

5th International Conference on

Pathology

May 09-11, 2016 Chicago IL, USA

Mechanisms of action of carcinogens for the complexities of the tumor types

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1. The etio-pathogenesis of tumors is thought to involve somatic mutations / genomic events, but how carcinogens induce genomic events is unclear.
2. For an agent to cause a tumor, five steps are involved (1): (i) The exogenous causative factor(s) enters, or perhaps only impinges on, a somatic cell. (ii) The exogenous agent(s) act on a critical structural or biochemical target(s) in the cell. (iii) A particular function of the target is disturbed. (iv) The disturbance in the function in the target has a pro-tumor genomic effect. (v) The relevant effect(s) / genomic event(s) produce the features of the thousand or so different types of tumors – from different parent cells, but nevertheless, all from the one genome.
3. This paper discusses the pathogenesis of chemical and radiation carcinogenesis under the following headings: (i) Toxicokinetics, including at the nuclear level (1). (ii) The intranuclear structures which may be affected. (iii) The action of carcinogens on susceptible nuclear component. (iiia) The dual dysfunction theory for uni-nucleotide events (1). (iiib) The tether drop theory for chromosomal aberration-like lesions (2). (iiic) The impaired polymerase complex theory for the focal replicative infidelity lesions (3).

Biography

Leon P Bignold graduated in Medicine from the University of Western Australia, and has post-graduate qualifications in internal medicine, experimental pathology, and diagnostic histopathology. From the 1980s, he has practiced and taught general and diagnostic histopathology at the University of Adelaide and the South Australian state government pathology service (SA Pathology, formerly Institute of Medical and Veterinary Science). He has written many articles on how genomic instability might explain the histopathological features of tumors, as well as related issues. In 2015, he published "Principles of Tumors: A Translational Approach to Foundations", Elsevier, Academic Press, Waltham, MA. With colleagues, he has also published a study of the origins of tumor pathology: "David Paul Hansemann: Contributions to Oncology" Birkhäuser, Basel, (2007) and a volume on the history of medicine: "Virchow's Eulogies" Birkhäuser, Basel, (2008). In 2006, he edited a volume "Cancer: cell structures, carcinogens and genomic instability".

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