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Meeting abstract

Pericentromeric demethylation and chromosomal instability induced by chemicals

Diddier Prada, Clementina Castro, Lisandro Sánchez, Roxanna Pérez, Rodrigo González and Luis A Herrera*

Address: Unidad de Investigación Biomédica en Cáncer-IIB-INCAN, Mexico

Email: Luis A Herrera* - herreram@biomedicas.unam.mx

* Corresponding author

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Background

Chromosomal instability, aneuploidy in particular, plays an important role in the initiation, progression and aggressiveness of cancer cells. However, the mechanisms implicated in the formation of aneuploid cells are still not fully understood. DNA methylation is critical for condensation of chromatin and for determination of patterns of genetic expression in somatic cells. Pericentromeric heterochromatin form highly methylated chromosome regions, which sometimes are altered inducing different forms of chromosomal instability, including ruptures, centromere decondensation, formation of isochromosomes and other chromosomal aberrations. However, the role of pericentromeric heterochromatin methylation in the formation of aneuploid cells and the mechanisms implicated in this alteration are not known. In this work we evaluated the role of pericentromeric methylation in the formation of aneuploid cells induced by chemical substances.

Materials and methods

Whole blood lymphocytes were cultivated and exposed to 5-azacytidine (10 μM) during 24, 48 and 72 h. Formation of micronuclei (MN), patterns of methylation of metaphasic chromosomes, fluorescent *in situ* hybridization, and DNA methylation using MSP (methylation-specific PCR) technique after bisulfite treatment, were analyzed on every period of study.

Results

5-azacytidine induced MN formation, being more evident at 72 h of treatment. A high proportion of MN was positive to chromosome 1, a chromosome with a high degree of pericentromeric chromatin methylation. We found a progressive lost of pericentromeric methylation of chromosomes 1, 9 and 16 by immunodetection. This lost of methylation was corroborated by MSP, which showed intense demethylation of non-CpG cytosines.

Conclusion

This would be the first report of association between chromosomal instability and pericentromeric demethylation induced by chemical substances, especially in non-CpG cytosines.