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Fifteen years' experience treating cells with inorganic arsenic, a molecule able to induce genetic/genomic instability and epigenetic changes even after its removal

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Treating V79-Cl3 cells with 10 μ M sodium arsenite (SA) for 24 h, we observed severe alterations in spindle morphology and aneuploidy; treating rat astrocytes with SA, we detected HSP70 induction and DNA damage. We assumed that SA induced in dividing cells early genetic instability. Subsequently, we stabilized those V79-Cl3 cells *in vitro* dividing at the end of SA-treatment and maintained for long without SA (ASO cells). In ASO cells, we observed chromosomal rearrangements, increased spontaneous mutations, genome-wide DNA hypomethylation (GWDH), similarly to exposed cells. We inferred that a short-term SA exposure has long-term effects and that GWDH enhances the genetic instability. Consequently, we evaluated GWDH in HaCaT keratinocytes at several time points during expanded growth following SA removal. We found a persistent GWDH and some specific gene promoters (*DNMT3A*, *DNMT3B*, *HMLH1*) methylation changes. We suggest that the SA-treated cells undergo epigenetic reprogramming at gene/genome level that is durable over many cell generations in the absence of SA, contributing to long-lasting genomic instability SA-induced. Obtaining several individual clones isolated at different time points from the growing ASO cells, we observed in someone, chromosomal and morphological instability, higher ROS and aberrant DNA methylation. We also noted that all the ASO clones with low SOD1 and high ROS acquired a transformed phenotype and moreover, increase of ROS was accompanied by defective telomerase activity. We propose that cells escaping the SA-induced death, perpetuate the memory of past exposure via ROS because of antioxidant and telomerase activity impairment and ultimately they acquire a transformed phenotype.

Biography

Fabio Caradonna has completed his PhD and Postdoc on Cellular Biology at University of Palermo. He is Specialist in Clinic Pathology and in Bioethics. He is a group leader of "Genetics and Cell Biology" lab of STEBICEF Department (University of Palermo). He is an official Reviewer of country and national projects and Editor in Chief of *Journal of Carcinogenesis & Mutagenesis*. He has an excellent experience in "Cytogenetics, Genotoxicity, DNA/chromosome methylation assessment". He is an Assistant Professor of Human Genetics and Cytogenetics, Supervisor for PhD thesis and has published 31 ISI papers, 13 book chapters and 58 meeting abstracts.

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