

Recurrent copy number abnormalities and copy neutral-loss of heterozygosity in colorectal cancer identified by high-density SNP array

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Two forms of genetic instability have been observed in colorectal cancer (CRC): chromosomal instability, that is present in 85% cases and is characterized by structural and numerical chromosomal abnormalities (aneuploidy); and microsatellite instability (MSI), characterized by a deficiency of the mismatch repair system and associated to a normal or quasi-normal karyotype. Recent advances in molecular cytogenetics techniques are likely to introduce a revolution in the field. In the present study we analysed a series of 57 CRC samples and their related normal mucosae by high resolution genomic arrays (Affymetrix SNP 6.0 arrays) and set up a series of bioinformatics tools that allow the generation of a rapid report on broad (>25% of a chromosomal arm) and small somatic copy number abnormalities (CNAs), somatic homozygous deletions, focal high level amplifications, and regions of loss of heterozygosity (LOH). MSI tumors represented 14% of our CRC series and showed a median values of somatic broad CNAs of 3 (range 1-6), while microsatellite stable (MSS) tumors showed a median value of 12 (range 0-24). Therefore all MSI tumors were below a threshold of 6 CNAs, while 16.2 % of MSS were below this threshold, representing a group of microsatellite and chromosomal stable tumors. No correlation was observed between the number of tumor associated CNAs and the number of somatic copy neutral-LOH regions, suggesting that different mechanisms underlie such chromosomal abnormalities. Analysis of recurrent CNAs identified somatic homozygous deletions that cannot be ascribed to regions of inherent fragility.

Keywords: Colorectal cancer; SNP array, copy number abnormalities, loss of heterozygosity.