Adenomatous Polyposis of the Colon

Alternative Names
APC
Familial Polyposis of the Colon
FPC
Polyposis, Adenomatous Intestinal
Familial Adenomatous Polyposis
FAP
Gardner Syndrome
GS
Adenomatous Polyposis Coli, Attenuated
AAPC
Deleted in Polyposis 2.5
DP2.5

WHO International Classification of Diseases
Diseases of the digestive system

OMIM Number
175100

Mode of Inheritance
Autosomal dominant

Gene Map Locus
5q21-q22

Description
The syndrome of familial adenomatous polyposis has a wide spectrum of clinical manifestations including adenomatous polyps of the colon and small bowel, adenocarcinoma of ampulla of Vater, tumors of the central nervous system, bone lesions, and various soft tissue tumors. Familial adenomatous polyposis of the colon is an autosomal dominant disease in which virtually all affected individuals develop colorectal cancer before the age of 40.

Molecular Genetics
The gene responsible for familial adenomatous polyposis of the colon (APC gene) is mutated in the germ line of patients. The genetic diagnosis of familial adenomatous polyposis of the colon was initially done using linkage analysis. The low-penetrance susceptibility APC 11307K allele confers a relative risk of 1.5–2.0 for colorectal cancer. The APC allele with lysine (K) at codon 1307, commonly referred to in the literature as I1307K, results from the T-A transition at nt 3920 in APC, which causes an extended mononucleotide tract (A8). This mononucleotide repeat impairs replication fidelity, forming a mutational hotspot.

Epidemiology in the Arab World

Egypt
[See also: Palestine > Niell et al., 2003]

Morocco
[See also: Palestine > Niell et al., 2003]

Palestine
Niell et al. (2003) tested whether selection has operated on the I1307K allele frequency. They estimated the age of the allele, to understand its origin in the context of the Jewish diasporas and subsequent founder events. They found a common progenitor haplotype spanned across APC 11037K from the centromeric marker D5S135 to the telomeric marker D5S346 and showed that it existed in Sephardi Jews of Syrian, Egyptian, Moroccan, Yemeni, and Palestinian origins, as well as in Muslim and Christian individuals of Arab descent. The ancestor of modern I1307K alleles existed 87.9 to 118 generations ago (approximately 2,200 to 2,950 years ago). Since the conserved I1307K haplotype is shared among Jews and Arabs and that the most recent ancestor of I1307K existed sometime between 947 BCE and 195 BCE, future genetic testing for this polymorphism might be offered to individuals of different ethnic backgrounds.

Syria
[See also: Palestine > Niell et al., 2003]
Yemen
In 1999, Patael et al. analyzed the presence of the I1307K polymorphism in Ashkenazi and Yemenite Jews using denaturing gradient gel electrophoresis (DGGE). They found a common four-marker haplotype (three intragenic markers and a single downstream marker 30-70 Kb from the APC gene - D5S346) containing the I1307K allele in Ashkenazi and Yemenite Jews. The haplotype excluded D5S82, which was found in 23.4% of unselected Yemenite Jews.

Drucker et al. (2000) conducted a study to estimate the prevalence of the I1307K mutation in several ethnic groups and to elucidate the clinical features of the mutation carriers with colorectal carcinoma (CRC). Mutation screening in four consecutive CRC patients of Yemenite origin identified three carriers of the mutation. On the other hand, screening of 189 Yemenites randomly selected from the general population demonstrated the presence of nine individuals carrying the mutation, hence an I1307K carrier frequency in Yemenite Jews of approximately 4.7%.

References

Contributors
Ghazi O. Tadmouri: 22.5.2005

[See also: Palestine > Niell et al., 2003]