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Multicentric Origin of Colon Carcinoma

Hsu *et al.* (*1*) report that colonic polyps in patients with Gardner syndrome are multiclonal in origin. They pose the question of whether colonic carcinomas arising in such patients would also be multiclonal.

In fact, a colon carcinoma of a black female heterozygous for glucose-6-phosphate dehydrogenase (G6PD) deficiency was found to be multiclonal in origin by E. Beutler *et al.* (*2*). Hsu *et al.* suggest that this observation "may have been due to stromal contamination in the samples." We (*2*) are incorrectly cited as being one of the sources of this suggestion. The actual findings were that some metastases contained primarily G6PD-A and others primarily G6PD-B. Only 7 of 24 tumor nodules contained equal amounts of G6PD-A and G6PD-B, and we proposed that in these nodules the findings might be due to stromal contamination. The fact that many tumors in the patient contained either G6PD-A or G6PD-B was interpreted unequivocally as showing that the origin of the tumor was multicentric. Although these observations are more than 15 years old, we still consider them to be valid. While they may not answer the question specifically posed regarding Gardner syndrome, they do show that colon carcinoma may, at least at times, be multicentric in origin. One can only speculate regarding the mechanism that transforms several cells to give rise to what seems to be a single neoplasm. It could be due, for example, to a viral infection transforming a patch of cells rather than a single cell.

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We agree that our summary of the study by Beutler *et al.* (*1*) was too brief to do justice to that work. Their findings that the primary tumor contained both G6PD isoenzymes may indeed have been due to stromal cell contamination; they pointed out that the primary tumor was mostly fibrous stroma (*1*). We did not include their findings that most of the liver and omental metastases contained either G6PD-A or G6PD-B. Beutler *et al.* did not unequivocally interpret those findings as showing that the origin of the tumor was multicentric. Rather, they stated that "the studies . . . suggest that the metastases represented clones . . . [and] it appears that this tumor arose from . . . a patch of cells. . . ." In the summary, the authors stated that "the findings were regarded as consistent with a multicentric origin of carcinoma of the colon" (*1*).

Furthermore, the finding of metastases containing either G6PD-A or G6PD-B in most cases and both isoenzymes when stromal contamination was present is consistent with a clonally derived primary tumor and the presence of an undetected synchronous or metachronous clonal primary tumor or tumors. Synchronous and metachronous colon cancers occur not infrequently in advanced colon cancers (*2*); and the patient described by Beutler *et al.* had advanced cancer and died 3 months after laparotomy for obstruction (*1*). Therefore, although the study of Beutler *et al.* suggested a multicentric origin, we do not yet have unequivocal documentation of the colonal origin of colon carcinoma.

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