FAP (FAMILIAL ADENOMATOUS POLYPOSIS)

Background: Familial Adenomatous Polyposis (FAP; OMIM 175100) is a genetic disorder which typically presents with colorectal cancer in early adult life secondary to extensive adenomatous polyps of the colon. Polyps also develop in the upper gastrointestinal track and malignancies may occur in other sites, including the brain and the thyroid. Helpful diagnostic features include pigmented retinal lesions known as congenital hypertrophy of the retinal pigment (CHRPE), jaw cysts, sebaceous cysts, and osteomata.

Screening for mutations in the MYH gene is offered to individuals with multiple polyps who have a negative family history and who are APC mutation negative. Mutations in the MYH gene have recently been shown to cause FAP when two copies of the MYH gene with a mutation are inherited (autosomal recessive pattern). MYH is more likely to be the gene involved when there is no prior family history of colorectal cancer. Testing is done first for two common mutations (Y165C and G382D). If neither of these two mutations is present, full sequencing of the MYH gene can be done. There is no tendency for other extracolonic tumors associated with MYH.

Assay: Direct mutation analysis by sequencing.

Utility: To identify individuals at very high risk of developing colon cancer so that they can be targeted for aggressive prevention programs and to reassure individuals in families with a known mutation that they are not at any higher risk for colorectal cancer than individuals in the general population if they have not inherited the familial mutation.

Sensitivity: Molecular genetic testing will detect a mutation in the APC gene in approximately 70% of affected individuals. Mutations in non-coding sequences, insertions, deletions or other rearrangements will not be detected by sequencing. A substantial proportion of people with multiple polyps in the colon, perhaps as many as 30% who have 15 to 100 polyps, have biallelic MYH mutations.

Turnaround: 6 weeks for APC screening  
6 weeks for MYH screening  
2-3 weeks for familial/targeted mutation  
7-10 days for prenatal diagnosis

Fees: APC for $1,410 for Sequencing  
MYH for $660 for Sequencing  
APC/MYH for $360 for Familial Mutation(s)  
APC/MYH for $460 for Prenatal Diagnosis (cost includes MCC studies)

CPT codes: APC Screen: 81201  
MYH Screening: 81406  
Familial Mutation: 81202 for APC or 81403 for MYH  
Prenatal Diagnosis: 81202, 81265 for APC; 81403, 81265 for MYH