

Author's Accepted Manuscript

Radiation-Induced DNA-Protein Cross-Links:
Mechanisms and Biological Significance

Toshiaki Nakano, Xu Xu, Amir M.H. Salem,
Mahmoud I. Shoukamy, Hiroshi Ide



www.elsevier.com

PII: S0891-5849(16)31075-9
DOI: <http://dx.doi.org/10.1016/j.freeradbiomed.2016.11.041>
Reference: FRB13096

To appear in: *Free Radical Biology and Medicine*

Received date: 29 August 2016
Revised date: 21 November 2016
Accepted date: 23 November 2016

Cite this article as: Toshiaki Nakano, Xu Xu, Amir M.H. Salem, Mahmoud I Shoukamy and Hiroshi Ide, Radiation-Induced DNA-Protein Cross-Links Mechanisms and Biological Significance, *Free Radical Biology and Medicine* <http://dx.doi.org/10.1016/j.freeradbiomed.2016.11.041>

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting galley proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Radiation-Induced DNA–Protein Cross-Links: Mechanisms and Biological Significance

Toshiaki Nakano¹, Xu Xu¹, Amir M. H. Salem^{1,2}, Mahmoud I. Shoukamy^{1,3}, Hiroshi Ide^{1*}¹Department of Mathematical and Life Sciences, Graduate School of Science, Hiroshima University, Higashi-Hiroshima 739-8526, Japan²Department of Pathology, Medical Research Division, National Research Centre, El-Bohouth St., Dokki, Giza 12311, Egypt³Department of Zoology, Biological Science Building, Faculty of Science, Minia University, Minia 61519, Egypt

*Corresponding author: Department of Mathematical and Life Sciences, Graduate School of Science, Hiroshima University, Higashi-Hiroshima 739-8526, Japan. Tel & fax: +81 82 4247457. ideh@hiroshima-u.ac.jp

Abstract

Ionizing radiation produces various DNA lesions such as base damage, DNA single-strand breaks (SSBs), DNA double-strand breaks (DSBs), and DNA–protein cross-links (DPCs). Of these, the biological significance of DPCs remains elusive. In this article, we focus on radiation-induced DPCs and review the current understanding of their induction, properties, repair, and biological consequences. When cells are irradiated, the formation of base damage, SSBs, and DSBs are promoted in the presence of oxygen. Conversely, that of DPCs is promoted in the absence of oxygen, suggesting their importance in hypoxic cells, such as those present in tumors. DNA and protein radicals generated by hydroxyl radicals (i.e., indirect effect) are responsible for DPC formation. In addition, DPCs can also be formed from guanine radical cations generated by the direct effect. Actin, histones, and other proteins have been identified as cross-linked proteins. Also, covalent linkages between DNA and protein constituents such as thymine–lysine and guanine–lysine have been identified and their structures are proposed. In irradiated cells and tissues, DPCs are repaired in a biphasic manner, consisting of fast and slow components. The half-time for the fast component is 20 min–2 h and that for the slow component is 2–70 h. Notably, radiation-induced DPCs are repaired more slowly than DSBs. Homologous recombination plays a pivotal role in the repair of radiation-induced DPCs as well as DSBs. Recently, a novel mechanism of DPC repair mediated by a DPC protease was reported, wherein the resulting DNA–peptide cross-links were bypassed by translesion synthesis. The replication and transcription of DPC-bearing reporter plasmids are inhibited in cells, suggesting that DPCs are potentially lethal lesions. However, whether DPCs are mutagenic and induce

Download English Version:

<https://daneshyari.com/en/article/5501813>

Download Persian Version:

<https://daneshyari.com/article/5501813>

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