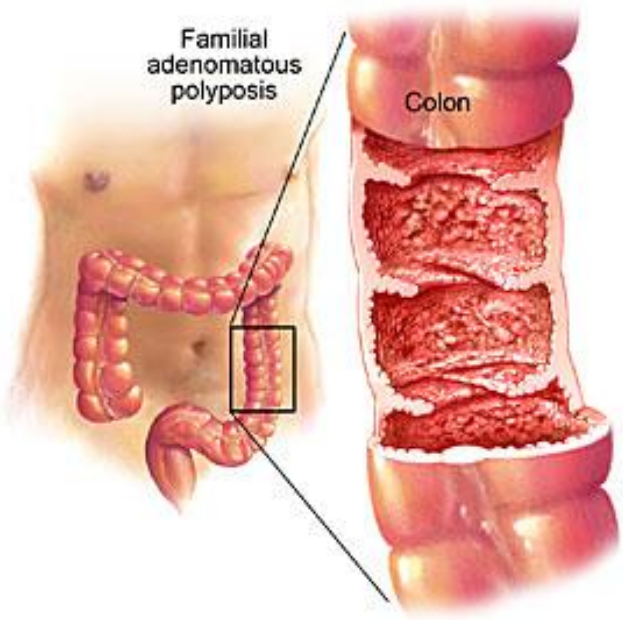
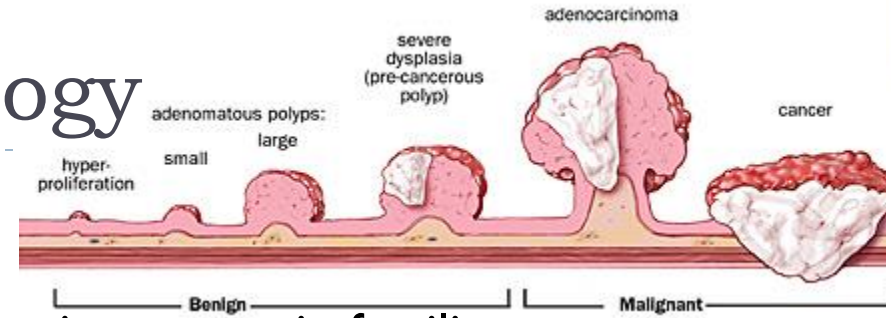
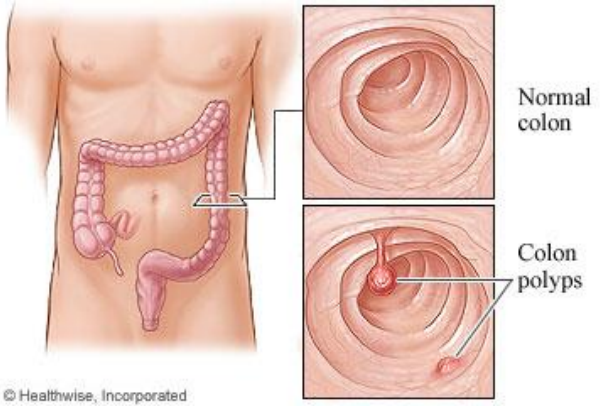


Familial Adenomatous Polyposis (FAP)

