coreBio II - genetics: Wed. 14 March 2018

phenotypes and gene names

How is mutant (disease-associated) allele first identified?
Often determines original name (name in paper)

Others may identify allele (gene) differently (and earlier)

Might take awhile to recognize the two and the same or different.

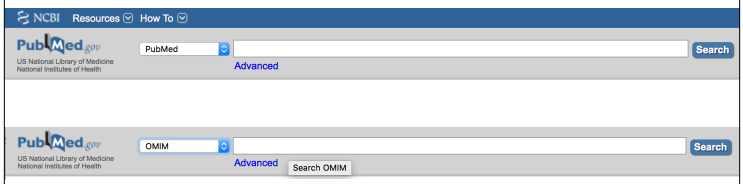
complexities of gene names (and histories)

- MIN-1: Moser et al. (1990) identified a dominant, fully penetrant mouse mutation named Min (multiple intestinal neoplasia)
- causes a phenotype closely resembling familial adenomatous polyposis (**FAP**; 175100).
- BUT THEN: number of intestinal tumors in Min/+ mice found to strongly affected by genetic background: C57BL-6J-Min/+ mice had ~29 tumors compared to AKR-Min/+ F1 progeny showed ~6 tumors
- postulated modifying gene, called Mom1 (modifier of Min-1) : associated with ~ 50% of genetic variation in tumor number
- Mom1 = gene for secretory type II phospholipase A2 (Pla2s)

check gene name on OMIM

using OMIM for your gene

go to PubMed - select OMIM

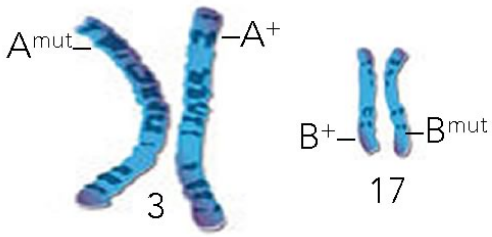


complexities of gene names (and histories)

- familial adenomatous polyposis (FAP; 175100) is the disease
- several genes within a 5.5-Mb region of DNA linked to FAP.
- All [FER (176942), MCC (159350), SRP19 (182175), TB2 (REEP5; 125265), APC] were expressed in normal colonic mucosa
- ? rough estimate of recombination frequency between these genes ?
- mutations in APC are implicated in FAP1
- APC protein found localized to cell membrane/cytoskeletal and nuclear fractions
- APC associated with both beta-catenin (CTNNB1; 116806) and alpha-catenin (CTNNA1; 116805).
- both proteins bind to the cell adhesion molecule E-cadherin (192090), the results suggested that APC is involved in cell adhesion

complexities of gene names (and histories)

- during mitosis, wildtype APC localized to the ends of microtubules embedded in kinetochores and formed a complex with the **checkpoint** proteins Bub1 (602452) and Bub3 (603719).
- plays a major role in tumor suppression by antagonizing the WNT (see WNT1; 164820) signaling pathway (alters gene expression).
- Inappropriate activation … contributes to cancer progression



estimate ratio of phenotypes if gene linked (10% rather than 50% crossover (unlinked)