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LETTER TO THE EDITOR

The relationship between aneuploidy and p53 overexpression during genesis of colorectal adenocarcinoma

Sir,

we read with interest the article by Auer and co-workers [1] in which they compared the DNA profile and the p53-immunoreactivity of normal colonic mucosa, the different types of colorectal adenoma and colorectal adenocarcinoma. They found p53-immunoreactivity in aneuploid adenomas (mild dysplasia 0%, moderate dysplasia 17%, severe dysplasia 24%) and aneuploid adenocarcinomas (66%), however not in diploid lesions or in normal colonic mucosa. The authors conclude that "genomic instability as reflected by crude aneuploidy occurs early during genesis of colorectal carcinoma and represents a high risk factor for p53-gene mutation".

Although this conclusion may be justified in general, the results of their study are compromised by the choice of methodology for the DNA measurements.

In the vast majority of investigations, cytological smears from touch preparations or after cell separation from paraffin blocks have been used for DNA cytometry. In this study, however, the authors performed DNA measurements on 4 μm sections, although several methodological objections have been raised.

Depending on such factors as the thickness of the section, the size of the nuclei and their position on the section, almost all of the cells will have lost part of their nucleus when the section is cut, and so the DNA profile obtained from a section will be different from that obtained from an imprint smear of the same specimen. This well-known phenomenon results in DNA histograms of limited quality [2–4]. In comparison with DNA histograms from cytological smears or after cell separation from paraffin blocks, the DNA stemline ploidy differs grossly after measurements on histological sections. Frequently even the loss of stemlines may be observed. This means that DNA histograms from histological sections cannot be reliably interpreted using terms as "diploid" or "aneuploid". Investigating sections of adenoid cystic carcinomas of the salivary gland, for example, the rate of false-positive diagnosis of aneuploidy was 42% when compared with cytospin preparations as standard [3]. Furthermore, the DNA distribution appears more scattered, so that also Auer's DNA histogram classification cannot be easily applied on DNA histograms from sections [2]. Consequently, DNA measurements on histological sections are no longer recommended in a recent consensus report on standardization of diagnostic DNA image cytometry [5].

The results of this study admittedly present an interesting trend but do not prove the authors' hypothesis.

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