

CONTROL OF GENE EXPRESSION

1 March 1996, 28 Feb 00, 8 Mar 04, 4 Mar 05, 3 Mar 06, 6 Mar 06, 5 March 08, 6Mar09, 5Mar10
 GMSLG, 7th, p 336-, 9th: 351-381

Jacob and Monod, 1961 (p 352): isolated mutants of *E coli* which were constitutively derepressed for β galactosidase (enzyme which hydrolyzes lactose). These produced 1000x baseline even in absence of lactose.

1) Mapped the collection of regulatory mutants, found they mapped at *two different places*:

lacO adjacent ("upstream") to *lacZ* and other lactose related genes. *LacO* acts only *cis* **no diffusible product**
lacI distant to the other lac genes *Lac I* acts *trans* makes **diffusible repressor**

2) performed *cis/trans* test with **heterogenotes**, (see p 360-361):

cis [on the same side] only acts when it is on the same piece of DNA (contiguous)
trans [across] makes *soluble product*: acts whether it is on same or other piece of DNA

heterogenote	Z gene product without inducer	Z gene product with inducer
I ⁺ O ⁺ Z ⁺	very low	high
I ⁻ O ⁺ Z ⁺	high	high
I ⁻ O ⁺ Z ⁺ / F' I ⁺	very low (LacI acts trans)	high
I ⁺ O ⁻ Z ⁺	high	high
I ⁺ O ⁻ Z ⁺ / F' O ⁺ Z ⁻	high (lacO acts only cis)	high

LACTOSE OPERON: POZYA (p. 357)
 A **polycistronic** message is produced from operon (several structural genes transcribed together.)

Lactose is the **inducer** of the operon.
 induced: makes 1000x more β galactosidase, permease and transacetylase

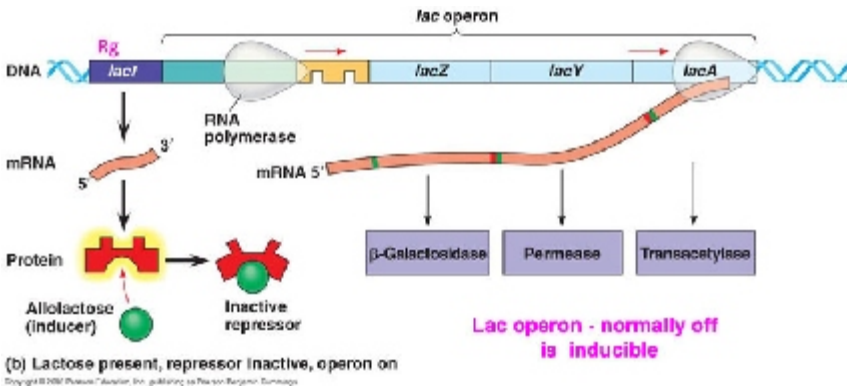
REPRESSOR

I gene codes for repressor which **acts trans**.
 If mutated = constitutive mutants, transcription not inhib.
 An allosteric **protein**: **active site** binds operator
allosteric site binds lactose
 Lactose inactivates, repressor
 Result: coordinate derepression of Z, Y and A.

PROMOTOR binding site of the RNA polymerase

OPERATOR binding site of the repressor

Polar mutations reduced downstream translation, act *cis*



Catabolite repression: (p 364, 365) If adequate glucose catabolites are present, keeps lac operon repressed, even with lactose.

High glucose synthesis of cAMP is **low**.
 Low glucose G protein is activated, adenylate cyclase activated, synthesis of **cAMP rises**.
lac expression is facilitated.

Catabolite Activator Protein (CAP): activated by binding cAMP binds to distal promoter activates transcription

Transcription only occurs when CAP-cAMP attaches to promoter, making it **more accessible to RNA polymerase**.

Repressor: page 365 for image of CAP repressor binding to DNA (Artificial inducer IPTG = isopropyl B-D-thiogalactoside)

Tryptophan Operon: p 369 illustration:
Tryptophan is corepressor:

Histidine Operon:
 Demerec found clusters of cistrons involved in metabolic pathways
 Often congruence in function and sequence in operon
histidyl-tRNA is the corepressor
 thus, mutants of his-tRNA synthetase also cause derepression.

THE TRYPTOPHAN OPERON

