APC: The Key to Colon Cancer
The APC protein and its role in controlling the cell cycle


Teachers: Susan Getzel and Anne Xiong
Mentor: W. L. Berger, MD

Abstract
Colorectal cancer affects 1 in 18 Americans, and is linked to mutations in the Adenomatous Polyposis Coli (APC) gene. The rapid division of colonocytes is regulated by the Wingless Type (Wnt) signaling pathway, mediated by β-catenin. In the nucleus, β-catenin binds to Transcription Cell Factor (TCF) and initiates transcription of cell cycle proteins. Alternatively, β-catenin binds to the 20-amino acid repeat region of the APC protein with the help of the scaffold protein axin. The enzyme GSK-3 then phosphorylates threonine and serine residues of the APC protein and subsequently β-catenin. Phosphorylated β-catenin is degraded, slowing mitosis. Mutations in APC allow β-catenin to accumulate, resulting in hyperproliferation of colonocytes, an early step in colon cancer development. As such, better understanding of APC and its function could potentially lead to better diagnosis and treatment in colorectal cancer.

Multi-Hit Hypothesis
Development of colon cancer requires multiple sequential changes in colonocytes.

Normal colonic mucosa: cells are aligned properly and replaced every 7 days due to constant damage

Hyperproliferative epithelium: too much β-catenin forms, causing excessive transcription

Adenoma: polyps (benign tumors) are formed

Carcinoma: tumor becomes malignant

Metastasis: tumor spreads to other tissues; the final stage of cancer development

The Wnt pathway is a cell signal cascade regulating cell division. Without the Wnt signal, the cell does not divide; with Wnt, division is promoted. When APC is mutated, mitosis occurs whether or not Wnt is present.

Familial vs. Sporadic Colon Cancer
This pedigree portrays a family in which sporadic colon cancer has occurred. Unlike the pedigree above, colon cancer is not common in this family. There are only two occurrences in unrelated males, and cancer appears late in life.

Think About It...
Considering the multi-hit hypothesis, it may take a decade for a polyt to become cancerous. When discovered early, the risk of dying from colon cancer drops considerably. Therefore, it is imperative to get a colonoscopy at least by your 50th birthday. Also, because colon cancer can be a result of hereditary factors, people with a familial history of colon cancer should consult with their physician about when they should start screenings. They may also wish to consult with a genetic counselor.

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