NUCLEAR ENVELOPE LIMITED CHROMATIN SHEETS IN P53 MUTATED BURKITT'S LYMPHOMA CELL LINES AFTER DNA AND SPINDLE DAMAGE

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The nuclear envelope-limited chromatin sheets (ELCS) represent flat folds of the nuclear envelope which lack pores and enclose the peripheral chromatin associated with fibrous lamina. Although their function is currently unknown, their presence is known to correlate with aneuploidy. Here we report that the extent of ELCS is significantly enhanced in p53 mutant Burkitt's lymphoma cell lines following irradiation (IRR) with 10 Gy, as determined by electron microscopy (EM). Polyploid giant cells are formed after irradiation and ELCS were more frequent in cells with large lobulated or segmented nuclei. DNA cytophotometric analysis of the segmented nuclei revealed extensive aneuploidy. Similar formation of segmented giant cells with abundant ELCS was also induced by treatment with 10 μM SKF, a drug which is known to cause reversible metaphasic arrest. The beta-tubulin network revealed by immunocytochemical fluorescence was not impaired after irradiation but was damaged after SKF. Giant cells often died by apoptosis, however typical ELCS were seen only in viable cells.

Detailed EM analyses in the both models revealed some novel features of ELCS: (1) Close contact of two segments of peripheral chromatin within the ELCS could be seen to result in their fusion and the formation of a median longitudinal fibril; (2) ELCS are systematically found in direct contact with the nucleolus-associated chromatin; (3) ELCS often form the 'tails' of sub-nuclei (lobes) which tend to converge in a radial pattern; (4) Large number of mitochondria are regularly seen nearby ELCS and microtubules are sometimes seen attached to them suggesting the motility of ELCS; (5) Rarely after IRR, but commonly after SKF, ELCS were found to be degrading and converting into the annulate lamellae. These annulate lamellae form into stacks, which then spiral and develop into autophagosomes.

Taken together, these features suggest that the formation of ELCS in the nuclei of p53 mutant cells may be associated with aneu-polyplody and with the elimination of amplified nucleolar DNA. Alternatively, ELCS may be involved in search of homologues for recombination repair, a process that is elevated after IRR in these cells. The data also suggest a role of microtubular network in the turnover of ELCS.