Ashley Lau

Physiology

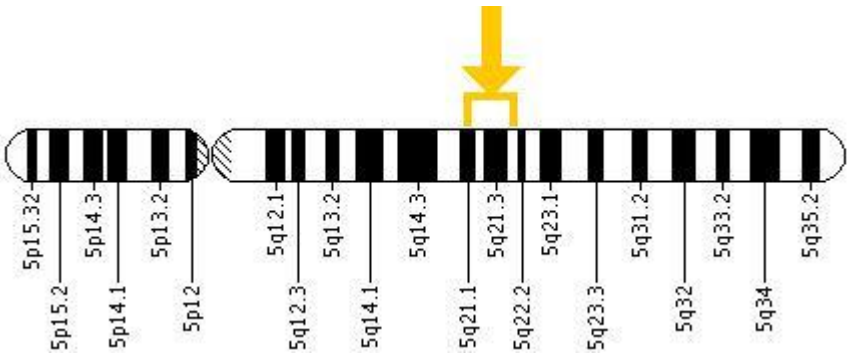


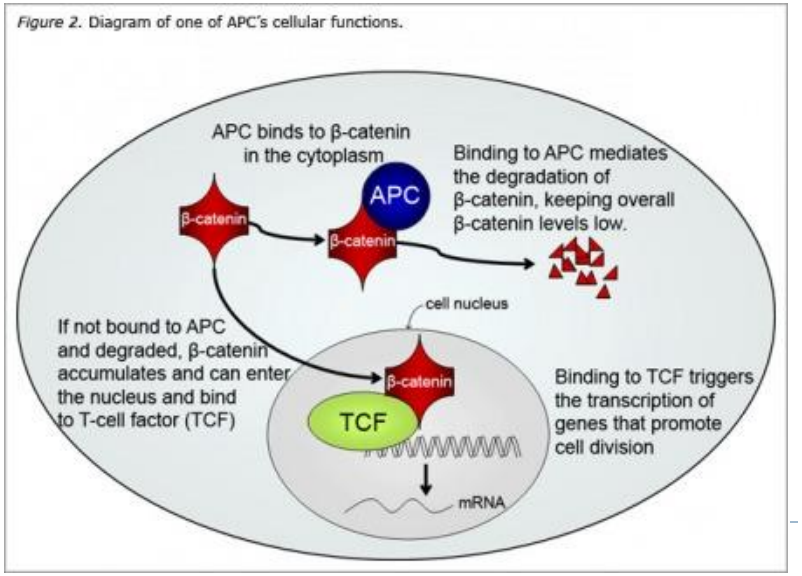


- Autosomal dominant; runs in families.
- Mainly early onset; symptoms generally appear between ages 7 and 40.
- FAP accounts for about 1% of all colorectal cancer cases.
- Major symptoms include adenomatous polyps and colon cancer. Other symptoms include abdominal pain, diarrhea, bleeding from the rectum, low blood count, change in bowel habits.
- Besides colon cancer, a mutation to the APC gene can also predispose you to other cancers such as small bowel, pancreatic, thyroid, and stomach cancer as well as brain tumors and hepatoblastoma (childhood liver tumor).
- Symptoms have a genotype-phenotype variation meaning that the phenotypes of the disease can vary depending on the area where the APC gene is mutated.

Molecular Cause

- The normal APC gene is a tumor suppressor gene.
  - The APC gene is located from base pair 112,043,201 to base pair 112,181,935 on chromosome 5
- The most common mutations for FAP are a deletion in codon 1309 and a deletion in codon 1061.
  - There can also be other types of mutations to the APC gene.





Treatments/Risks and Limitations

- There is no cure for FAP.
- Treatments vary from surgery to medication. The treatments' purpose is either to remove or slow down the growth of polyps.
- There are two medications being used to treat FAP:
  - Sunlindac (Clinoril): a sulfoxide nonsteroidal anti-inflammatory (NSAID) agent that is metabolized to the anti-inflammatory sulfide metabolite and sulfone metabolite. The sulfide metabolite has a apoptotic activity on colonic epithelial cells and is presumed to help the regression of adenomatous polyps.
  - Celecoxib (Celebrex): inhibits COX-2, which is overexpressed in colonic adenomas and might contribute to adenoma growth. Inhibiting COX-2 may make the polyps regress.
- There are three types of surgeries FAP patients can undergo:
  - Colectomy with ileorectal anastomasis (IRA): the colon is removed, but most of the rectum remains – the upper portion of the rectum is attached to the small intestine.
  - Colectomy with ileoanal pouch: both the colon and rectum are removed, leaving the anal canal and the sphincter muscles. A new rectum is made from the small intestine and is attached to the anal canal.
  - Proctocolectomy and ileostomy: both the colon and rectum are removed and a permanent ileostomy (opening in the abdomen) is formed.
- Endoscopic surveillance: visit doctor to check on polyp formation.
- Patients can also get chemotherapy or radiotherapy when they reach the cancer stage.
- Limitations of the treatments are that you might need multiple surgeries and the medications have side effects.

Proposed Cure/Limits

- Immunotherapy is a treatment that uses the immune system to fight off diseases.
  - This can be done by making the immune system work harder to attack cancer cells or by inserting immune system components.
  - Immunotherapy works by either improving the immune system on a general level or by training the immune system to attack specific cancer cells.
- The proposal is to make a cancer vaccine using cells from a removed polyp to train the immune system to attack the polyps.
  - Problems with making a vaccine would be that tumor cells are human cells, which makes them less likely to be recognized as foreign. Some cancer cells also shed molecules that inhibit immune responses.
    - Two possible solutions:
      - Identify molecules unique to the polyps and use them in vaccines to attack the specific cancer cells.
      - Use antigen presenting cells in the vaccine to present tumor antigens so the immune system will attack the tumors.
  - A limitation to this is the polyp donor. Using one person's tumor cells for a vaccine might not work for everyone. Making individualized vaccines would also require more work and time, as well as money.

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