03-621 Week 3

Advanced Quantative Genetics

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Mutations (Continued)

- Synonymous Substitutions Can Alter Phenotypes

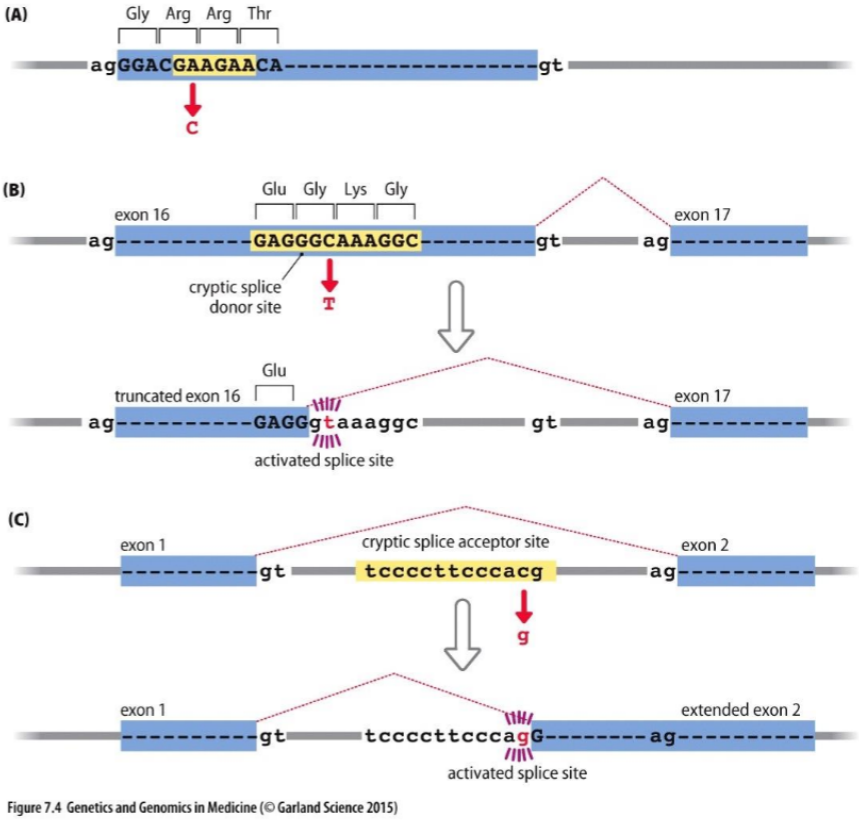


Figure 7.4 Genetics and Genomics in Medicine (© Garland Science 2015)

- Single-gene disorders can also be caused by mutations in **non-coding** RNA genes
- Large Copy Number Variations (CNVs) are common in the human genome
  - One section of DNA is duplicated many times
  - About 10-15% of the genome displays copy number variation
  - 1000 bp - 5 mbp in length
  - Most are in non-coding regions, but some contain genes
  - Too large for PCR analysis, can be detected using a microarray

- Variable nucleotide tandem repeats (VNTR) and short tandem repeats (STR) are inherited repeating stretches of DNA
  - Different individuals may have different numbers of repeats at a given locus.
  - If the number of base pairs in a repeated section is not a multiple of three, tandem repeats may cause frameshift errors.
- Some mutations that cause disease do not change the sequence of a gene product but alter the amount of gene product
  - For example, mutations in promotors or enhancers
  - Mutations in transfactors (e.g., histones)
  - Gene duplication or deletion

