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Sommario	Common Fragile Sites (CFSs) are regions in which DNA is prone to gaps, breaks or constrictions visible on metaphase chromosomes when cells are under replicative stressful conditions. CFSs are characterized by slow/late replication timing mainly due, among other characteristics, to nucleotide sequence which tend to form secondary structure, and to the number of active (or inducible) replication origins. Recent studies indicate that CFSs expression is associated with tissue specificity. In the first part of the work, induction and classification of CFSs in two human lung fibroblast cell line, IMR-90 and MRC-5, has been done. Cytogenetical identification of the most expressed CFSs in both fibroblast cell lines were done: 1p31.1 and 3q13.3, located on chromosome 1 and 3 respectively, are peculiar for this tissue. These regions have typical and confirmed CFSs' characteristics such as expression higher than 3%, high AT levels and enrichment in large genes. Using genomic databases, searching for causes of their instability were done comparing percentage of repetitive elements among the CFSs, non-fragile regions (NFRA) and standard genomic sequences. These CFSs are characterized by presence of large genes, NEGR1 found in 1p31.1, LSAMP and ARHGAP31 in the most fragile region of 3q13.3, that could be co-responsible for their genomic instability. Using probes

	delimitating fragile regions and combining FISH with IF anti-BrdU, analysis of relationship between replication timing and fragility was done. Furthermore, comparison between replication timing, in normal and stressful condition using APH, was done as well. The results obtained for these fragile regions reflect the replication timing impairments typical of fragile sites, in both normal and stressful conditions. The same probes when used in lymphocytes result in a normal replication timing, moreover also using CFSs probes specific in lymphocytes on fibroblast, results in normal replication timing. The results from replication timing analysis are strictly correlated with the structural and functional characteristics that are specific of the tissues in which these CFSs are expressed.
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