Editorial

Beyond *p53*

Timothy J. Yeatman, MD

For some time now, we have known that sporadic colon cancer is the product of alterations in both oncogenes and tumor suppressor genes, with the latter being more prevalent.¹ *p53*, in fact, is the most common tumor suppressor gene affected in human cancer. The report of Garcia-Patino et al.² highlights the potential importance and prevalence of tumor suppressor genes other than *p53* in human colon cancer. The authors describe genetic evidence for the absence of at least one allele (loss of heterozygosity [LOH]) in a large percentage of tumors at two different loci, 17q21 and 10q23, known to harbor the *BRCA1* and *PTEN* tumor suppressor genes, respectively. As with other tumor suppressor genes, *BRCA1* and *PTEN* can cause familial cancer syndromes when inherited in a mutant form. *BRCA1* is known to result in breast, colon, and ovarian cancers, whereas *PTEN* is associated with three different autosomal dominant disorders.

The authors elected to compare two sets of sporadically occurring tumor specimens using LOH analysis of 17q21 and 10q23 using tumor-derived DNA: those where one tumor sample was derived per patient and those where up to four noncontiguous samples were derived from each tumor per patient sample. This experimental design allowed them to determine the degree of heterogeneity between multiple patients and between multiple samples taken from geographically distinct portions of the primary tumor.

Their data in this report confirm their previous findings² and those of others³ that LOH in the 17q21 region is significant (38.4%) and that LOH in the 10q23 region is not uncommon (30.8%). Because several portions of a number of tumors were examined for LOH, it was determined that many of the tumors did not display LOH in all portions of the tumor, confirming the heterogeneous nature of colon tumors. Interestingly, a strong correlation was seen between the presence of 10q23 LOH in any one tumor with 17q21 LOH, suggesting that these losses may be linked in some way. Because *BRCA1* is thought to have a caretaker function regulating genome integrity, it is postulated that loss of 17q21 genetic material allows the development of 10q23 LOH in a high percentage of patients. Moreover, when multiple tumors from the same patient were examined, 10q23 LOH was always associated with 17q21 LOH but not the contrary. This pattern suggested a sequential acquisition of these genetic alterations, with 17q21 being acquired first and probably early in the adenoma carcinoma sequence.

Collectively, these observations provide new insight into the development and progression of sporadic human colon cancer and expand the list of affected genes implicated in this disease.

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From the Department of Interdisciplinary Oncology and Surgery, H. Lee Moffitt Cancer Center, Tampa, Florida.

Address correspondence to: Timothy J. Yeatman, MD, Department of Surgery, H. Lee Moffitt Cancer Center, 12902 Magnolia Dr., Tampa, FL 33612; Fax: 813-979-3893; E-mail: Yeatman@moffitt.usf.edu.

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