is not hard to envision that individuals with diseases other than cancer

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Bartek of the Danish Cancer Society Institute of Cancer Biology in Copenhagen, Denmark, has an established history of important contributions to the field of cell cycle control and has turned his attention to DNA damage signaling in the past several years.

could benefit from such new drugs as well."

SW: Where do you see your research leading in the future?

Both of us will continue to elucidate the molecular events involved in stress signaling and DNA repair, always while keeping an eye towards the potential opportunities for manipulating these pathways for patient benefit. For example, modulators of these DNA damage responses could be used to make tumors more sensitive to cytotoxic therapies, an approach already being used by the recent development of Parp inhibitors. This is certain to be only the first such examples of therapeutic benefits coming from small-molecule manipulation of DNA damage response pathways.

SW: Do you foresee any social or political implications for your research?

Improving cancer cure rates or decreasing the toxicities of cancer therapies would certainly qualify as a social implication of the work, and we are already in the process of developing small molecules targeting these pathways that we hope to use in these ways. Since these pathways are also important in many other disease processes, it is not hard to envision that individuals with diseases other than cancer could benefit from such new drugs as well.

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