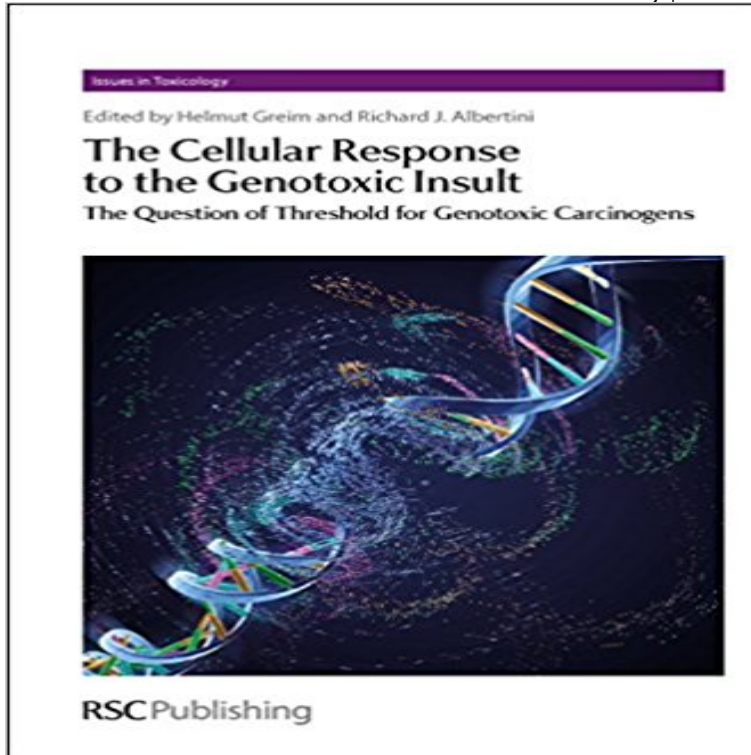


# The Cellular Response to the Genotoxic Insult: The Question of Threshold for Genotoxic Carcinogens (Issues in Toxicology)



Genotoxic carcinogens can lead to DNA mutations with the potential to cause cancer. Typically, a series of mutation events are needed before malignancy occurs so a single, small exposure may not result in disease. Also, cells have an armoury of defence mechanisms which, to a degree, counter the effects of mutagens. Distinguishing the point at which exposure to a carcinogen increases mutation rates beyond the background level is challenging. In fact, there is now general agreement that, for genotoxic carcinogens, no specific threshold can be identified. However, NOAELs (No Observed Adverse Effect Levels) may be used in the process of establishing a dose-response relationship. These denote the level of exposure at which there is no significant increase in adverse effects in the exposed population when compared to an appropriate control. Such a scientifically defensible threshold allows us to propose health based exposure limits for genotoxic carcinogens. This book describes the various cellular defence mechanisms individually and explains how they are regulated. The processes covered include metabolic inactivation, epigenetic regulation, scavenging mechanisms, DNA-repair and apoptosis. It also considers dose-dependent threshold mechanisms of carcinogenesis and the rate limiting parameters. Aimed at graduate level and above, the book discusses the consequences of genotoxic evaluation and urges readers to question the idea that even low exposures present a cancer risk.

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