Wrap up of Central Dogma: Genetic Variations (continued) and Genomes

Genome organization
Species-species sequence comparisons
Germline vs. Somatic mutations
General Central Dogma/Genome Points
Mutations can occur anywhere on DNA

Effect of mutation depends on the mutation and on WHERE in genome (ex. within a gene or in between genes?, in exon or in intron?)
human genome = $3.2 \times 10^9$ nucleotide pairs

 Avg gene = 27,000
 Avg protein=430 aa
 (so coding = )

coding vs. noncoding
(only 1.5% of human genome is “coding sequences” (codes for a.a.)
The SEQUENCE of these 3 billion nucleotides was determined

Completed Human Genome Project-2004

(President Bill Clinton makes the Announcement of the first draft on June 26, 2000 with the scientific project leaders, Craig Venter and Francis Collins)

Our genomes are not identical...what is the extent of variation?
Compare genomes of any two individuals:
~ 2.5 x 10^5 differences that are single nucleotide differences

ATTGCGTAGCCTGATGCCTAGTTGATAGCGCTT

ATTGCGTAGCCTGATGCCTAGTTGATAGCGCTT

 ATTGCGTAGCCTGATGCCTAGTTGATAGCGCTT  G GAATCGTAGACGTAG

ATTGCGTAGCCTGATGCCTAGTTGATAGCGCTT

ATTGCGTAGCCTGATGCCTAGTTGATAGCGCTT

 ATTGCGTAGCCTGATGCCTAGTTGATAGCGCTT  G GAATCGTAGACGTAG

Additional differences: duplicated/deleted sequences, esp. repetitive seq.

GTGACGCAATCGCTGACTTTTCTTTTCCGGAATCGTAGACGTAGCGTGCGCA

GTGACGCAATCGCTGACTTTTCTTTTCTTTTCTTTTCTTTTCCGGAATCGTAGACG

GTGACGCAATCGCTGA [CTTT]n CCGGAATCGTAGACGTAGCGTGCGCA
human genome = $3.2 \times 10^9$ nucleotide pairs

The vast majority of differences are in noncoding sequences

Human – human genetic variation ~ 0.1% of genome (avg of 1 diff/1000 nte)
The leptin gene in chimp vs. human

(5 nte differences out of 441 nte)

Common ancestor
5 million yrs ago

Genomes are 99% identical!
Sequence comparison of the leptin gene in mouse vs. human