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Relationship between chromatin structure and chromosomal rearrangements in myelodysplastic syndromes

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MDS is heterogeneous group of clonal hematologic disorders characterized by inefficient hematopoiesis. The incidence of MDS is about 4 cases per 100,000 people. The most typical cytogenetic abnormality arising due to still unknown cause and mediated by still unknown mechanism, is a partial or complete deletion of 5q. To address these questions, we isolated lymphocytes and CD34+ hematopoietic cells from healthy donors and MDS patients. By combining 3D-fluorescence *in situ* hybridization with BAC probes and high-resolution confocal microscopy, we reconstructed higher-order nuclear organization of the CDR (common deleted region) between bands 5q31 and 5q32. Radial and mutual positions of BAC probes, specific for individual chromosomal bands inside the CDR were determined and suggest that higher-order chromatin structure significantly contributes to formation of 5q deletions associated with MDS. Chromatin in the CDR region forms a giant loop that is, by its base, anchored to the nuclear envelope. Though the initial event and the mechanism of the loop base fragmentation has to be further studied, we suppose that close spatial proximity of loci at the loop base, stabilized by anchoring of these loci to the envelope, could simplify deletions of the whole CDR loop.

Biography

Iva Falk has completed her PhD in the field of Medical Technologies. She is working in the Department of Cell Biology and Radiobiology at the Institute of Biophysics of the Czech Academy of Sciences (Brno, CR). She is participating in research that concerns the role of chromatin structure in regulation of cellular processes. Other research interests include DNA damage and repair, carcinogenesis, tumor cells radio-sensitization, and radiobiology.

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