



Review

Epigenetic alterations induced by genotoxic occupational and environmental human chemical carcinogens: A systematic literature review

Grace Chappell^a, Igor P. Pogribny^b, Kathryn Z. Guyton^c, Ivan Rusyn^{a,*}^a Department of Veterinary Integrative Biosciences, Texas A&M University, College Station, TX, USA^b National Center for Toxicological Research, US Food and Drug Administration, Jefferson, AR, USA^c International Agency for Research on Cancer, Lyon, France

ARTICLE INFO

Article history:

Received 12 January 2016

Received in revised form 24 March 2016

Accepted 25 March 2016

Available online 31 March 2016

Keywords:

Epigenetics

Toxicology

Cancer

Genotoxicity

Hazard assessment

ABSTRACT

Accumulating evidence suggests that epigenetic alterations play an important role in chemically-induced carcinogenesis. Although the epigenome and genome may be equally important in carcinogenicity, the genotoxicity of chemical agents and exposure-related transcriptomic responses have been more thoroughly studied and characterized. To better understand the evidence for epigenetic alterations of human carcinogens, and the potential association with genotoxic endpoints, we conducted a systematic review of published studies of genotoxic carcinogens that reported epigenetic endpoints. Specifically, we searched for publications reporting epigenetic effects for the 28 agents and occupations included in Monograph Volume 100F of the International Agency for the Research on Cancer (IARC) that were classified as “carcinogenic to humans” (Group 1) with strong evidence of genotoxic mechanisms of carcinogenesis. We identified a total of 158 studies that evaluated epigenetic alterations for 12 of these 28 carcinogenic agents and occupations (1,3-butadiene, 4-aminobiphenyl, aflatoxins, benzene, benzidine, benzo[a]pyrene, coke production, formaldehyde, occupational exposure as a painter, sulfur mustard, and vinyl chloride). Aberrant DNA methylation was most commonly studied, followed by altered expression of non-coding RNAs and histone changes (totaling 85, 59 and 25 studies, respectively). For 3 carcinogens (aflatoxins, benzene and benzo[a]pyrene), 10 or more studies reported epigenetic effects. However, epigenetic studies were sparse for the remaining 9 carcinogens; for 4 agents, only 1 or 2 published reports were identified. While further research is needed to better identify carcinogenesis-associated epigenetic perturbations for many potential carcinogens, published reports on specific epigenetic endpoints can be systematically identified and increasingly incorporated in cancer hazard assessments.

© 2016 Elsevier B.V. All rights reserved.

Contents

1. Introduction	28
2. Methodology	29
3. Categories of epigenetic alterations induced by chemicals and associated occupations included in the systematic review	31
3.1. DNA methylation	31
3.2. Histone modifications	31
3.3. Non-coding RNAs	32
4. Epigenetic effects associated with carcinogenic chemicals and associated occupations	34
4.1. Benzo[a]pyrene	34
4.1.1. Routes of exposure, associated cancers, and genotoxicity	34
4.1.2. DNA methylation	34

* Corresponding author at: Department of Veterinary Integrative Biosciences, Texas A&M University, 4458 TAMU, College Station, TX 77843-4458, USA.
E-mail address: irusyn@cvm.tamu.edu (I. Rusyn).

4.1.3.	Histone modifications	34
4.1.4.	Non-coding RNA	35
4.2.	Aflatoxins (naturally occurring mixtures)	35
4.2.1.	Routes of exposure, associated cancers, and genotoxicity	35
4.2.2.	DNA methylation	35
4.2.3.	Histone modifications	35
4.2.4.	Non-coding RNA	36
4.3.	Benzene	36
4.3.1.	Routes of exposure, associated cancers, and genotoxicity	36
4.3.2.	DNA methylation	36
4.3.3.	Histone modifications	36
4.3.4.	Non-coding RNA	37
4.4.	Formaldehyde	37
4.4.1.	Routes of exposure, associated cancers, and genotoxicity	37
4.4.2.	DNA methylation	37
4.4.3.	Histone modifications	37
4.4.4.	Non-coding RNA	37
4.5.	Coke production, occupational exposures	38
4.5.1.	Routes of exposure, associated cancers, and genotoxicity	38
4.5.2.	DNA methylation	38
4.5.3.	Non-coding RNA	38
4.6.	1,3-butadiene	38
4.6.1.	Routes of exposure, associated cancers, and genotoxicity	38
4.6.2.	DNA methylation	38
4.6.3.	Histone modifications	38
4.7.	Sulfur mustard	38
4.7.1.	Routes of exposure, associated cancers, and genotoxicity	38
4.7.2.	DNA methylation	39
4.7.3.	Non-coding RNA	39
4.8.	Vinyl chloride	39
4.8.1.	Routes of exposure, associated cancers, and genotoxicity	39
4.8.2.	DNA methylation	39
4.9.	4-Aminobiphenyl	39
4.9.1.	Routes of exposure, associated cancers, and genotoxicity	39
4.9.2.	Histone modifications	39
4.9.3.	Non-coding RNA	39
4.10.	Benzidine	39
4.10.1.	Routes of exposure, associated cancers, and genotoxicity	39
4.10.2.	DNA methylation	39
4.11.	4,4'-Methylenebis(2-chlorobenzeneamine)	40
4.11.1.	Routes of exposure, associated cancers, and genotoxicity	40
4.11.2.	Histone modifications	40
4.12.	Occupational exposure as a painter	40
4.12.1.	Routes of exposure, associated cancers, and genotoxicity	40
4.12.2.	DNA methylation	40
5.	Summary	40
6.	Future research needs	40
7.	Conclusions	41
	Conflict of interest	41
	Disclaimer	41
	Acknowledgements	41
	References	41

1. Introduction

Epigenetic alterations represent non-genotoxic mechanisms of carcinogenesis that may occur independently or concomitantly with genotoxic aberrations. Further, the epigenomic landscape may directly influence the genotoxic potential of a chemical; for example, several studies have indicated preferential binding of reactive chemicals to regions of DNA that harbor specific histone modification marks and/or DNA methylation patterns [1–6].

There are several major types of epigenetic and epigenomic alterations: DNA methylation, histones/chromatin structure, nucleosome positioning, and expression of non-coding RNAs, all of which can alter gene activity without change to the DNA sequence. A wealth of data demonstrates that changes in these epigenetic marks may occur as a consequence of exposure to environmental

chemicals [7,8], and may play a role in the etiology of various human diseases, including cancer [9]. It has been demonstrated that chemically-induced epigenetic alterations occur early during exposure and may also have significance as biomarkers of carcinogen exposure.

To enable incorporation of epigenetic endpoints in chemical safety assessments, further characterization of the role of epigenetic alterations induced by chemical exposure is necessary [10]. Specifically, additional studies are needed to characterize the relationship between epigenetic alterations and toxicity phenotypes, and the epigenetic-specific dose-response [11]. Several recent publications [9,12] reviewed the current state of knowledge of epigenetics and cancer, and the application of epigenetic endpoints in cancer hazard assessments, including for chemical carcinogens. Despite the fact that the utilization of epigenetic

Download English Version:

<https://daneshyari.com/en/article/2149552>

Download Persian Version:

<https://daneshyari.com/article/2149552>

[Daneshyari.com](https://daneshyari.com)