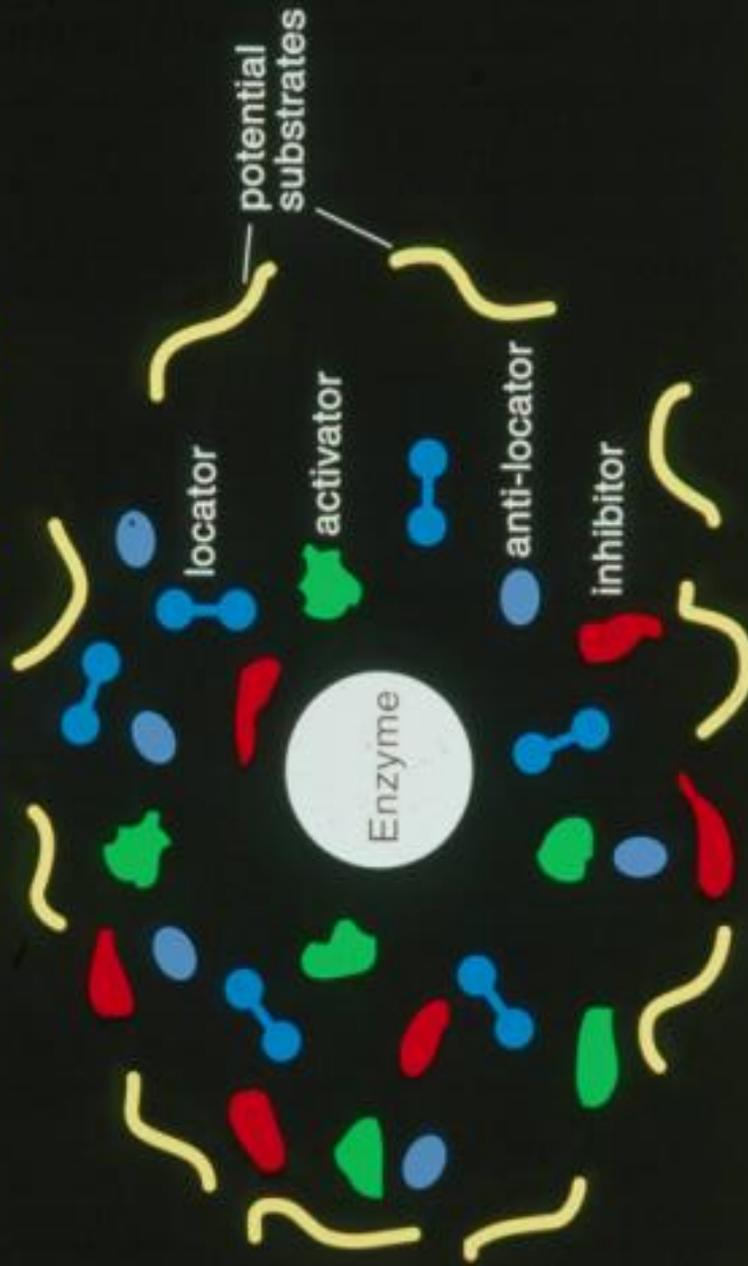


**"Those who bear names that are difficult both to spell and to pronounce are relatively unlikely to be remembered by succeeding generations, regardless of their achievements."**

**In Medicine's 10 Greatest Discoveries  
Friedman M. and Friedland G., Yale University Press, 1988**

## The General Scene



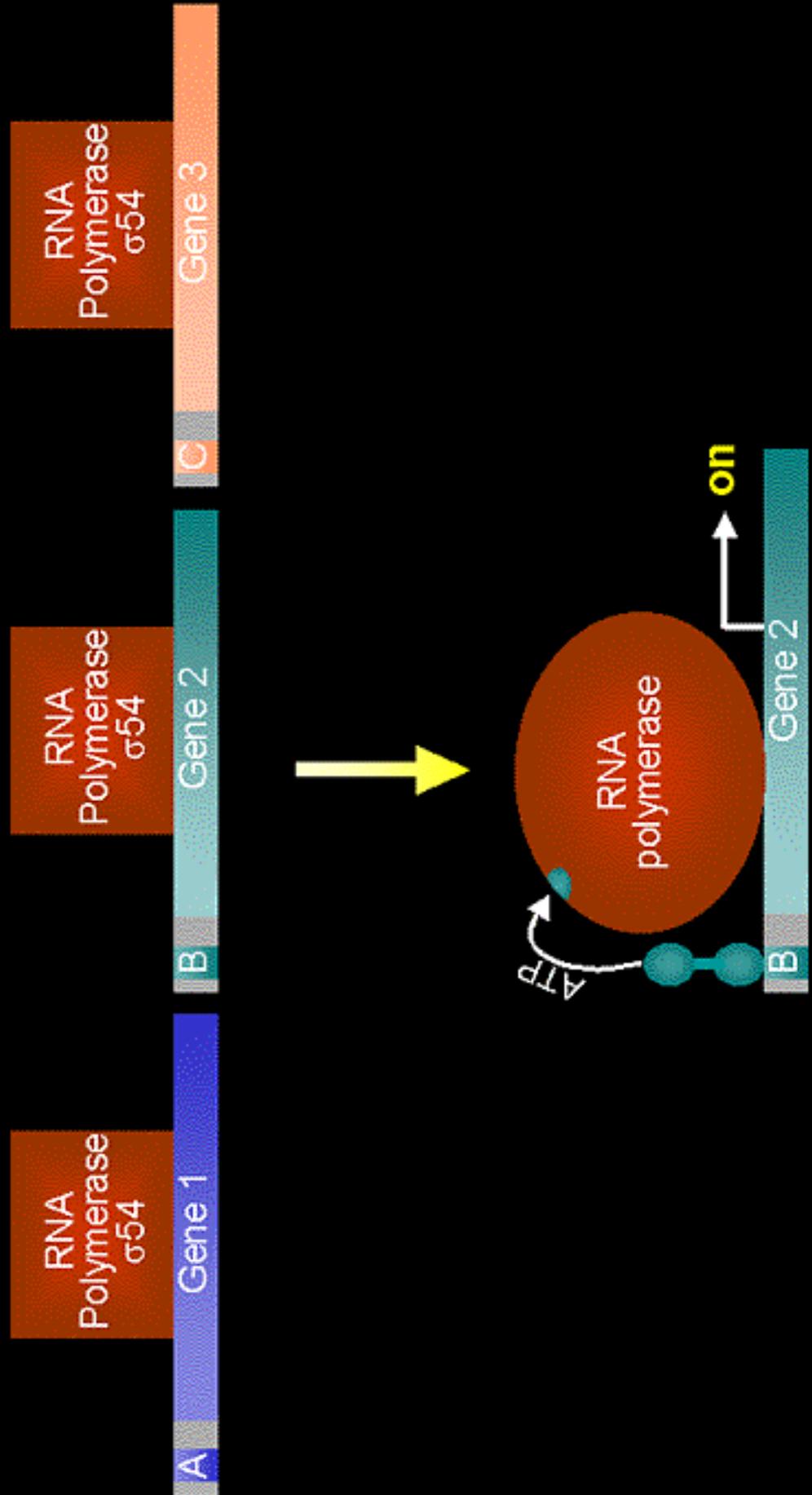
Transcription, splicing, DNA replication, Ser/Thr kinases and cell cycle, Tyr kinases and signal transduction, protein degradation, etc-

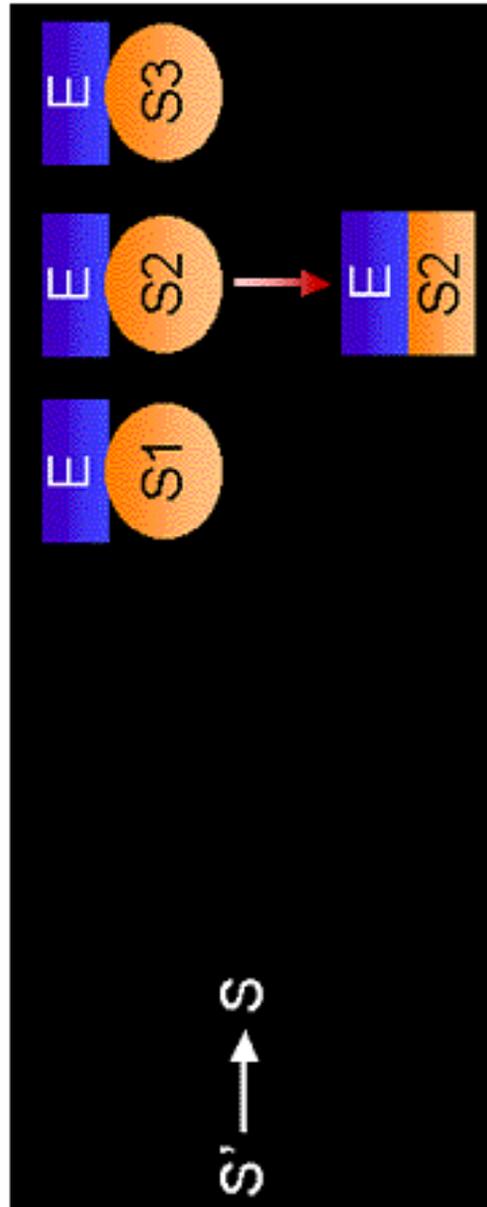
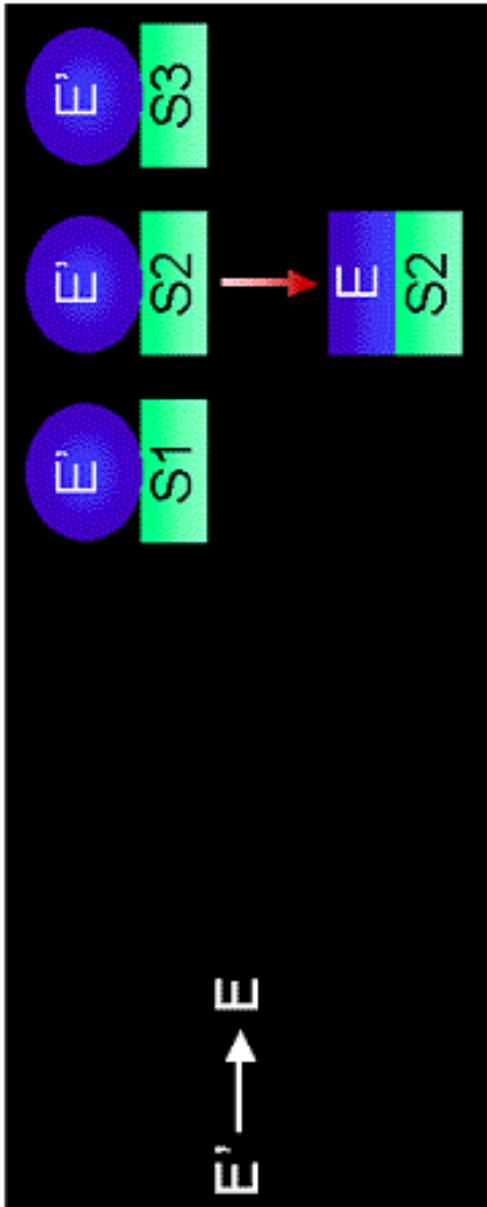


