Control of Gene Expression

E. coli lac Operon

Regulation of Inducible lac Operon

a. Lactose absent from medium

b. Lactose present in medium

Inducible lac Operon

When lactose is absent from the medium, the active Lac repressor binds to the operator of the lac operon, blocking transcription.

When lactose is present in the medium, some of it is converted to the inducer allolactose. Allolactose binds to the Lac repressor, inactivating it so that it cannot bind to the operator. This allows RNA polymerase to bind to the promoter, and transcription of the lac operon occurs. Translation of the mRNA produces the three lactose metabolism enzymes.
Repressable *trp* Operon

a. Tryptophan absent from medium

- **Regulatory gene**
- **RNA polymerase binds and transcribes operon**
- **trp operon**
- **mRNA**
- **trp repressor (inactive)**
- **Tryptophan biosynthesis enzymes**

When tryptophan is absent from the medium, the Trp repressor is inactive in binding to the operator and transcription proceeds.

b. Tryptophan present in medium

- **Regulatory gene**
- **RNA polymerase binds and transcribes operon**
- **trp operon**
- **mRNA**
- **trp repressor (inactive)**
- **Tryptophan-binding site**
- **Tryptophan (corepressor)**
- **RNA polymerase cannot bind to promoter**

When tryptophan is present in the medium, the amino acid binds to, and activates, the Trp repressor. The active repressor binds to the operator and blocks transcription.

Chromatin Remodeling

- **DNA**
- **Promoter**
- **Nucleosomes**
- **Gene**
- **Activator**
- **Chromatin remodeling exposes promoter**
- **Promoter not accessible to proteins for transcription initiation**
- **Promoter now accessible to proteins for transcription initiation**

**Transcriptional regulation**
- Chromatin remodeling to make genes accessible for transcription
- Regulation of transcription initiation

**Posttranscriptional regulation**
- Variations in pre-mRNA processing
- Removal of masking proteins
- Variations in rate of RNA breakdown
- RNA interference

**Translational regulation**
- Variations in rate of initiation of protein synthesis
- Variations in rate of protein processing
- Removal of masking segments
- Variations in rate of protein breakdown

**Determine availability of finished proteins**

**Determine which genes are translated**

**Determine types and availability of mRNAs to ribosomes**

**Determine rates at which proteins are made**
Organization of Eukaryotic Gene

DNA

Enhancer

Promoter proximal region

Transcription unit of gene

Exon

Intron

Exon

Intron

Exon

3' UTR

5' UTR

Promoter

TATA box

Transcription begins

Initial general transcription factor

Additional general transcription factors

RNA polymerase

Site where transcription starts

Transcription complex

Interaction Between Activators

Coactivator (multiprotein complex)

Activators

Enhancer

Promoter

Gene

Maximal transcription

Interaction between activators at the enhancer, coactivator, and proteins at the promoter and promoter proximal region

Combinatorial Gene Regulation

A unique combination of activators controls gene A.

Activators — 2 5 7 8

Gene A

Enhancer

Transcription

Gene A, controlled by activators 2, 5, 7, and 8 binding to regulatory sequences in its enhancer
DNA methylation silences genes

- The hemoglobin genes for instance are highly methylated and thus silenced in most vertebrate body cells except red blood cells.

- DNA methylation sometimes silences large blocks of genes or even whole chromosomes like one of the X chromosome in female mammals (Barr bodies).

- DNA Methylation underlies genomic imprinting in which either the paternal or maternal allele of a particular gene is silenced.

Histone acetylation activates genes

The DNA around acetylated histones is less tightly wrapped around the histones in the nucleosome and thus more accessible to DNA binding proteins including transcription factors and RNA polymerase.
Development of Colorectal Cancer

- Colon wall
- Normal colon epithelial cells
- Colon
- Loss of tumor-suppressor gene APC (or other)
- Small benign growth (polyp)
- Activation of ras oncogene
- Larger benign growth (adenoma)
- Loss of tumor-suppressor gene DCC
- Malignant tumor (carcinoma)
- Loss of tumor-suppressor gene p53
- Additional mutations