What to FOCUS on when reading Ch.18 *(Regulation of Gene Expression)* & to STUDY well in your slides

- **After studying, practice teaching the contents of your slides out loud to your imaginary classroom. Practice sketching all the components of eukaryotic vs prokaryotic genes, using proper terminology, defining terms, describing steps to activate gene expression in prokaryotes vs eukaryotes etc.**

- **Once you are done studying & teaching the material, check off those boxes next each of the topics below that you know you have fully mastered.**
  - **Restudy unchecked topics until you are able to check them ALL off !**

Eukarotyic Gene Expression Topics to Know

Concept 18.2: Eukaryotic gene expression is regulated at many stages

☐ Even though all cells of an organism have the same genes, a **typical human cell probably expresses about 20% of its genes at any given time**, leading to differential gene expression. What is meant by '**differential gene expression**'?

☐ In all organisms, prokaryotes and eukaryotes, what is the **common control point of gene expression**?

☐ Eukaryotic cells have a structure that provides additional opportunities for regulating gene expression. Name the **10 stages of gene expression in eukaryotes that can serve as points of Regulation.** (Fig.18.6)

Chromatin not only packs DNA into a compact form that fits inside the nucleus but also helps regulate gene expression in several ways. The location of a gene's promoter relative to **nucleosome** (See Figure 16.23) and to the sites where the **DNA attaches to the chromosome scaffold proteins** or **nuclear lamina proteins** can affect whether a gene is transcribed.

☐ Are genes within **heterochromatin or euchromatin** usually expressed? Distinguish between the structure of heterochromatin and euchromatin? How do these structures help control gene expression.

☐ **Chemical modifications of histones** can influence chromatin structure and gene expression. What occurs in **histone acetylation**?

☐ What effect does **histone acetylation** have on gene expression?

☐ Explain how **histone acetylation** promotes transcription by opening the chromatin structure.

☐ What effect does **histone deacetylation** have on gene express? Why?

☐ What occurs in **DNA methylation**?

☐ What role does **DNA Methylation** play in gene expression?

☐ The **inactivate mammalian X chromosome** (bar body) is heavily methylated. What is the result of this methylation?

☐ What is **genomic imprinting** and how is it maintained?

☐ Explain what is meant by **epigenetic inheritance**, and give an example of epigenetic changes discussed in the text.

☐ **Chromatin-modifying enzymes provide initial control of gene expression** by making a region of DNA either more or less able to bind the transcription machinery. Once the chromatin of a gene is optimally modified for expression, the **initiation of transcription is the next major step at which gene expression is regulated**. These involve proteins that bind to DNA and either facilitate or inhibit binding of RNA polymerase. What are eukaryotic gene '**control elements'**?

☐ Distinguish between the locations of **distal vs proximal control elements** relative to the gene promoter and transcription unit?

☐ What are '**enhancers**' specifically? Are these enhancers **distal or proximal control elements**?

☐ What are '**activators**' and how do they affect gene expression?

☐ What are '**repressors**' (sometimes referred to as "silencers")?

☐ What are the **3 ways in which we currently believe repressors** help turn off gene expression?

☐ How are **general transcription factors** and **specific transcription factors** similar?

☐ How are **general transcription factors** and **specific transcription factors** different?

☐ Where do **general transcription factors** bind to the DNA of a gene?

☐ Where do **specific transcription factors** bind to the DNA of a gene?

On average, **each enhancer region of a gene is composed of about ~ 10 control elements** (DNA segments), each of which can bind only 1 or 2 **gene**-**specific** transcription factors. While **general** transcription factors that bind to control elements in the promotor region help a cell activate **low** levels of transcription of **all** eukaryotic genes in a nucleus that are not bound to histones in nucleosomes or other nuclear scaffolding or mechanical support proteins, **the specific transcription factors** (activators or repressors) **activated or produced in a cell determine which specific genes are expressed in high quantities or not at all in that cell as long as general transcription factors could bind too.**

☐ What is the **transcription initiation complex** that must form in eukaryotes for a gene to be expressed?

☐ Explain how **enhancers** and **specific** transcription factors known as **activators** interact with **general** transcription factors and **mediator proteins** and **RNA Polymerase II** to activate a particular's gene expressions.

☐ (Merging Figure 18.9 & 18.11) Could you draw and label from memory a eukaryotic gene that includes all of the following gene elements in the correct locations relative to one another alongside the transcription initiation complex: **TATA box within promotor, promoter, enhancers and silencers** (distal control elements)**, proximal control elements, activators** (that bind to proximal and distal control elements)**, general transcription factors** (that bind within the promotor)**, specific transcription factors** (that includes activators and repressors), **RNA polymerase II, DNA, DNA bending protein, mediator proteins.**

☐ **In prokaryotes, functionally related genes are usually clustered together in a single operon**. Operons have largely not been found in eukaryotic cells, and the genes coding for the enzymes of a particular metabolic pathway are often scattered over different chromosomes. Describe how eukaryotes engage in **"coordinate control**" with regards to activating or deactivating all at once genes for proteins that function together to accomplish an activity in the cell such as a biochemical pathway?

