**Lac operon**

**Regulation of Lac operon in presence of glucose (positive regulation of lac operon)**

* A regulatory mechanism known as **catabolite repression** restricts expression of the genes required for catabolism of lactose, arabinose, and other sugars in the presence of glucose, even when these secondary sugars are also present.
* The effect of glucose is mediated by cAMP, as a coactivator, and an activator protein known as **cAMP receptor protein,** or **CRP** (the protein is sometimescalled CAP, for *c*atabolite gene *a*ctivator *p*rotein).
* When glucose is absent, CRP-cAMP binds to a site near the *lac* promoter and stimulates RNA transcription 50-fold.
* **CRP-cAMP is therefore a positive regulatory element responsive to glucose levels, whereas the Lac repressor is a negative regulatory element responsive to lactose**.
* CRP-cAMP has little effect on the *lac* operon when the Lac repressor is blocking transcription, and dissociation of the repressor from the *lac* operator has little effect on transcription of the *lac* operon unless CRPcAMP is present to facilitate transcription; when CRP is not bound, the wild-type *lac* promoter is a relatively weak promoter. The open complex of RNA polymerase and the promoter does not form readily unless CRP-cAMP is present.
* CRP interacts directly with RNA polymerase through the polymerase’s *\_* subunit.
* The effect of glucose on CRP is mediated by the cAMP interaction CRP binds to DNA most avidly when cAMP concentrations are high.
* In the presence of glucose, the synthesis of cAMP is inhibited and efflux of cAMP from the cell is stimulated. As cAMP declines, CRP binding to DNA declines, thereby decreasing the expression of the *lac* operon.
* Strong induction of the *lac* operon therefore requires both lactose (to inactivate the *lac* repressor) and a lowered concentration of glucose (to trigger an increase in [cAMP] and increased binding of cAMP to CRP).

