Genetics of Behavior
Cancer Genetics

BIT 220
Chapter 26 (pp.. 664-671)
Chapter 28
Technical Sidelight

- **Page 664** - genes and homosexuality
- gene on X- q28 region
- early studies suggested locus for male sexual preference
- later studies did not confirm, but still many think link between genetics and sexual preference
- also study of size of hypothalamus - smaller in homosexual men
Chromosomal changes-Association with Behavior

• Some more obvious- Down syndrome - IQ lower than normal; genes and gene dosage influence intelligence

• Alzheimer’s disease - more prevalent in people with Down syndrome- does chromosome 21 involve susceptibility to Down?

• Yes- gene for amyloid β protein on 21
Alzheimer’s

• APP (amyloid precursor protein) - cleaved to produce amyloid β protein
• excessive amounts of long Aβ - leading to deposit in the brain and may be a cause for Alzheimer’s
• patients lose memories and intellectual functions
Single-gene mutations and behavior

• PKU - defective liver enzyme, phenylalanine hydroxylase- phenylalanine not converted to tyrosine, builds up in blood
• range of PKU phenotypes - mild to severe
• Other diseases:
  – Lesch-Nyhan syndrome: enzyme defective
  – HD- neurodegenerative
Complex traits- affect behavior

- Studied in monozygotic twins
- reared together or apart- tells us of influence of environmental influences on genetics (MZT vs. MZA)
- less than 0.3% of live births
Intelligence

• See page 670 for parameters of intelligence
• IQ - intelligence quotient - is it a valid test?
• Very high IQ correlation between MZ twins; less so between DZ twins; unrelated people living together - correlation zero
• what does that tell us?
Personality

• Minnesota Study - MZA
• personality traits still similar
• also studied substance abuse issues - more MZ twins alcoholic then DZ twins - so suggests trait influenced by genetics
• all these things very tricky to prove
Chapter 28 - Cancer & Genetics

• Metastasis - when malignant tumors move to other body locations, forming secondary tumors
• Genetics, environment (sunlight, chemical exposure diet, etc.), age influence the risk of cancer
• Cancer many forms - slow vs. fast growers, different tissues involved, some more responsive to treatment
Cancer cells

- Unregulated growth
- Normal cells form monolayer; cancer cells pile up in culture (don’t exhibit contact inhibition)
- Cell cycle important proteins; cyclins and cyclin-dependent kinases (CDKs)
Cancer and the cell cycle

- CDKs - transfer phosphate groups; requires the presence of cyclins
- Cyclins enable CDKs to do their work
- Helps with cell-cycle “checkpoints”
- In tumor cells, checkpoints are deregulated
- Cyclins or CDKs mutated
Oncogenes

- Gene products can regulate cell cycle
- Table 28.1 (p. 699) retroviral oncogenes:
  - abl
  - fos
  - myb
  - myc
  - H-ras
  - src
Gene association with Cancer

- Two main ways:
  - 1. Proto-oncogenes
  - 2. Tumor Suppressor genes
Proto-oncogenes

- Cellular homologues of viral oncogenes (a.k.a. normal cellular oncogenes, \textit{c-onc})
- e.g., \textit{v-src} and \textit{c-src}; very similar genes (few a.a. different)
- \textit{c-onc} genes a lot of conservation in structure among species
- \textit{c-onc}’s have introns; \textit{v-onc}’s do not
C-onc genes to tumors

- Mutant c-onc’s can develop into cancer
- Human bladder cancer - **Figure 28.4**
- Looked at transforming normal cells into cancerous cells - by foci formation on soft agar (foci - cancer cells form small clumps)
- *c-H-ras* responsible
Chromosomal rearrangements and cancer

- CML- chronic myelogenous leukemia
- *Philadelphia chromosome* - reciprocal translocation between chromosomes 9 and 22
- **Figure 28.6**
- *c-alb* oncogene involved (on chromosome 9); *ber* gene on chromosome 22
- they join to form - white cells become cancerous
Tumor Suppressor genes

• Need additional mutants to the oncogenes to get full development of cancer
• TS genes- involved in the 2 hit hypothesis (Knudson)
• Figure 28.8
• discussed inherited and sporadic retinoblastoma
Cellular role - TS genes

• More cancers defect in TS gene, not oncogene
• normal TS proteins function in cell division, differentiation, apoptosis, DNA repair
• Table 28.2 (p. 705) examples of inherited cancers
Examples some TS genes

• p53 - 53 kilodalton TS protein (393 aa)
• gene called TP 53
• somatic mutations of TP53 involved in many cancers
• contains 3 domains:
  – TAD - N-term. transcription-activation domain
  – DBD - DNA binding core domain
  – OD - oligomerization domain  Figure 28.10
p53

- Most mutations in DBD
- cannot bind to target genes, so targets not transcribed
- recessive loss-of-function mutations
- also important in cellular stress response
- normal p53 important in DNA damage repair
pBRCA1 and pBRCA2

- Mutant forms of these TS genes implicated in breast and ovarian cancer
- brca1- map to ch 17; brca 2 - map to ch 13
- 220-350 kd proteins
- in nucleus - putative transcription factors
- mutations in these about 7% of all breast cancers and 10% of ovarian cancers
- carriers high probability of disease
Genetic pathways to Cancer

• Malignant tumor formation - not mutation in single proto-onc or TS gene; must have accumulation of several mutations/several genes
• therefore, pathways diverse and complex
• involves APC (adenomatous polyposis coli)
• See Figure 28.12
6 steps to malignant cancer

• 1. Cancer cells self sufficient in division and growth signaling
• 2. Cancer cells ignore growth inhibitory signals
• 3. Cancer cells evade apoptosis
• 4. Cancer cells replicate limitlessly
• 5. Cancer cells nourish themselves
• 6. Cancer cells can evade other tissues and colonize them