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Letter to the Editor

Chromosomal instability, aneuploidy, and gene mutations in human sporadic colorectal adenomas

To the Editor:

We read with interest the article of Giaretti et al. [2] associating specific gene mutations with aneuploidy of sporadic colorectal carcinomas, and the central role of the *KRAS2* gene in this process, but we would like to raise some points of discussion on the data presented.

The majority of sporadic colorectal cancers present chromosomal instability (CIN), which is believed to be reflected by DNA aneuploidy, and this is thought to be one of the key genomic events in colorectal adenoma to carcinoma progression [3]. Despite extensive research efforts in the area, the mechanisms which give rise to this phenotype are still largely unknown [1,4–7]. Giaretti et al. [2] found a significant association of specific mutations on *KRAS2* and *APC* genes, and genomic losses on 1p34–36, with aneuploidy. Within *KRAS2* mutations the authors found that only G–C and G–T transversions, and not G–A transitions, were strongly associated with DNA aneuploidy (and, by inference, CIN). It would be interesting to speculate about the biological consequences that these different mutations have, and how this affects mechanisms involved in maintenance of the integrity of the genome, and more specific the chromosomes. Also putting these data in perspective of other findings, gives further food for thought. As said before, adenoma to carcinoma progression is largely believed to be determined by the onset, or at least acceleration of chromosomal instability. For instance, in a study by Hermsen et al. [3], progressed adenomas appeared to show more commonly G–A transitions than G–C and G–T transversions in the *KRAS2* gene. Also at the other hand of the spectrum of precursors of colorectal cancer, *KRAS* mutations appear to play a role. *KRAS* mutations are frequently found in aberrant crypt foci and most of these lesions hardly ever progress to malignancy [8]. The role of *KRAS* in aneuploidy in the context of colorectal carcinogenesis still seems to hold some enigmas.

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