# Allosteric Change in Enzyme



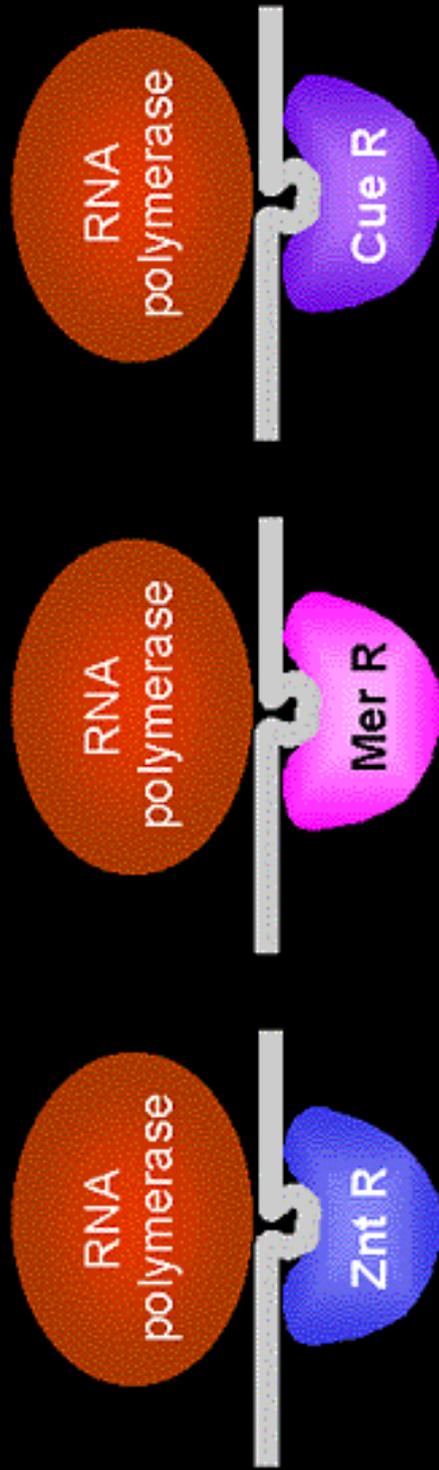
# Allosteric Change in Enzyme





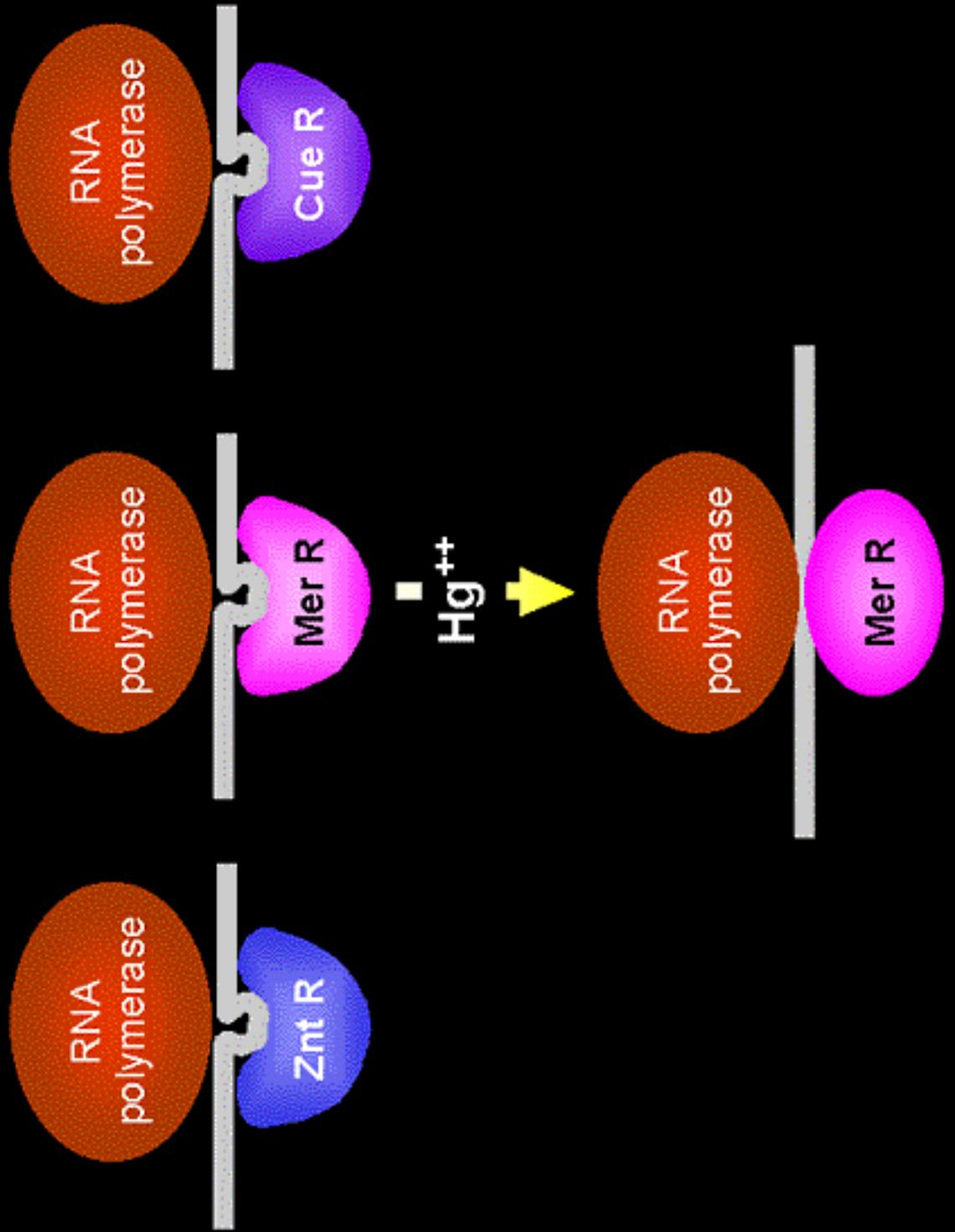
# Allosteric Change in Substrate

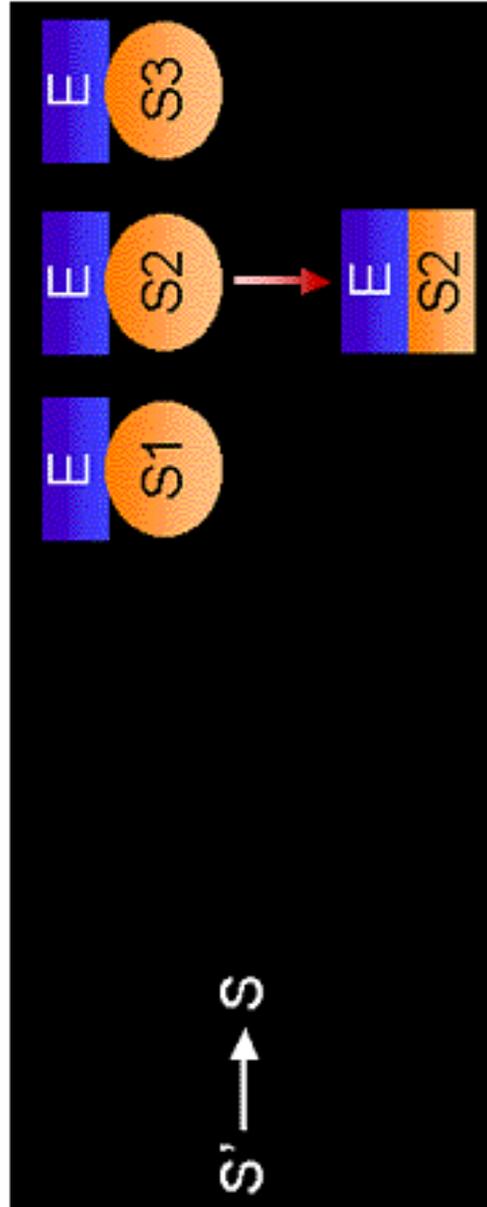
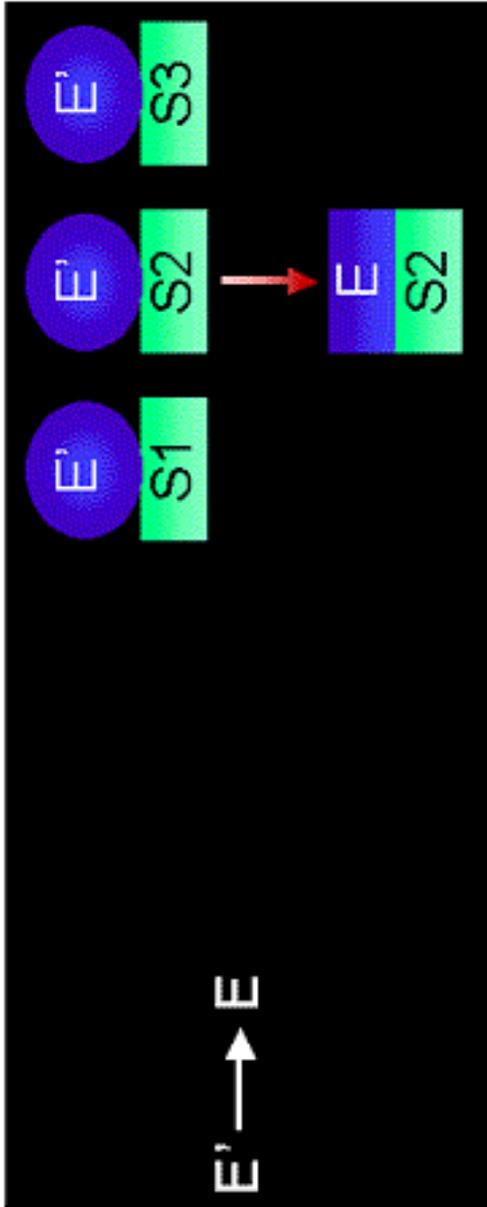
$S' \rightarrow S$