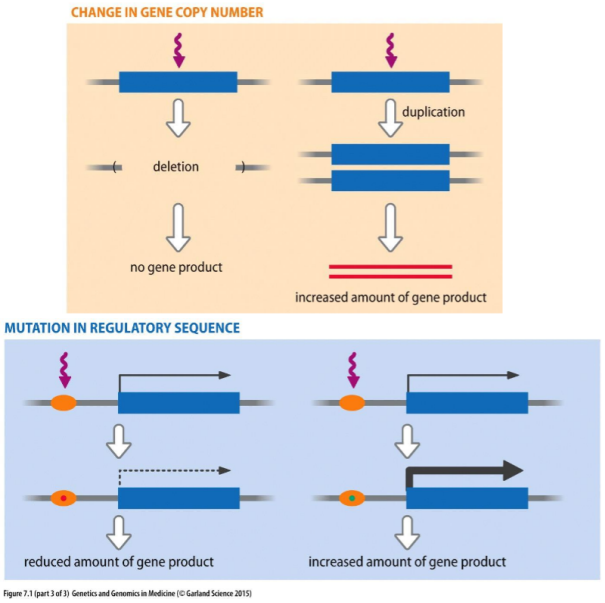


Figure 7.1 (part 3 of 3) Genetics and Genomics in Medicine (© Garland Science 2015)

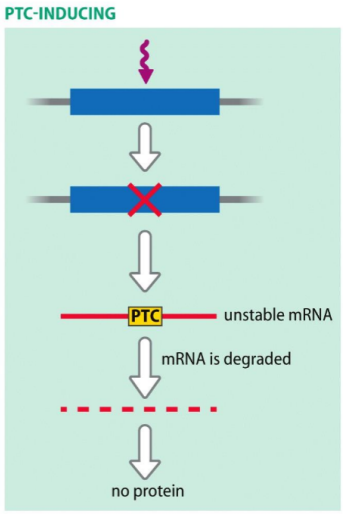
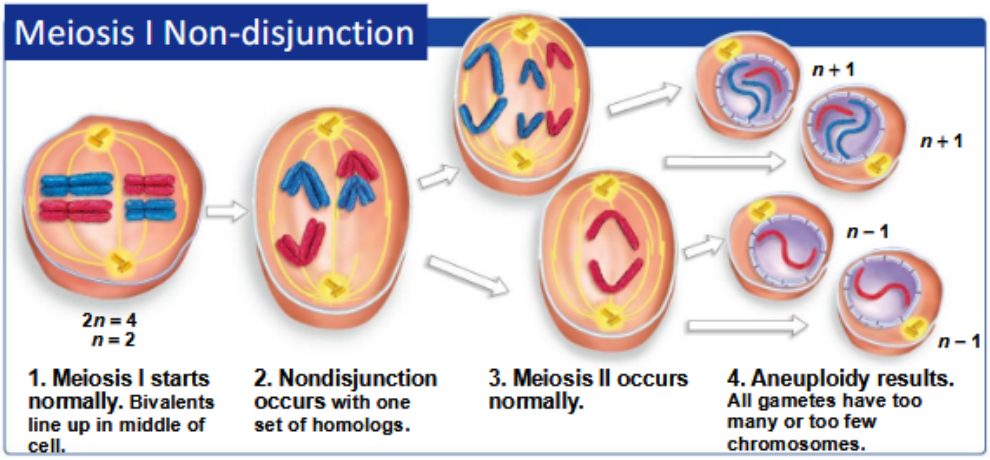


Figure 7.1 (part 1 of 3) Genetics and Genomics in Medicine (© Garland Science 2015)

- Gene dosage changes via Meiotic Non-disjunction
  - Frequency: in all recognized pregnancies
  - 8% of *recognized* pregnancies have major chromosomal abnormalities. $> 94\%$ of this 8% undergo spontaneous abortion.
  - Aneuplodies change the amount of gene product expressed ("gene dosage"), across many genes.
  - Among the fetuses in 100000 recognized pregnancies, about 8000 have major chromosomal abnormalities, 7500 of these undergo spontaneous abortion, and 500 are born alive.


Meiosis I Non-disjunction
2n = 4
n = 2
n + 1
n + 1
n − 1
n − 1
1. Meiosis I starts normally. Bivalents line up in middle of cell.
2. Nondisjunction occurs with one set of homologs.
3. Meiosis II occurs normally.
4. Aneuploidy results. All gametes have too many or too few chromosomes.