Published in final edited form as:

Chem Biol Interact. 2010 November 5; 188(2): 265–266. doi:10.1016/j.cbi.2010.06.002.

Cell Death or Survival: The Double-Edged Sword of Environmental and Occupational Toxicity

Rodrigo Franco¹ and Mihalios I. Panayiotidis^{2,3}

¹Redox Biology Center and School of Veterinary Medicine and Biomedical Sciences. University of Nebraska-Lincoln. Lincoln, NE 68583 rfrancocruz2@unl.edu.

²Department of Pathology, Medical School, University of Ioannina, University Campus 45110, Ioannina, Greece.

³School of Community Health Sciences, University of Nevada, Reno, NV 89557, USA.

Keywords

Environmental Stress; Cell death; Carcinogenesis; Oxidative Stress

EDITORIAL

Exposure to environmental toxicants such as pollutants, chemicals, allergens and natural toxins have detrimental effects on health and are considered to contribute substantially to the etiology of human diseases of major public health significance. In this regards, research towards understanding how environmental risk factors affect the development and progression of disease will lead to further improvements in public health. Environmental sciences focus on the study of the basic biological processes that are altered or regulated by environmental factors, and as a result trigger disease processes or alter the course of disease progression. Thus, research with potential for future translation into the clinic must be pursued to understand the fundamental changes caused by exposure to environmental agents that will drive the scientific basis for public health decisions. Although a large number of toxicological studies have been performed to understand the biological basis of the cellular environmental stress response, there is still a lack of evidence for a mechanistic explanation of these effects [1,2].

Both national and international public health agencies strive to prevent human disease induced by toxic agents and/or their mixtures found in the environment. Thus it is of outmost importance not only to identify these potential harmful sources but also to be able to understand the mechanistic basis of their progression to human disease. Epidemiological studies have provided a large amount of evidence linking/correlating environmental agent exposure to adverse health effects, in humans, where the effect of a toxic agent has been linked to a particular disease phenotype. Scientists have now undertaken the enormous task

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To whom correspondence should be addressed: Rodrigo Franco. Redox Biology Center and School of Veterinary Medicine and Biomedical Sciences. 114 VBS 0905. University of Nebraska-Lincoln, Lincoln, NE 68583. Tel: 402-472-8547. Fax: 402-472-9690. rfrancocruz2@unl.edu. .

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CONFLICT OF INTEREST The authors declare that there is no conflict of interest

to identify and characterize the molecular mechanisms involved in disease development/progression after environmental toxicant exposure. Reconstructing those events in between exposure and disease development will provide us with the necessary knowledge to: 1) identify possible routes for intervention; 2) identify methods to diagnose environmental diseases before they are clinically evident (early biomarkers of disease); 3) develop early interventions to prevent progression; and 4) identify targets for the design of new therapeutic approaches..

In multicellular organisms, a balance between the cell proliferation and cell death (mainly induced by apoptosis) determines the total number of cells. A disruption of this delicate balance leads to the development of a variety of human diseases such as cancer and neurodegeneration. Exposure to environmental agents has been reported to mediate alterations in the expression or function of signaling molecules that control both survival and cell death pathways. In general environmental exposures have been reported to mediate cellular toxicity (death) or transformation, which exemplifies the double-edged sword of environmental toxicity. In this Special Issue, we have assembled a number of concise reviews and original research articles by experts in different areas encompassing the study of the molecular mechanisms by which cell fate is determined by environmental toxicity.

The impact of environmental toxicity on the mechanisms of cell death progression is poorly understood, yet the consequences of modifying/regulating cell death pathways can result in a potential increased risk of developing diseases associated with changes in apoptotic cell death rates [1,2]. Metal toxicity arises from numerous sources, including contaminated air, water, soil and food [3-5]. This special issue addresses first the mechanisms by which cell toxicity is triggered by metals such as cadmium (Dr. Templeton) and chromium (Dr. Ceryak).