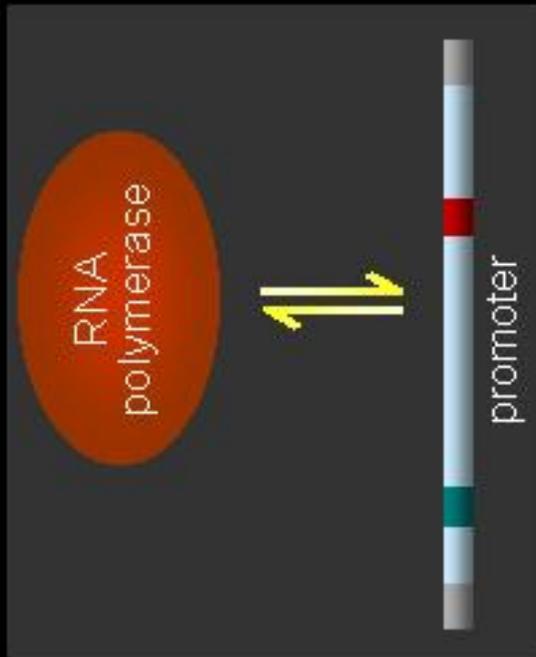
# Allosteric Change in Substrate

$S' \rightarrow S$

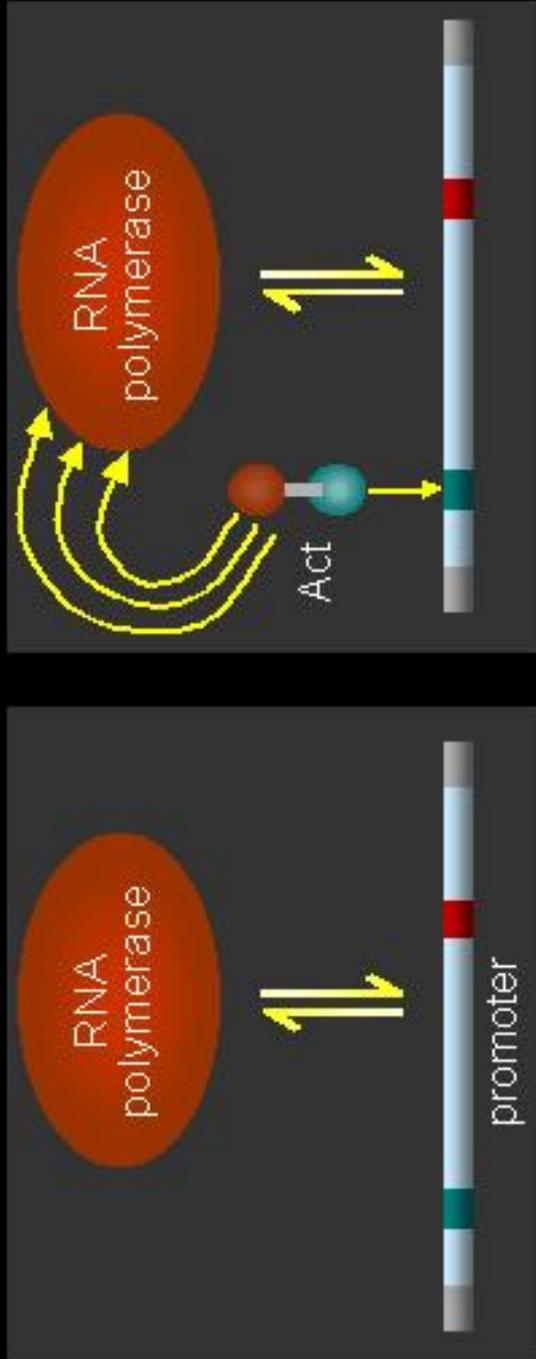




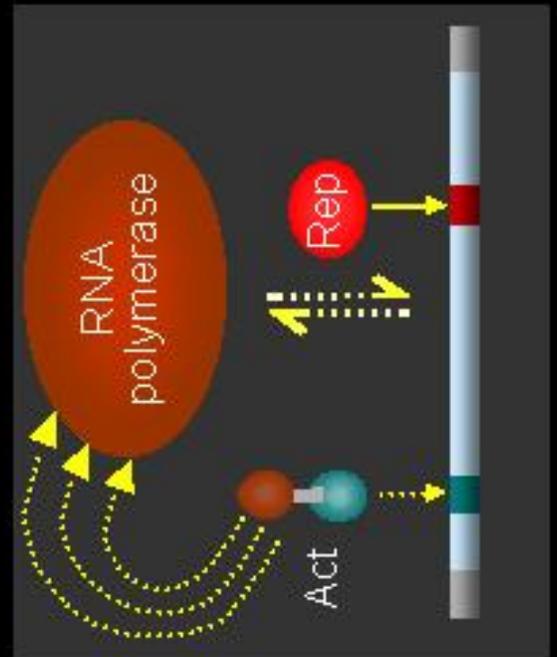
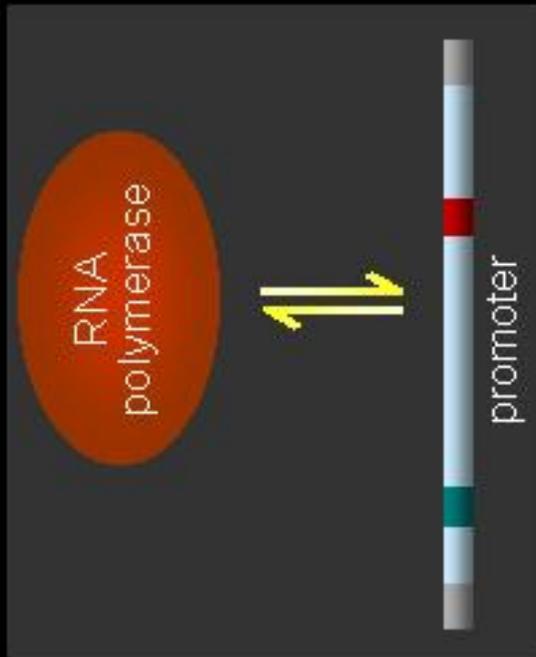
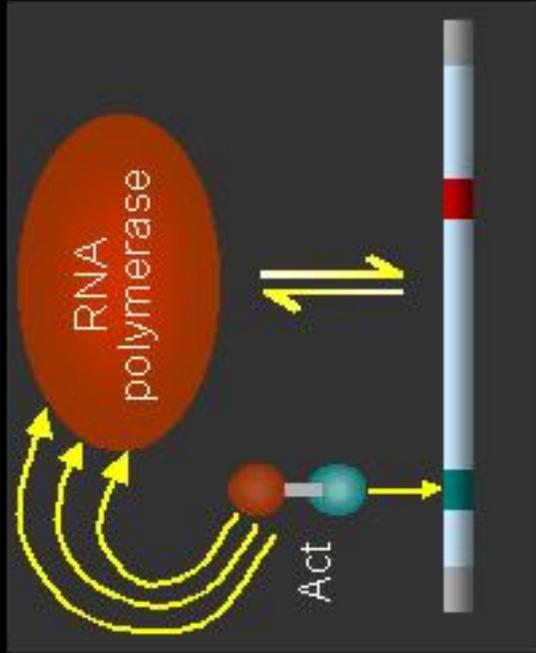
# Regulated Recruitment (Mass Action)



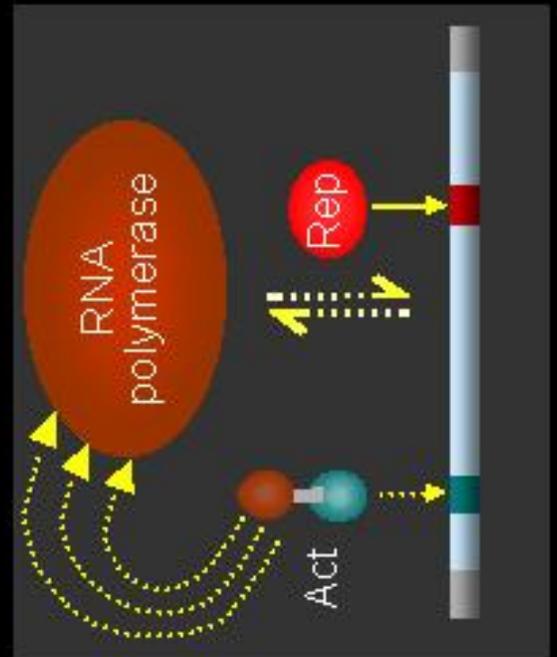
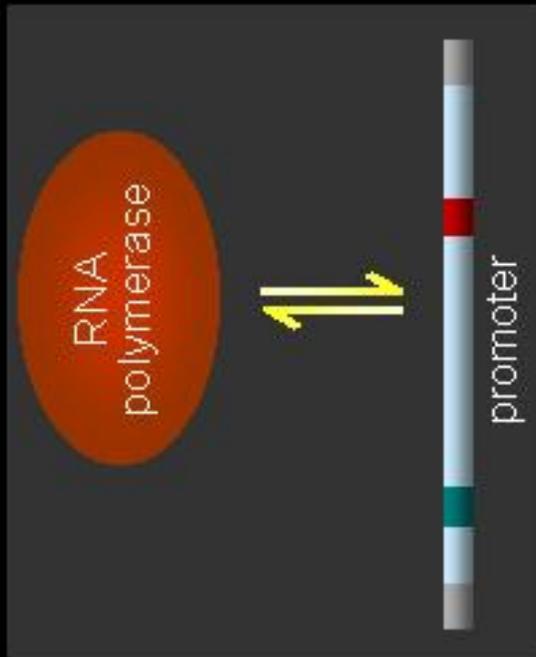
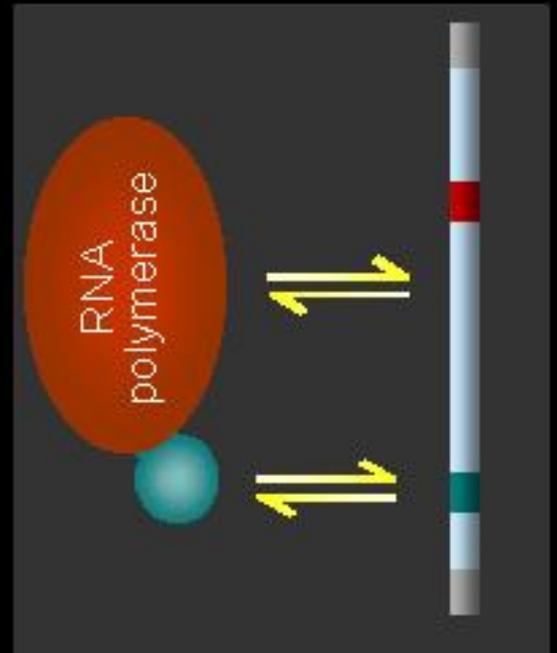
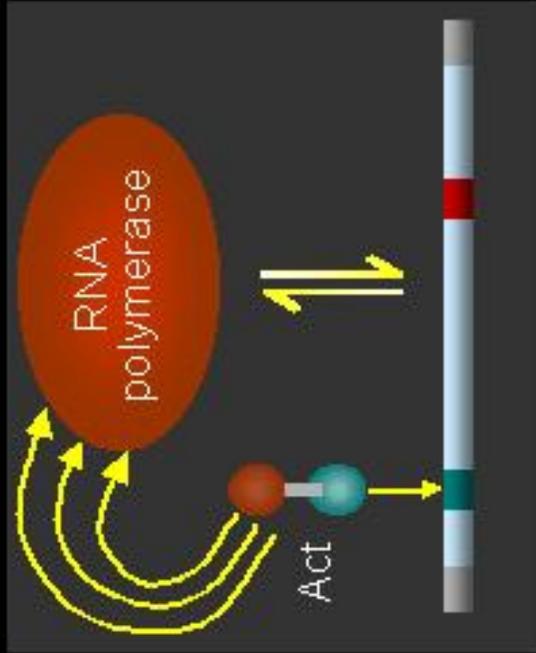
# Regulated Recruitment (Mass Action)



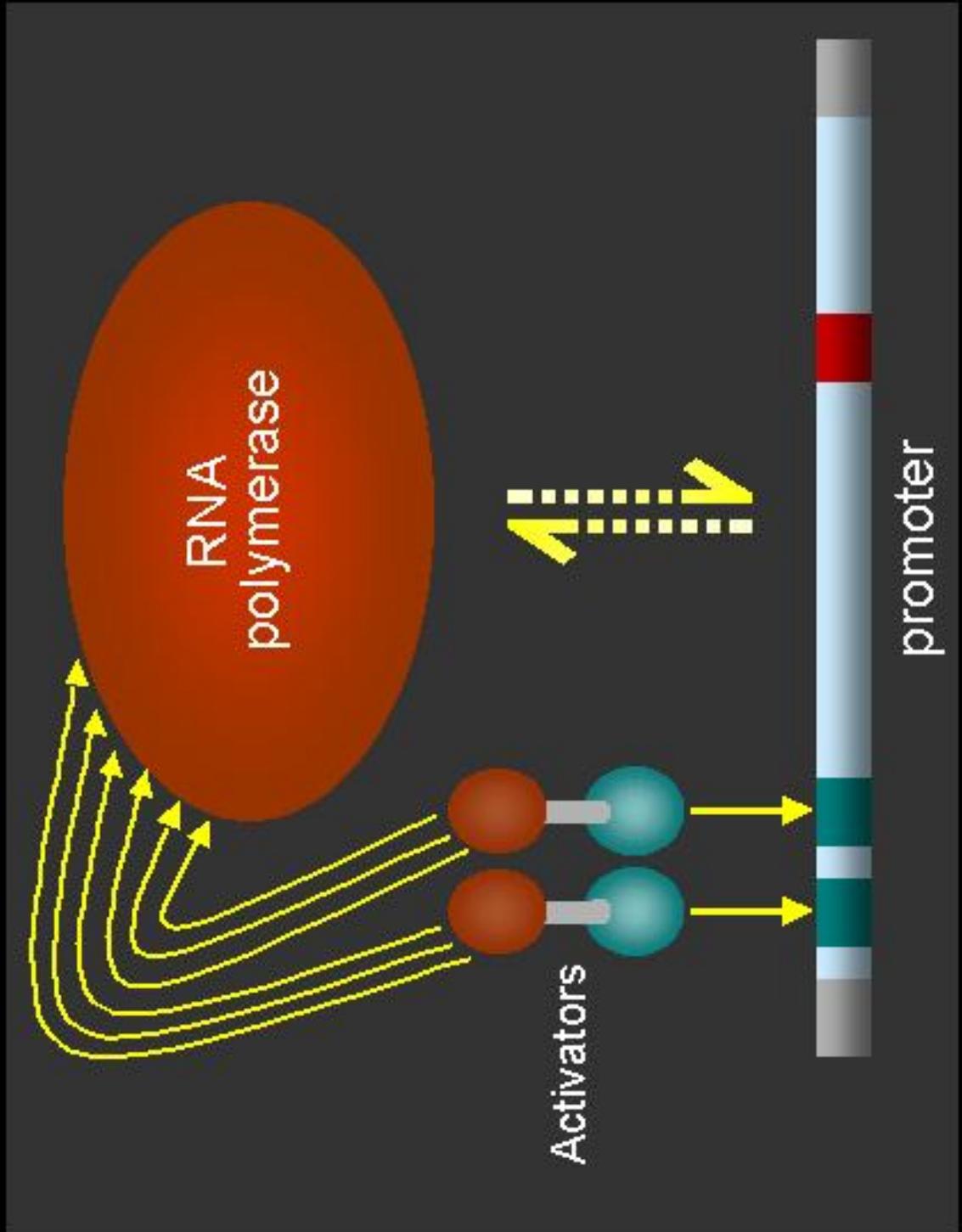
# Regulated Recruitment (Mass Action)

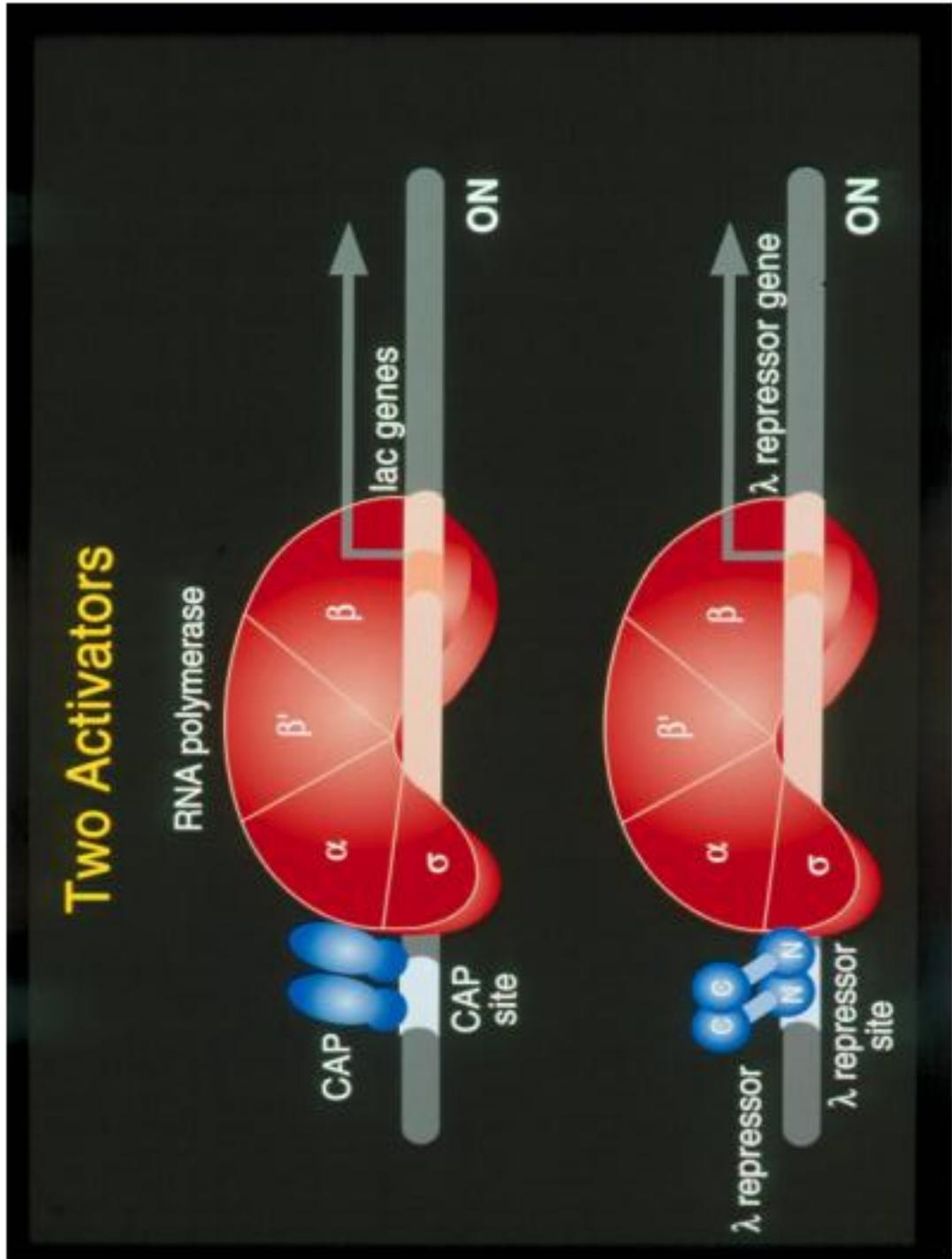


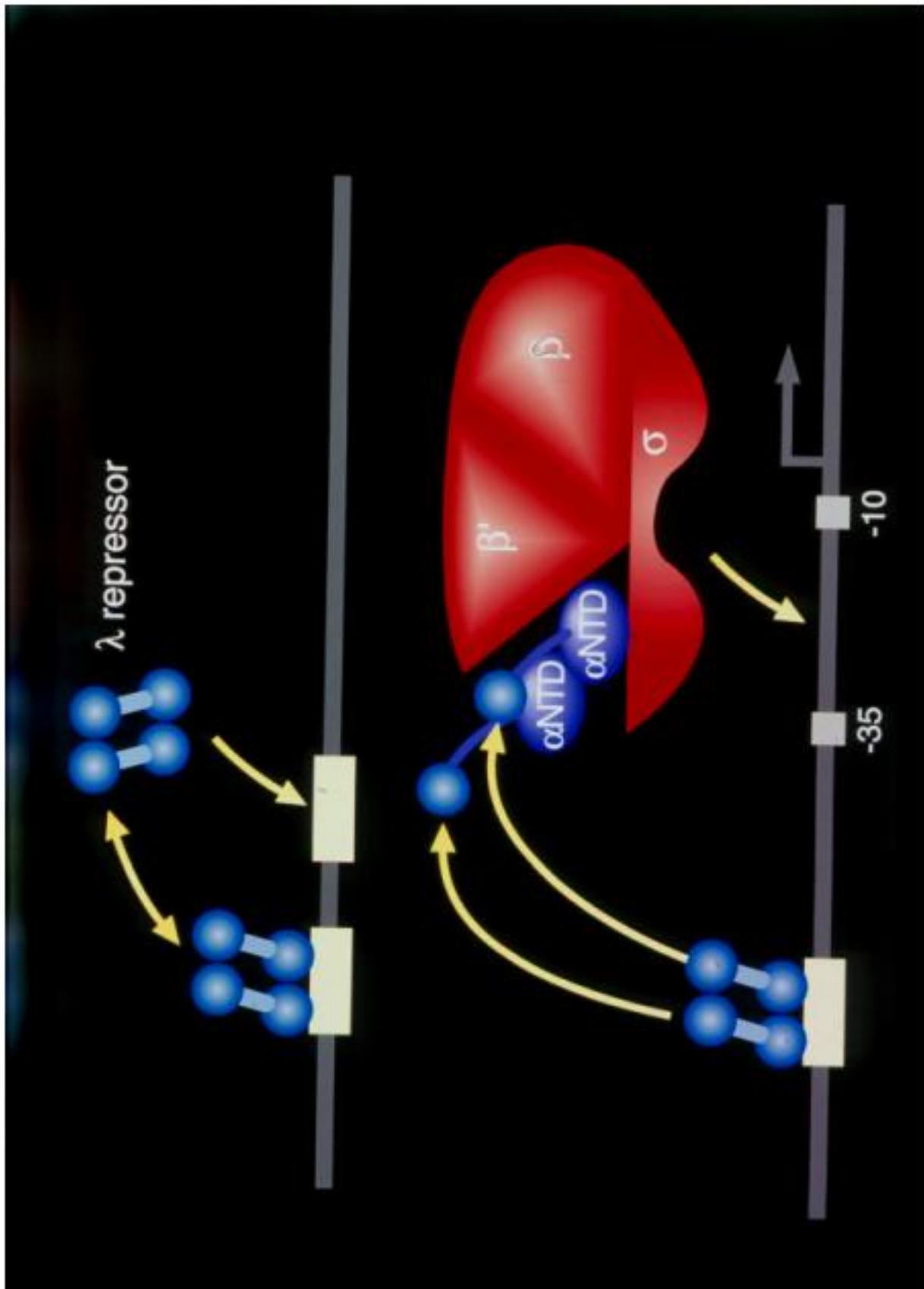
# Regulated Recruitment (Mass Action)

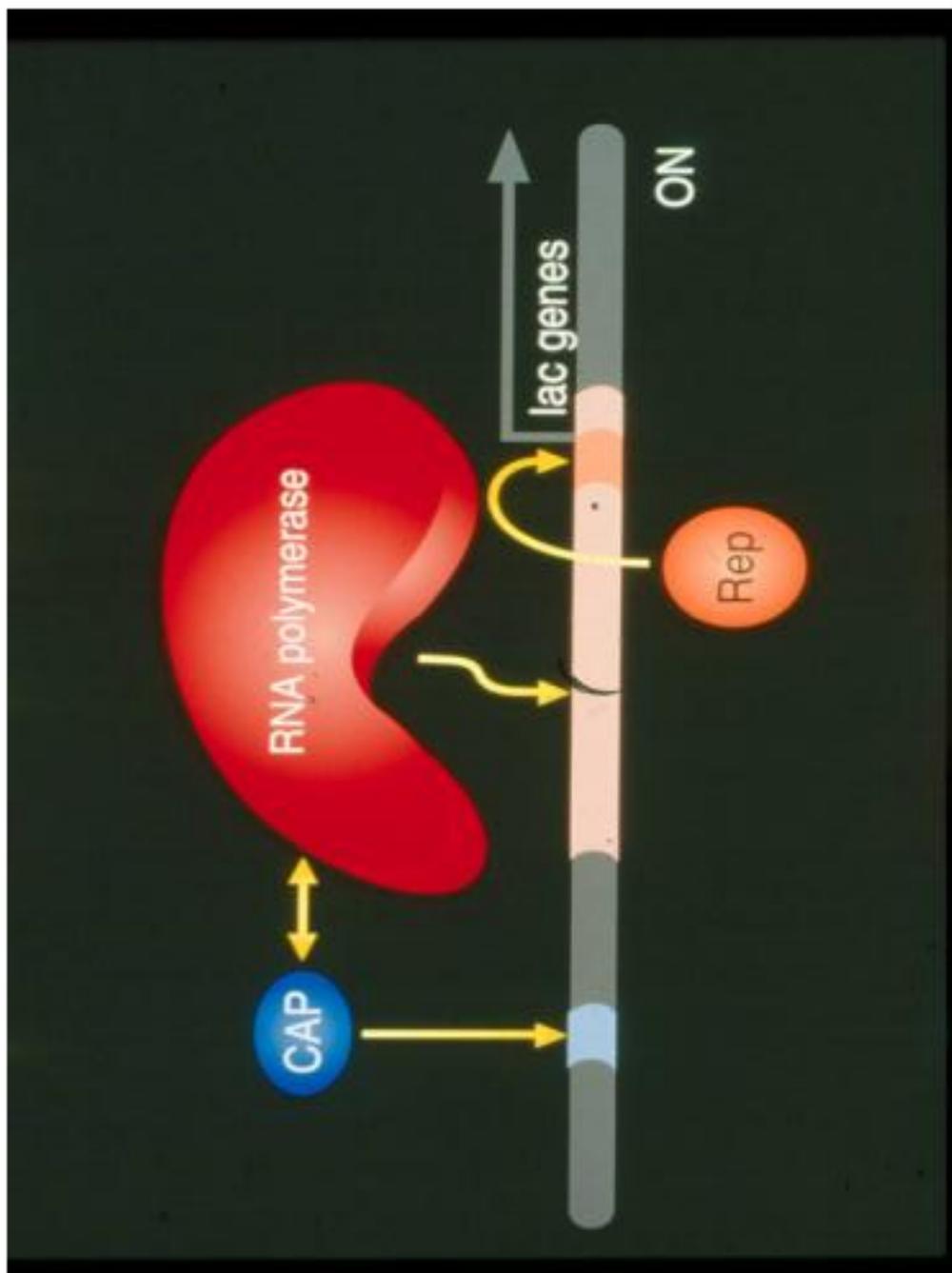


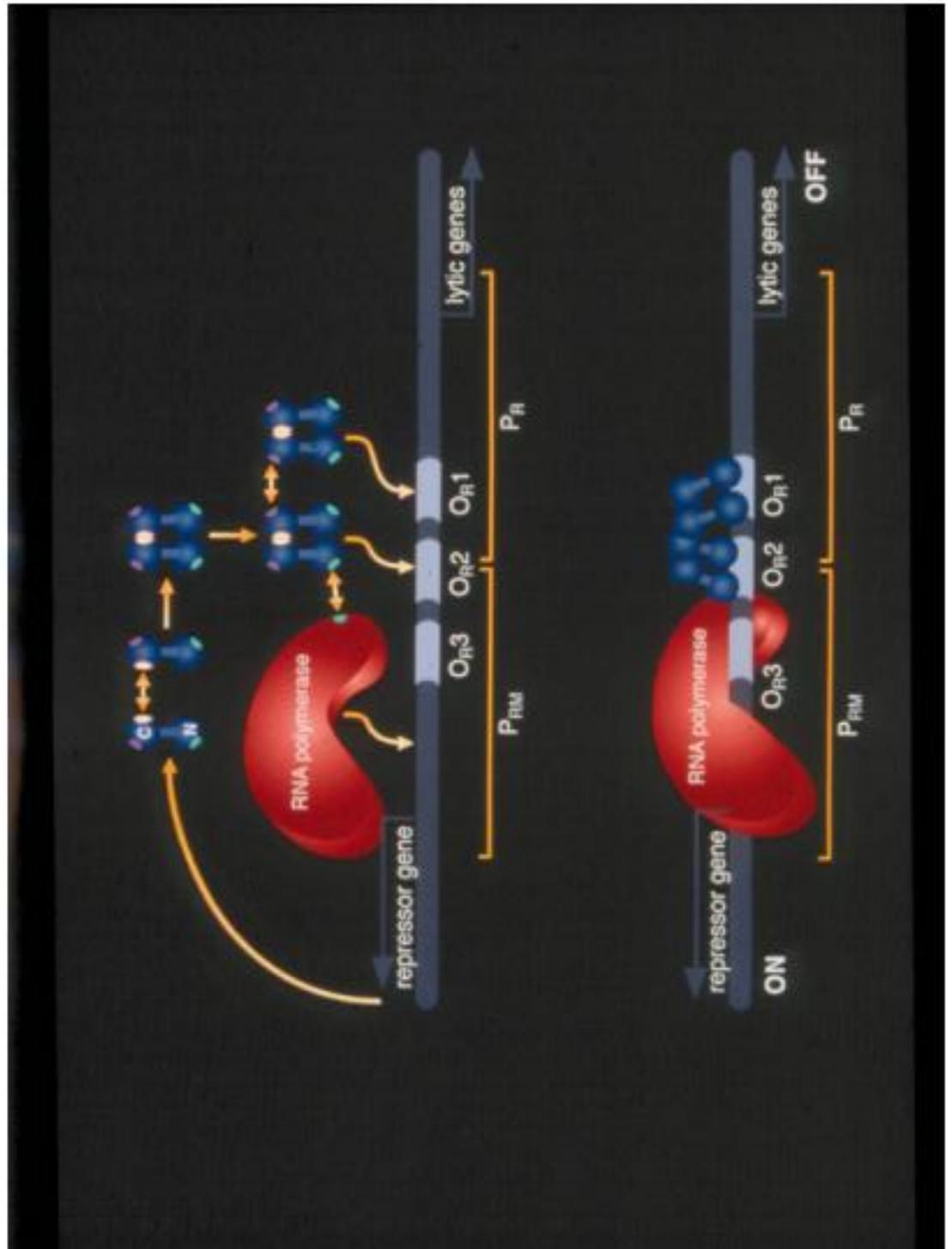
# Regulated Recruitment (Mass Action)



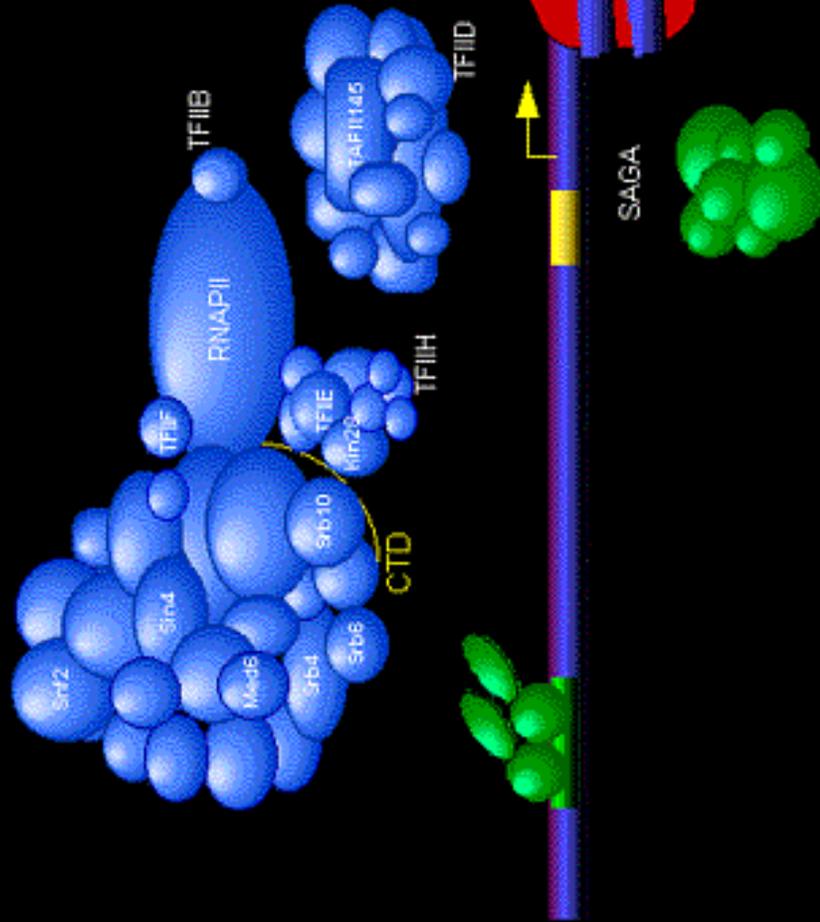








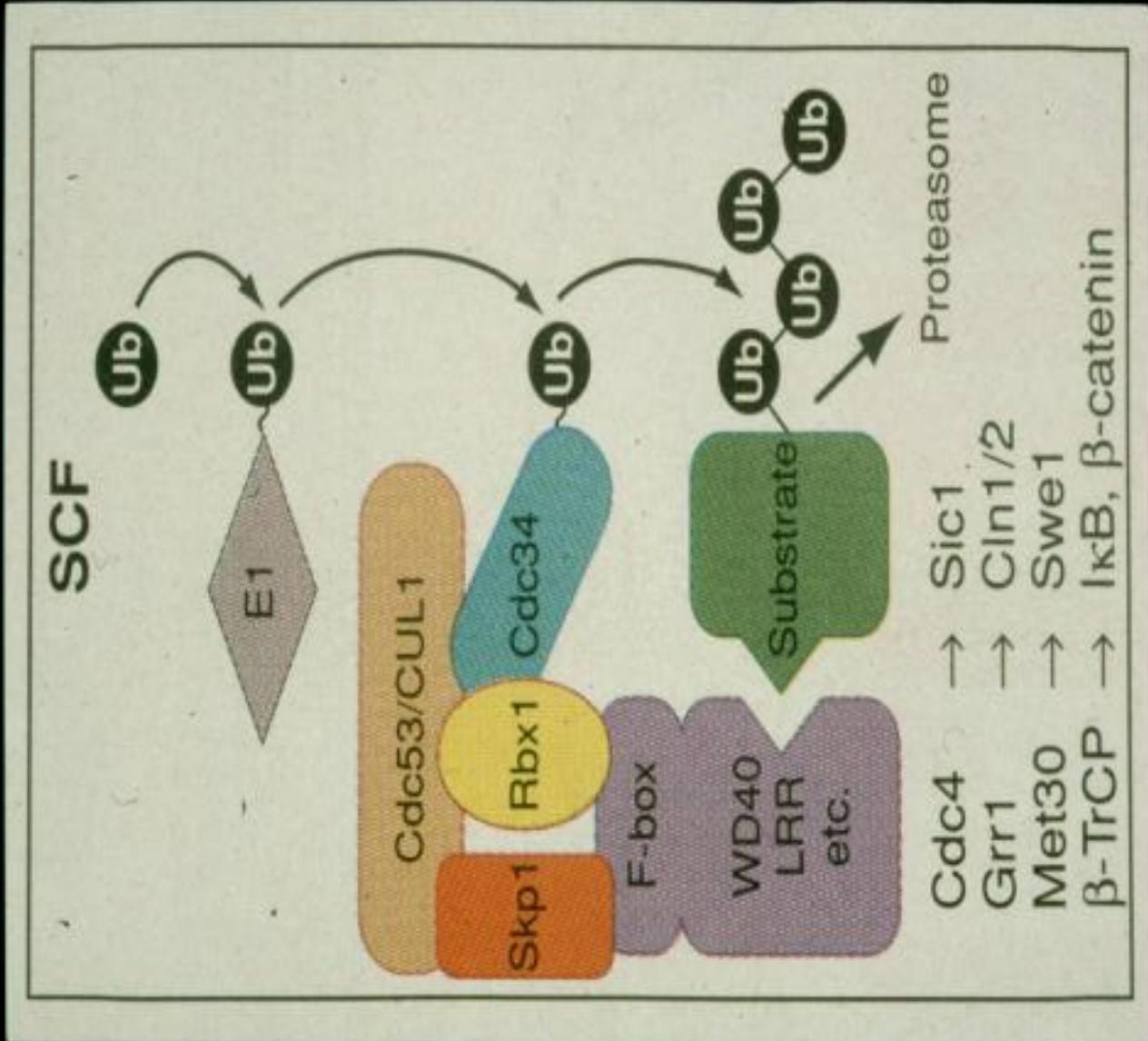
## Components of transcription apparatus: Summary



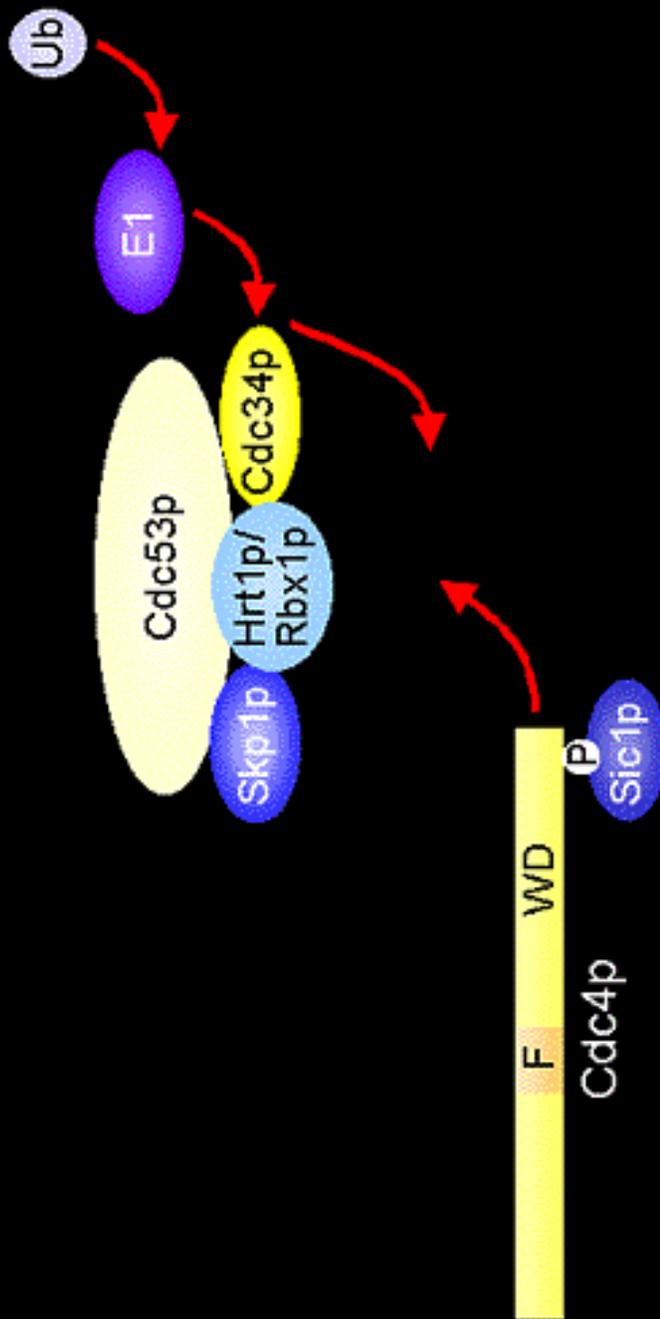
Evidence for global roles of RNA Polymerase II, TFIIH and Srb/mediator complex

Many components have roles at specific subsets of genes

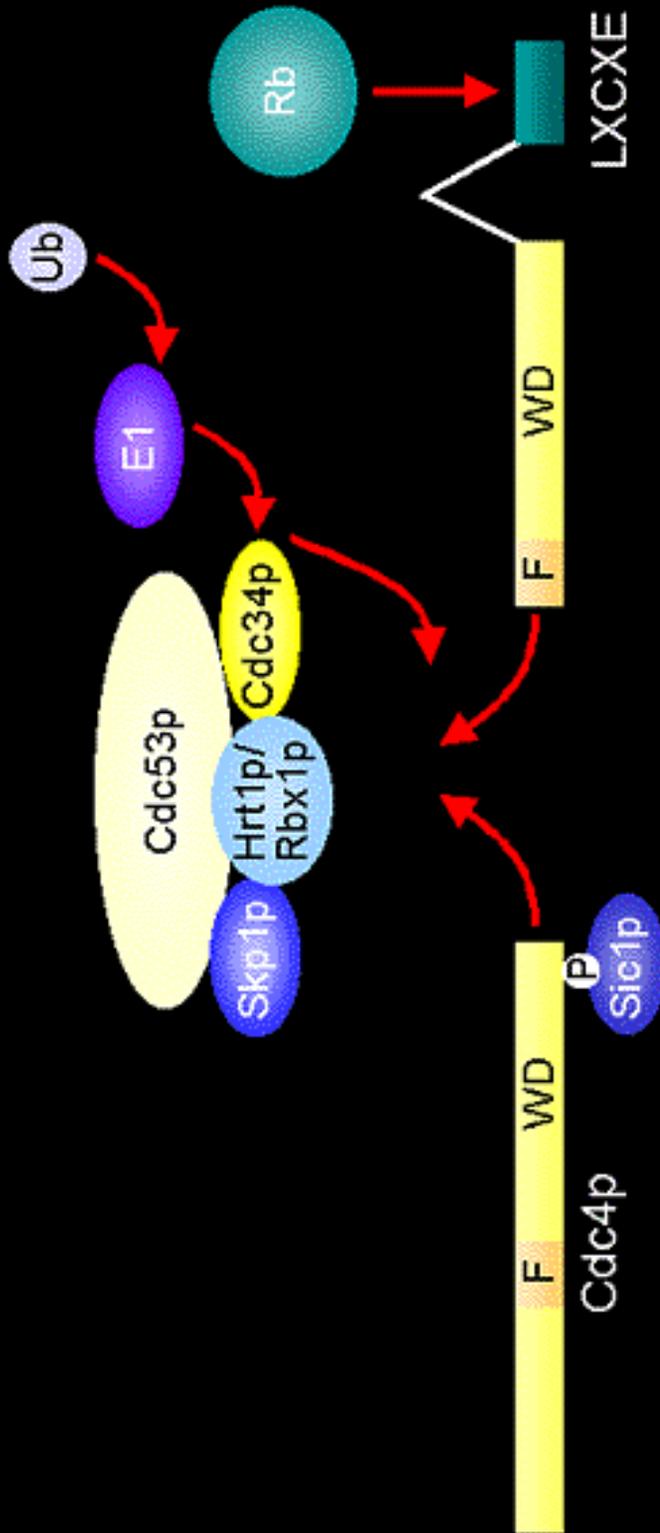
Co-ordinate regulation of genes can occur through specific components (Srb10)



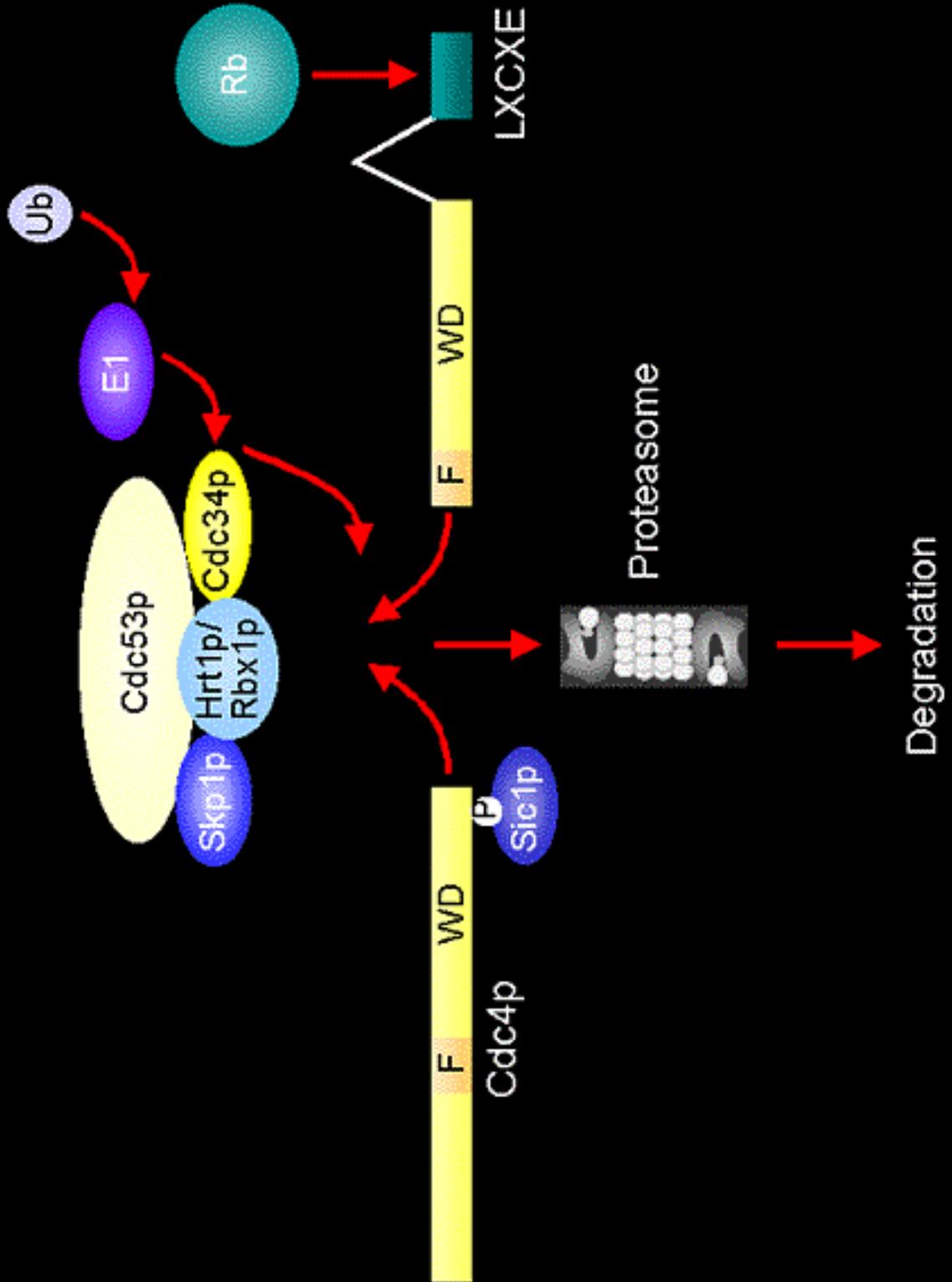
# F-box Protein as Locator



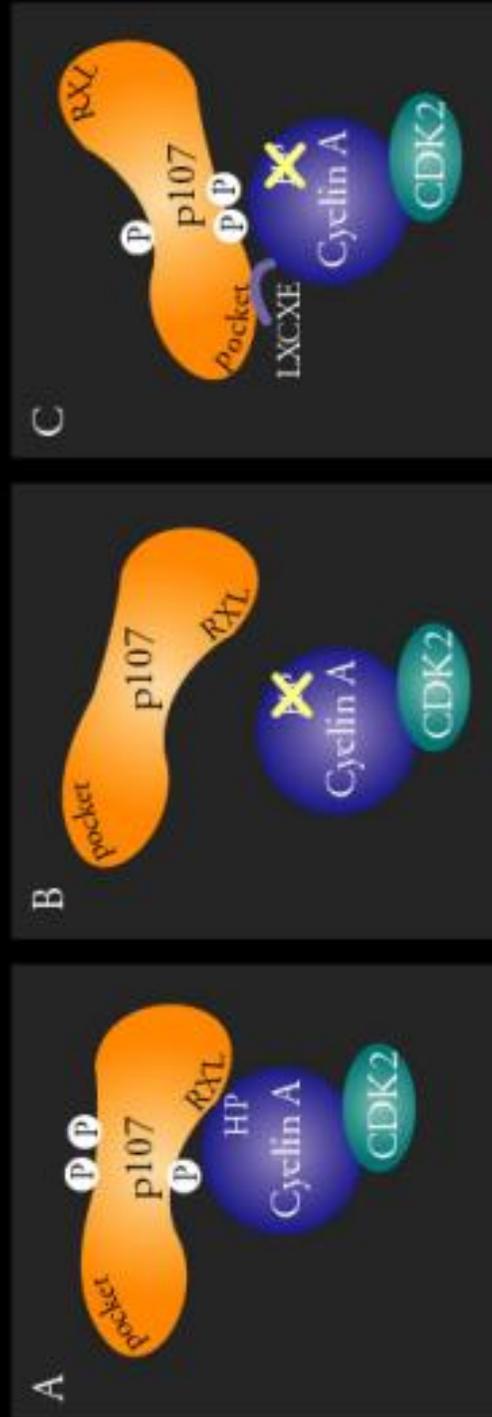
# F-box Protein as Locator



# F-box Protein as Locator



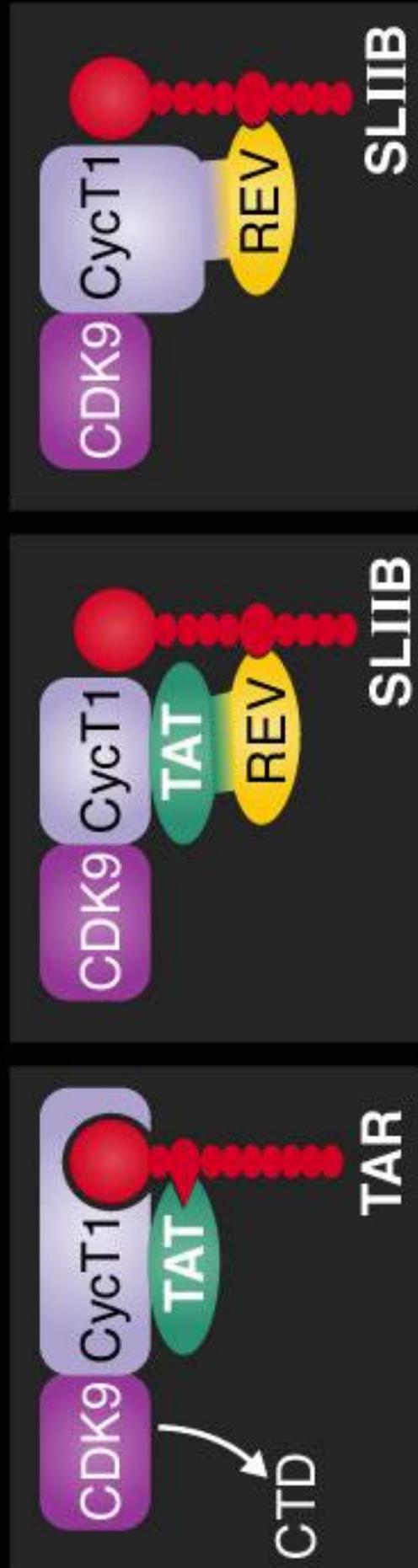
## Activator Bypass (In Vitro)



## Enzyme Activation

B. A. Schulman et al. (1998) PNAS 95, 10453

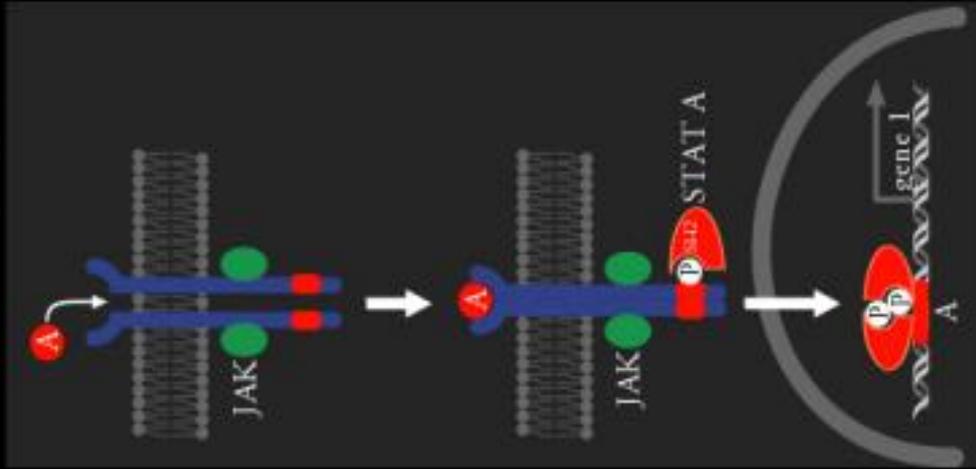
# TAT Bypass



Bieniasz *et al.* (1999) PNAS 96, 7791

## STAT Activation

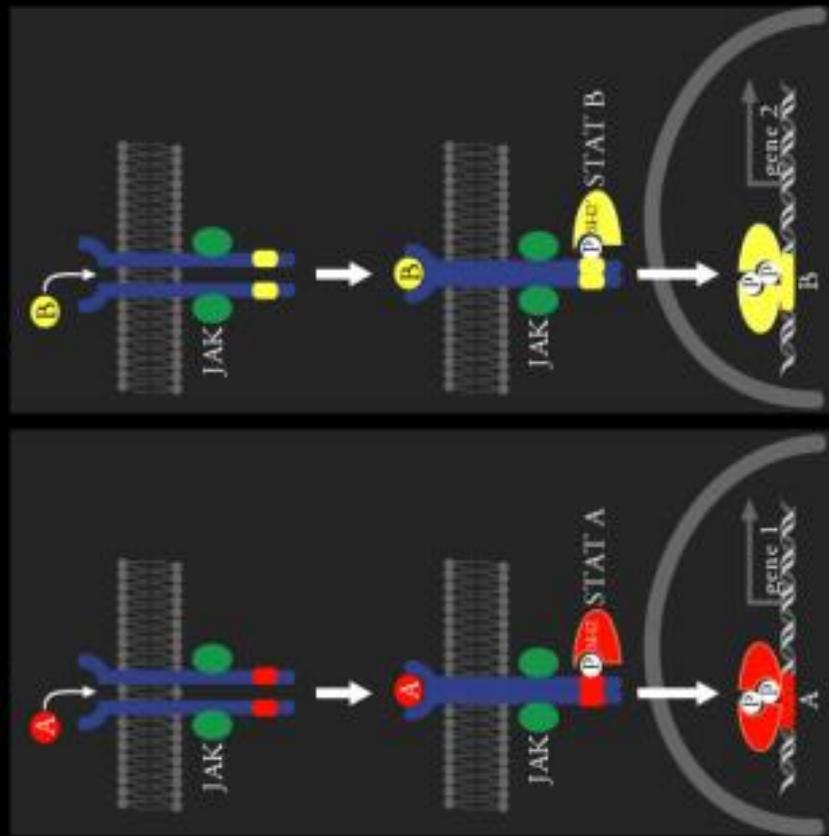
Cytokines: IFN $\alpha$ , b, g, IL-6, etc.

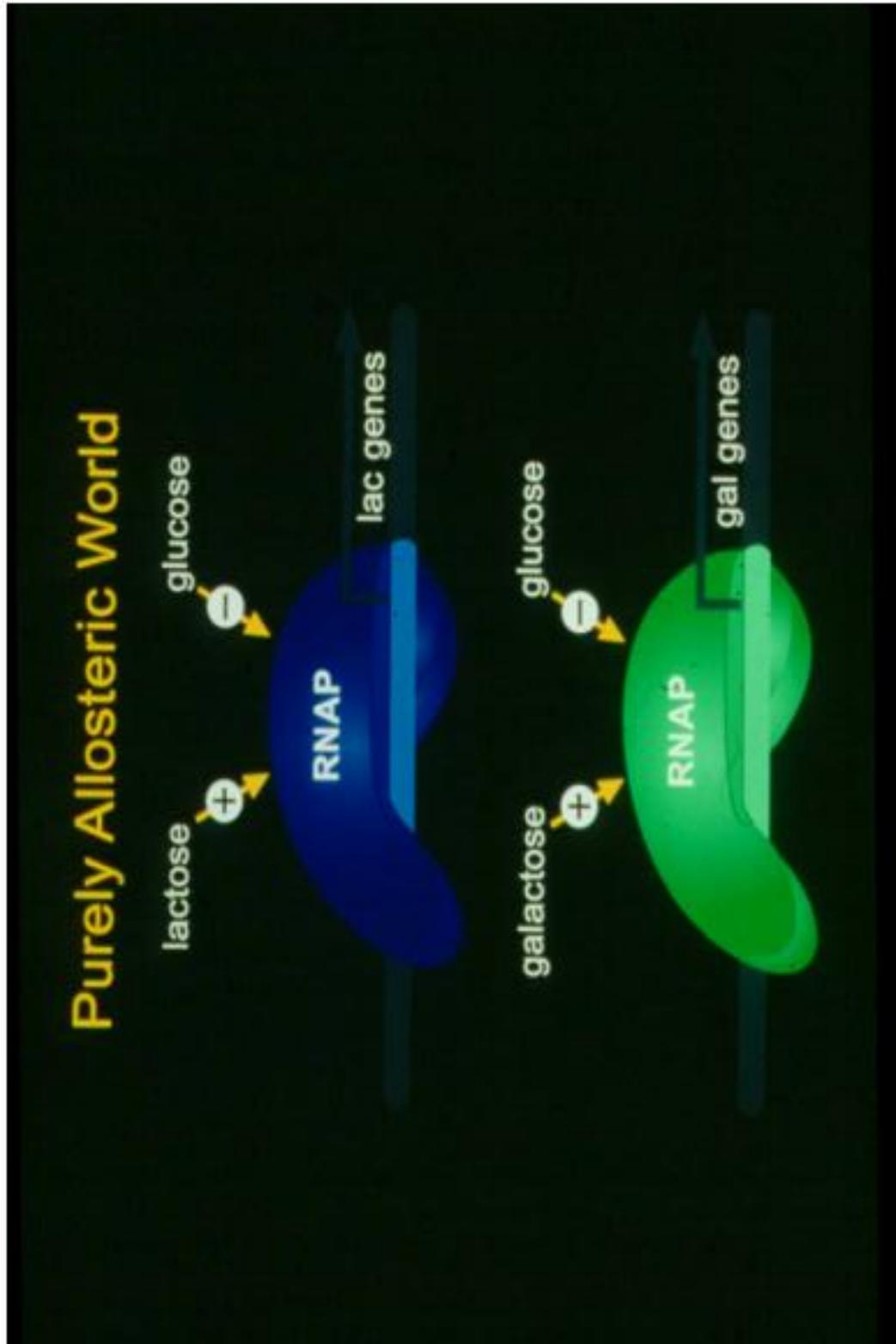


Activator Bypass:  
overproduction of JAK/STAT  
activates pathway

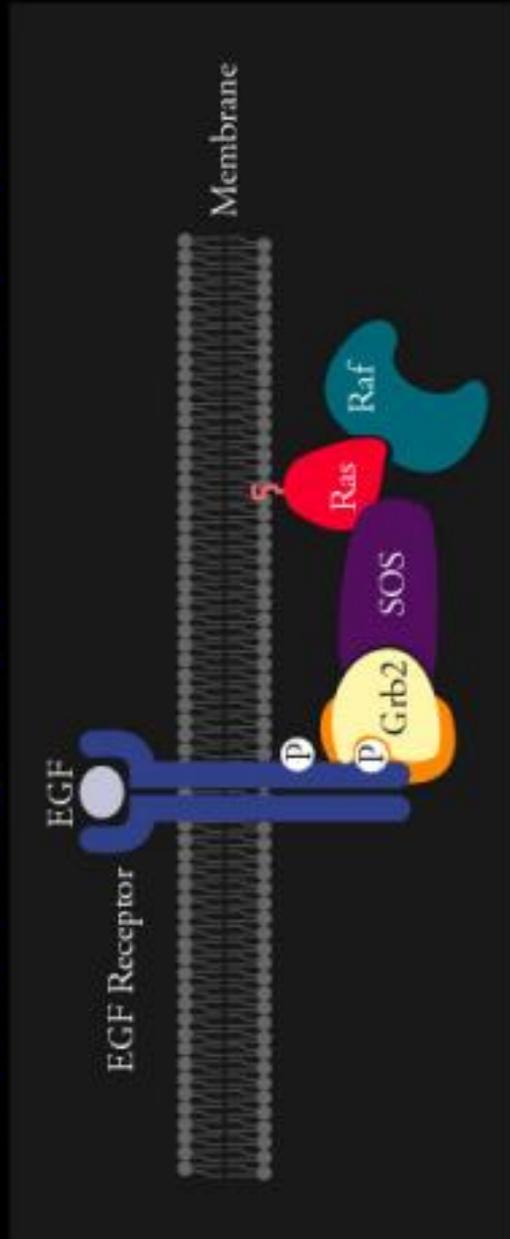
## STAT Activation

Cytokines: IFN $\alpha$ , b, g, IL-6, etc.





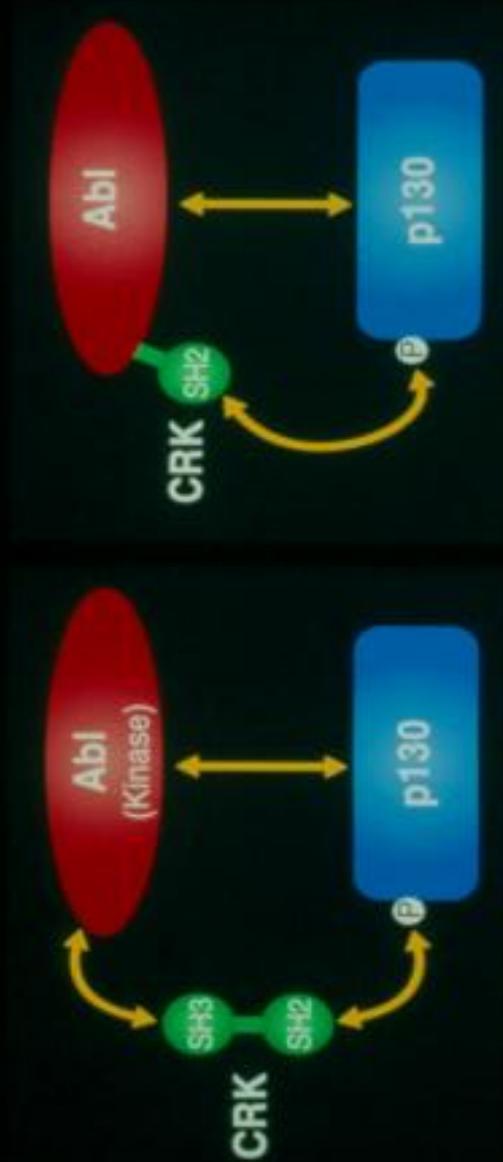
## Activator Bypass (Mammalian Cells)



### Activator Bypass

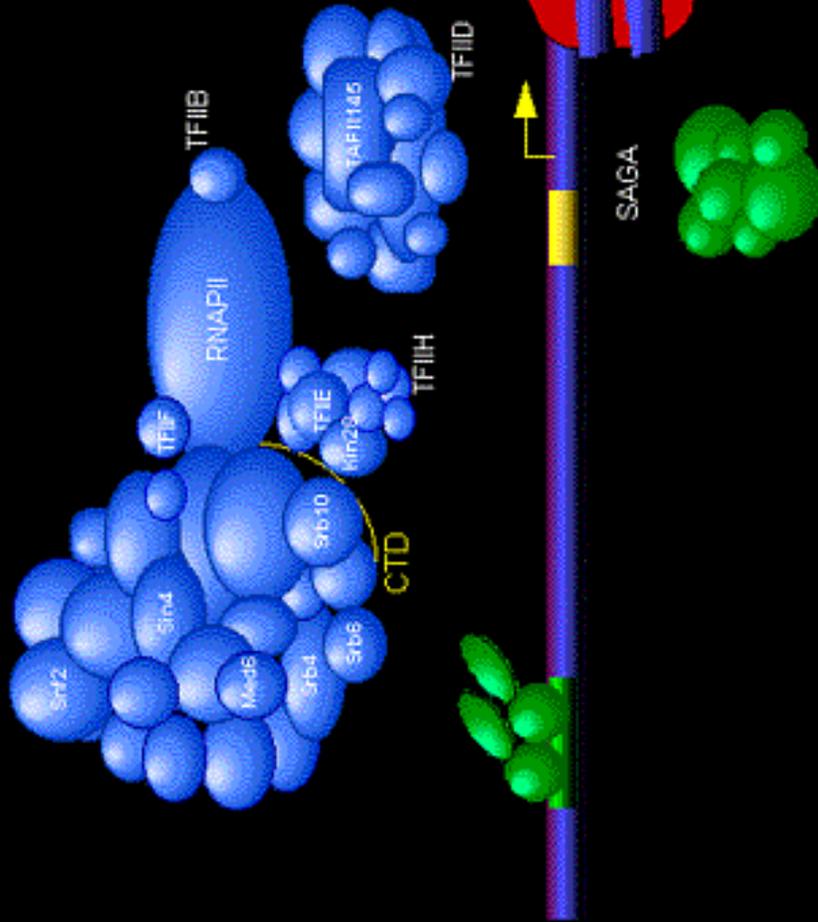
- Overproduce SOS'
- Tether SOS to membrane
- Tether Raf to membrane

## An Activator Bypass Experiment (Abl)



Mayer *et al.*, *Current Biology* 5, 296, 1995

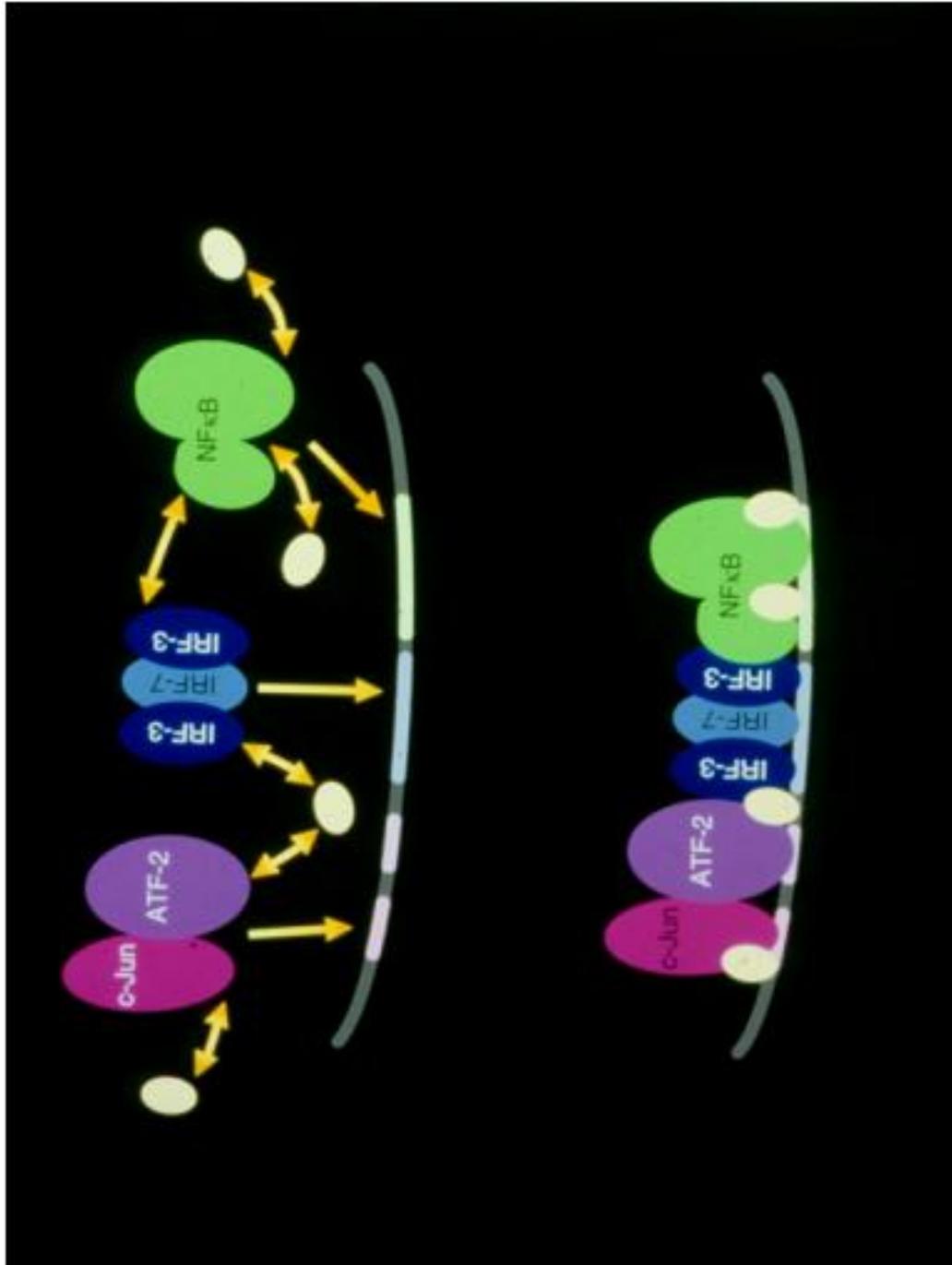
## Components of transcription apparatus: Summary



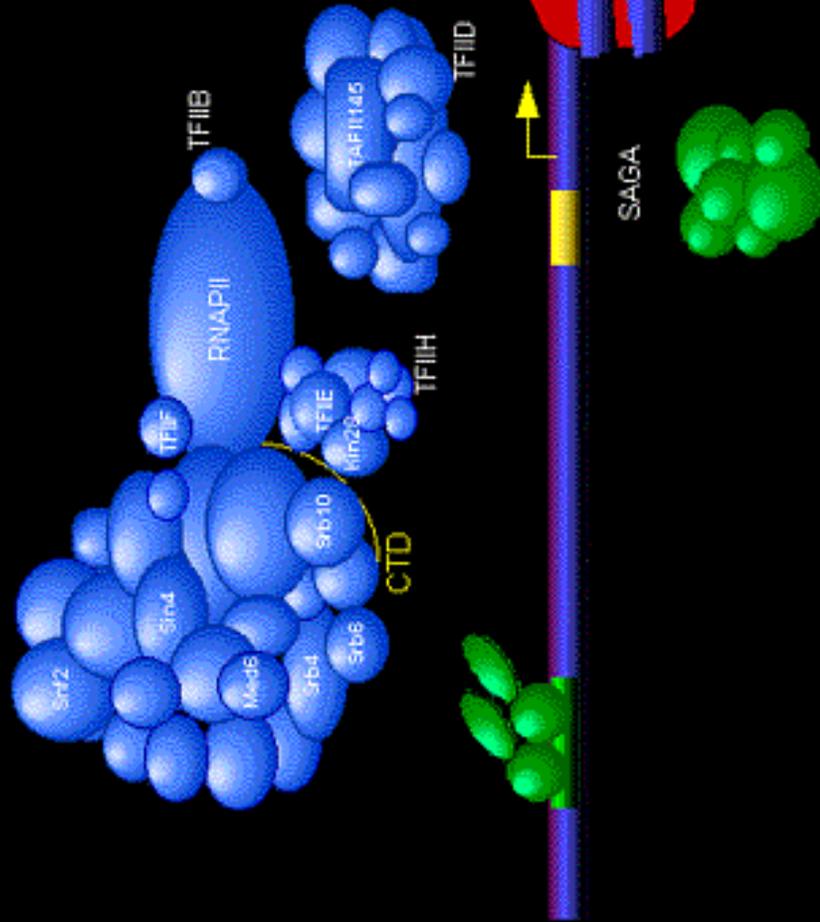
Evidence for global roles of RNA Polymerase II, TFIIH and Srb/mediator complex

Many components have roles at specific subsets of genes

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## Components of transcription apparatus: Summary



Evidence for global roles of RNA Polymerase II, TFIIB and Srb/mediator complex

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