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Cancer Prone Disease Section

Short Communication

Familial adenomatous polyposis (FAP)

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Identity

Other names: Adenomatous polyposis of the colon; Gardner syndrome
Inheritance: Autosomal dominant disorder; frequency is about $2.5/10^5$ newborns; neomutation in 20%; variable expressivity; penetrance close to 100% by the age of 40 yrs.

Clinics

Phenotype and clinics

Multiple adenomatous polyps of the colon and the rectum. Polyps also develop in the upper gastrointestinal tract. Other: pigmented retinal lesions (congenital hypertrophy of the retinal pigment epithelium), jaw cysts, sebaceous cysts, desmoid tumours, and osteomas.

Neoplastic risk

Colorectal cancer(s) develop from the polyps through a dysplastic stage. Malignancies may be found in other sites: liver (hepatoblastoma), brain (medulloblastoma), thyroid.

Prognosis

Colorectal cancer in early adult life (median age: 40 yrs) is the first cause of death in this disease.

Genes involved and Proteins

APC

Location: 5q21

Protein

Description: Tumour suppressor gene; the APC normal gene product interacts with the adherens junction proteins a and b-catenin.

Mutations

Germinal: FAP is caused by a highly heterogeneous spectrum of point mutations that represents a problem for molecular genetic diagnosis; but all the mutations are chain terminating and some correlations between the position of the mutation and the phenotypic consequences have been described:
- Germline mutations between codons 1250 and 1464 are associated with profuse polyposis;
- An attenuated adenomatous polyposis coli (AAPC) is associated with mutations located very close to the 5-prime end of the APC gene;
- The extent of congenital hypertrophy of the retinal pigment epithelium (CHRPE) depends on the position of the protein-truncating mutation in APC; CHRPE lesions are almost always absent if the mutation occur before exon 9, but are consistently present if it occurs after this exon;
- Patients with a mutation between codons 1445 and 1578 do not express CHRPE; however, these patients developed severe desmoid tumours.

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