☐ Once mRNA encoding a particular protein reaches the cytoplasm, list 4 mechanisms that can regulate the amount of the protein that is active in the cell?

☐ Explain how **RNA processing's Alternative RNA Splicing** is a mechanism of **post-transcriptional gene regulation**, resulting in different proteins (or different polypeptides) derived from the same initial RNA transcript.

☐ Post-trancriptional control includes regulation of mRNA degradation. How do BOTH **mRNA Degradation** and the **prevention of translation initiation** affect translation? How do BOTH affect gene expression?

☐ How can proteins be **activated**, (chemically) **processed**, or **degraded**? *Describe an example of each process.*

☐ An article in Scientific American about proteasomes was entitled "Little Chambers of Horrors." What are '**proteasomes**' and how do they work?

☐ Explain the **proteasomes' role in regulating gene expression**.

Concept 18.3: Noncoding RNAs play multiple roles in controlling gene expression

☐ How much (%) of the human genome **codes for proteins**?

☐ It is now known that much of the RNA that is transcribed is not translated into protein. What 2 crucial items or processes seem to be **regulated by noncoding RNAs**, helping control eukaryotic gene expression?

☐ Often the noncoding RNAs that regulate gene expression is microRNA. Explain how **miRNA-protein complexes** are made in eukaryotes.

☐ Explain the 2 **modes of action of microRNAs** (miRNA's) in post-transcriptional regulation.

☐ Imagine that the mRNA being degraded by a miRNA in the cytoplasm codes for a protein that promotes cell division in a multicellular organism. What would happen, both in the cell and to the organism, if a mutation disabled the gene encoding the miRNA that triggers this degradation?

☐ What role do **small interfering RNAs** (siRNA) play in cells?

Concept 18.4: A program of differential gene expression leads to the different cell types in a multicellular organism

☐ What 3 processes lead to the transformation of a single-celled zygote into the mature multicellular organism?

☐ What is **cell differentiation**? How does that relate to **morphogenesis**?

☐ Due to **cytoplasmic determinants** and **induction**, early embryonic cells receive two types of instructions that allow them to each know which genes to express or not, thus leading to differential gene expression in these cells and, as a consequence, different phenotype formations

☐ Explain what **Cytoplasmic Determinants** that are present in the zygote and in early embryological cells are.

☐ How do **Cytoplasmic Determinants** lead to cells in the same embryo to express different genes, allowing different cells to develop along particular and distinct paths from each other even though all the cells inherited copies of the exact same DNA from the original zygote they formed from?

☐ Explain what **Induction** during embryological development is and how it leads to one cell expressing different genes and engaging in different activities than another in the same embryo.

☐ What is meant by **determination** during embryological development?

☐ What are **maternal effect genes** ? When are they expressed? What are their products? Where are their products found? What do their products do in the zygote and early embryo?

☐ What is controlled by **homeotic genes** that activate in embryonic cells?

Concept 18.5: Cancer results from genetic changes that affect cell cycle control.

☐ What is the difference between **oncogenes** and **proto-oncogenes**?

☐ List & describe the 5 genetic changes (mechanisms) that can that can convert a proto-oncogene into an oncogene (See figure 18.23)

☐ There seem to be 2 categories of genes involved in cancer: **oncogenes**, which code for proteins that help in cell proliferation or cell growth *(= cell duplication through passing through the cell cycle and completing mitosis),* and so should not be stuck "on," much like the accelerator in a car; and **tumor-suppressor genes**, which function like the brakes on a car and must function unless temporarily released. What is the normal role of proteins built from instructions in **tumor-suppressor genes**?

☐ How do **mutations in tumor suppressor genes** play a role in the onset of cancers?

☐ The proteins encoded by many proto-oncogenes and tumor-suppressor genes are often components of the cell signaling pathways. Interference with normal signaling pathways then seems to be an important factor in cancer development. Mutations in the ras proto-oncogene, which codes for a type of G protein, occur in about 30% of human cancers while mutations in the p53 tumor-suppressor gene, accounts for more than 50% of cancers. What is the importance of the **ras gene**? What does it code for and what role does that protein have?

☐ Is a functioning **ras gene** an oncogene or proto-oncogene? Why?

☐ What is the importance of the **p53 gene** sometimes called the "guardian angel of the genome?"

☐ Why is the **p53 gene** considered a tumor-suppressor gene?

☐ In what **3 ways** does p53 protein prevent cells from passing on mutations to daughter cells due to DNA damage?

☐ How many changes must occur at the DNA level for a typical cell to become fully cancerous?

- Why is said that people inherit predispositions to cancer not cancer itself?

- **Stimulatory and inhibitory pathways regulate the cell cycle**, commonly by influencing transcription. Could you describe the signaling pathways that regulate cell division in Figured 18.24 & Figure 18.25 and explain how aberrations in such pathways (due to gene mutations) can lead to cancer?

- Why does the incidence of cancer increase with age?