Finishing up on Central Dogma:
Germline vs. Somatic mutations
General Central Dogma/Genome Points

Gene Regulation
When do mutations get passed on to the next generation?
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Two final notes on Central Dogma

1) Not all RNA sequence is translated into protein sequence

2) Viruses exhibit some variations on DNA $\rightarrow$ RNA
   (but NOT on RNA $\rightarrow$ protein)
We have seen two different classes of RNA:

1) **mRNA** (messenger RNA) serves merely to carry information = intermediate product of a gene

2) **RNA** with its own function: structural or catalytic = final gene product
   ex. Transfer RNA (tRNA) and ribosomal RNA (rRNA)
Central Dogma: Flow of information

- DNA → RNA → protein
- RNA → protein
- Variations seen among Viruses

all cellular organisms
“gene”

Segment of DNA that provides necessary information to encode a product (includes sequences that do not directly code for a.a.)

~25% of our genome is Transcribed into RNA (only 1.5% of genome is coding)

How many genes in human genome? ~25,000 (still figuring this out!)
(B) PROCARYOTES

DNA \[\rightarrow\] TRANSCRIPTION

mRNA \[\rightarrow\] TRANSLATION

protein

(A) EUARYOTES

cytoplasm

nucleus

DNA

transcription unit

"primary RNA transcript"

5' CAPPING RNA SPlicing
3' POLY-ADENYLATION

RNA cap

mRNA AAAAA

EXPORT

mRNA AAAAA

TRANSLATION

protein
Chemical Biology 03
Oct 22, 2010

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General Central Dogma/Genome Points

Gene Regulation
Gene Regulation: Every Step in Gene Expression is a potential target for Regulation

- 25,000 genes present in all human cells
- Subset of proteins unique to a particular cell type under a particular set of conditions
Transcriptional Regulation

Regulation is achieved by:

1) Regulatory DNA sequence
   • next to promoter
   • up to several 1000 base-pairs “upstream” (before) promoter
   • sometimes even in introns or “downstream” of gene

2) Regulatory Protein
   • binds DNA double helix in a sequence-specific manner
   • Some are Positive Regulators ("activators" and "enhancers")
   • Some are Negative Regulators ("repressors" and "silencers")
Transcriptional Regulation

Examples of DNA-binding domains of Regulatory Proteins
Regulatory Proteins bind Double-stranded DNA (like TATA binding Protein)
Transcriptional Regulation

How do proteins bound so far away influence transcription machinery?

Transcription initiation

gene regulatory proteins

RNA polymerase II

gene regulatory proteins

regulatory sequence

spacer DNA

promoter

TATA

RNA transcript

the gene control region for gene X
Network of Regulatory Proteins

~ 2000 - 3000 genes in our genome = Transcriptional Regulatory Proteins

The transcriptional activity of any given gene is determined by abundance, activity, cooperation, competition of different Regulatory Proteins

The presence & activity of a regulatory protein is influenced by cell type and by extracellular environment
Recall that genes are scattered over many chromosomes
Each gene acts independently: has its own TATA box and associated regulatory regions.