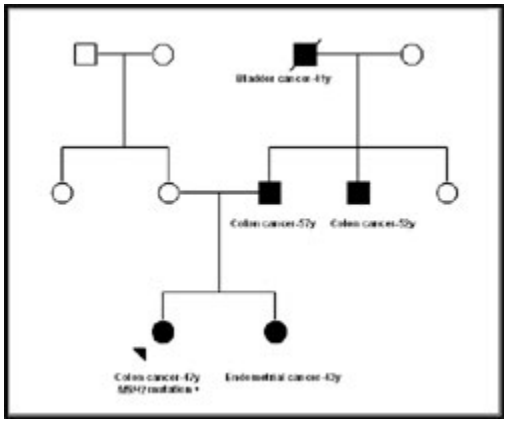
Question 14 – Week of May 19

A woman with a personal history of colorectal cancer tests positive for an MSH2 mutation. If her sister's endometrial cancer is also related to familial HNPCC syndrome, in what gene is the sister most likely to test positive for a mutation [FIGURE]?



A. MSH2
B. MYH
C. MSH6
D. APC

Answer: A

The figure shows a pedigree of an HNPCC family fulfilling the Amsterdam criteria. When a pathogenic mutation is identified in an affected family member, the same gene mutation is responsible for all the HNPCC related cancers in the other family members as well. APC gene mutations cause FAP and have not been associated with HNPCC. The MYH gene is another new gene that has been identified recently and mutations in this gene have usually been reported to cause an attenuated FAP phenotype.

References:

1. Vasen HF, Watson P, Mecklin JP, Lynch HT. New clinical criteria for hereditary nonpolyposis colorectal cancer (HNPCC, Lynch syndrome) proposed by the International Collaborative group on HNPCC. Gastroenterology 1999;116(6):1453-1456.
2. Lynch HT, Smyrk T, Lynch JF. Molecular genetics and clinical-pathology features of hereditary nonpolyposis colorectal carcinoma (Lynch syndrome): Historical journey from pedigree anecdote to molecular genetic confirmation. Oncology 1998;55(2):103-108.
3. Sieber OM, Lipton L, Crabtree M, et al. Multiple colorectal adenomas, classic adenomatous polyposis, and germ-line mutations in MYH. N Engl J Med 2003;348(9):791-799.