Causes of genome instability: the effect of low dose chemical exposures in modern society

ABSTRACT

Genome instability is a prerequisite for the development of cancer. It occurs when genome maintenance systems fail to safeguard the genome's integrity, whether as a consequence of inherited defects or induced via exposure to environmental agents (chemicals, biological agents and radiation). Thus, genome instability can be defined as an enhanced tendency for the genome to acquire mutations; ranging from changes to the nucleotide sequence to chromosomal gain, rearrangements or loss. This review raises the hypothesis that in addition to known human carcinogens, exposure to low dose of other chemicals present in our modern society could contribute to carcinogenesis by indirectly affecting genome stability. The selected chemicals with their mechanisms of action proposed to indirectly contribute to genome instability are: heavy metals (DNA repair, epigenetic modification, DNA damage signaling, telomere length), acrylamide (DNA repair, chromosome segregation), bisphenol A (epigenetic modification, DNA damage signaling, mitochondrial function, chromosome segregation), benomyl (chromosome segregation), quinones (epigenetic modification) and nano-sized particles (epigenetic pathways, mitochondrial function, chromosome segregation, telomere length). The purpose of this review is to describe the crucial aspects of genome instability, to outline the ways in which environmental chemicals can affect this cancer hallmark and to identify candidate chemicals for further study. The overall aim is to make scientists aware of the increasing need to unravel the underlying mechanisms via which chemicals at low doses can induce genome instability and thus promote carcinogenesis.

Keyword: Genome instability; Chemical exposures; Modern society