Other environmental exposures have been reported to exert specific toxic effects in the nervous system. It has been largely suggested that methylmercury and pesticides are potent neurotoxins [6-12]. The mechanisms by which pesticides (Dr. Franco) and methylmercury (Dr. Ceccatelli) exposures induce neurotoxicity are reviewed in this Special Issue.

Exposure to asbestos remains an area of great concern in the field of occupational lung disease, which has become one of the leading causes of occupationally-related cancer death [13,14]. Dr. Kamp contributes to this Special Issue with a review manuscript that addresses the molecular mechanisms involved in asbestos-induced apoptosis.

Fluoride has been described as an essential element for normal development and growth of animals. Fluoride is abundant in the environment and the main source of fluoride to humans is drinking water [15,16]. However, high levels of fluoride are known to induce toxicity (fluorosis) in various organs. Barbier and Del Razo discuss the current state of knowledge regarding the mechanisms involved in fluoride toxicity.

On the other end of this double-edged sword of environmental toxicity, exposure to environmental agents has also been demonstrated to impair the cellular machinery governing the progression of cell death and thus induce cellular transformation and carcinogenesis [17-20]. Many environmental, occupational and industrial chemicals are known to generate oxidative stress that contributes to the pathophysiology of cancer [21-23]. We continue this special issue with a review manuscript from Dr. Panayiotidis regarding the role of reactive oxygen species (ROS) and oxidative stress in environmental carcinogenesis with an emphasis on the importance of this research area for biomarker development in the early detection of cellular transformation.

Furthermore, cancer research has generated a large body of evidence linking epigenetic changes to the genome with the carcinogenic process. Modifications in the DNA methylation machinery have been hypothesized to serve as excellent candidates for the association between environmental exposure and cancer development. These epigenetic changes have been strongly implicated in virtually every step during tumor development and progression [22]. Dr. Panayiotidis also contributes with a review manuscript regarding the epigenetic mechanisms involved in silencing of tumor suppressor genes and/or activation of proto-oncogenes, which determine cell fate and are critical during carcinogenesis, as observed in many environmental-and occupational-induced human cancers.

DNA damage is considered a central event in cellular transformation. Tumor suppressor gene BRCA1 is considered an important component of mammary homeostasis through its participation in the control mechanisms of cell growth and DNA repair. There is strong experimental evidence linking BRCA1 to environmentally induced toxic-stress responses and carcinogenesis [24,25]. Dr. Georgakilas contributes to this special issue with an original research manuscript that reports on the role of BRCA1 in the repair of oxidatively-induced clustered DNA lesions.

Viral infections are considered now a major environmental factor involved in the etiology of cancer. Human T-cell leukemia/lymphoma virus type 1 (HTLV-1) causes neoplastic transformation of human T-cells [26,27]. Dr. Chlichlia's work reviews the mechanisms by which HTLV-1 Tax, considered to be responsible for the early stages of leukemogenesis in infected hosts, regulates cellular transformation and cell death.

Our goal as guest editors of this special issue is to present the current state of knowledge regarding how environmental toxicity regulates cellular fate and the molecular events involved by presenting a general and diverse view of major environmental exposures. We acknowledge that other major environmental exposures have been left out due to space restrictions. We apologize in advance to our colleagues for this omission. To this end, we would like to express our gratitude to all authors for contributing their expertise in this special issue of "Cell Death or Survival: the Double-Edged Sword of Environmental Toxicity" in Chemico-Biological Interactions. Last, but certainly not least, we would like to thank Dr. James A. Bond (Editor-in-Chief) for the opportunity he has given us, as well as for his patience, support and advice while putting this special issue together. We would also like to acknowledge the *ad hoc* reviewers participating in the peer review process. Finally, this work would not have been possible without the help from Xian Li and Emma O'Connell at Elsevier

Enjoy!!

Acknowledgments

This work was supported by National Institutes of Health Grant P20RR17675 Centers of Biomedical Research Excellence (COBRE) (Franco R) and the School of Community Health Sciences and a Junior Faculty Research Award from the University of Nevada-Reno (Panayiotidis MI).

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