Contribution ID: **223** Type: **poster preferred**

Involvement of chromatin organization at different cell-cycle stages in the conversion of DNA lesions into chromatid breaks and exchanges

Tuesday, 16 October 2012 16:43 (1 minute)

The formation of diverse chromosomal aberrations following irradiation at different cell-cycle stages remain a long standing controversy, probably because most of the studies have focused on elucidating the enzymatic repair mechanisms involved using simple DNA substrates. Yet, recognition, processing and repair of DNA damage occur within the nucleoprotein complex of chromatin which is dynamic in nature, capable of rapid unfolding, disassembling, assembling and refolding. Using conventional cytogenetics and premature chromosome condensation to visualize interphase chromatin, we discuss in the present work the current status of knowledge and evidence to support the hypothesis that chromatin organization at different cell-cycle stages is an important determinant in the conversion of sub-microscopic DNA lesions into chromatid breaks and the formation of exchanges. Specifically, using G2-checkpoint abrogation by caffeine, we have investigated the formation and repair kinetics of chromatid breaks during G2-M transition and the correlation of G2-checkpoint efficiency to prevent chromatid breakage with G2 chromosomal radiosensitivity. Our results demonstrate that radiation-induced chromatid breaks during G2-M transition are irreparable. This observation is important since it justifies the use of an increased yield of chromatid breaks at metaphase following G2-irradiation, as a reliable predictive biomarker for individual radiosensitivity. Furthermore, we present data to demonstrate the vital importance of chromatin organization and the proximity of breaks in determining the kinds and frequencies of exchanges. When cells are irradiated at metaphase and chromosomes are analyzed in daughter cells in the subsequent G1 or G2 phase, the ratio of inter-change to intra-change it shifts to almost entirely to the intra-change category and even more to the intra-arm intra-change. Consequently, the type and yield of radiation-induced chromosomal aberrations at a given cell-cycle-stage depends on the combined effect of DNA repair processes and chromatin organization, which is cell-cycle-regulated and subject to up- or down-regulation following mutagen exposure or genetic alterations. This hypothesis is used to revisit unresolved issues and in particular to explain the variability in radiosensitivity observed at various cell-cycle-stages, among mutant cells and cells of different origin, or among different individuals.

Primary author: Dr TERZOUDI, Georgia (Radiobiology Laboratory, Institute of Nuclear & Radiological Sciences & Technology, Energy & Safety, National Centre for Scientific Research "Demokritos"Athens, Greece)

Co-authors: Dr GEORGAKILAS, Alexandros (Department of Biology, Thomas Harriot College of Arts and Sciences, East Carolina University, Greenville, NC 27858, USA, Department of Physics, National Technical University of Athens, Zografou Campus, GR 15773 Athens, Greece); Dr PANTELIAS, Gabriel (Radiobiology Laboratory, Institute of Nuclear & Radiological Sciences & Technology, Energy & Safety, National Centre for Scientific Research "Demokritos"Athens, Greece); Dr HATZI, Vasiliki (Radiobiology Laboratory, Institute of Nuclear & Radiological Sciences & Technology, Energy & Safety, National Centre for Scientific Research "Demokritos"Athens, Greece)

Presenter: Dr PANTELIAS, Gabriel (Radiobiology Laboratory, Institute of Nuclear & Radiological Sciences &

Technology, Energy & Safety, National Centre for Scientific Research "Demokritos"Athens, Greece)

Session Classification: Poster Session 1

Track Classification: DNA Damage and Repair