Lactose Operon: Positive Control

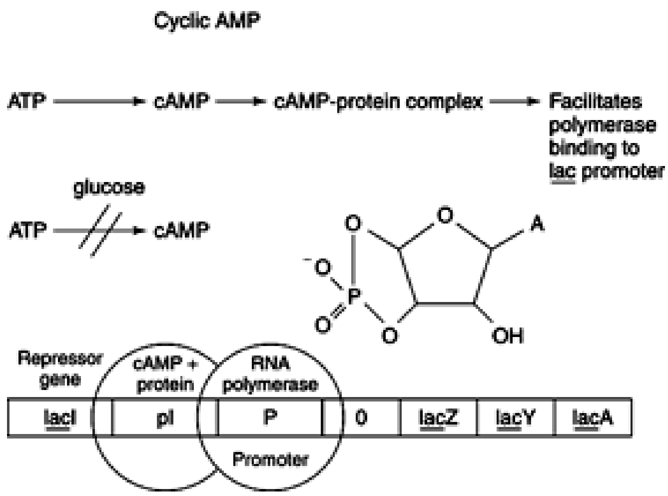

Figure 3

Catabolite repression is a two-part system. The first component is the small-molecule regulator, **cyclic AMP**. Glucose decreases cyclic AMP synthesis. The second component is cyclic AMP binding protein, **CAP**. CAP binds cAMP and thereby helps RNA polymerase bind to the promoter. When bound to cAMP, CAP binds to a sequence at the 5′ end of the *lac* promoter. CAP binding bends the DNA, allowing protein-protein contact between CAP and polymerase. It therefore behaves in the opposite manner of repressor. Repressor (LacI) binds to operator DNA only in the absence of its small-molecule ligand, while CAP binds to promoter DNA in the presence of its small-molecule ligand.

These two complementary systems allow the bacterial cell to metabolize lactose in response to *two* stimuli. “Switching on” the expression of the *lac* operon requires both the absence of glucose and the presence of lactose. This series of switches allows complex expression patterns to be built up from simple components. For this reason, the *lac* system is a model for other, apparently more complex, biological control systems, such as hormone action or embryonic development.

Corepressors

As mentioned above, the synthesis of tryptophan from precursors available in the cell requires 5 enzymes. The genes encoding these are clustered together in a single operon with its own promoter and operator. In this case, however, the **presence** of tryptophan in the cell **shuts down** the operon. When Trp is present, it binds to a site on the Trp repressor and **enables** the Trp repressor to bind to the operator. When Trp is not present, the repressor leaves its operator, and transcription of the 5 structural genes begins.

The usefulness to the cell of this control mechanism is clear. The presence in the cell of an essential metabolite, in this case tryptophan, turns off its own manufacture and thus stops unneeded protein synthesis.

As its name suggests, repressors are **negative control** mechanisms, shutting down operons

- in the absence of a substrate (lactose in our example) or
- the presence of an essential metabolite (tryptophan is our example).

However, some gene transcription in E. coli is under positive control.

Positive Control of Transcription: CAP

Absence of the lac repressor is essential but not sufficient for effective transcription of the lac operon. The activity of RNA polymerase also depends on the presence of another DNA-binding protein called **catabolite activator protein** or **CAP**. Like the lac repressor, CAP has two types of binding sites: