A. Controlling Gene Expression using Regulatory RNAs:
   - Regulation by RNA uses
   - RNA can shift between one structure and another =
   - Changes in structure can be result
   - Secondary structure changes occur

1. Intramolecular mechanisms of regulation
   a. mRNA structure prevents translation
      - Translational regulation of
      - At one conformation of mRNA,
      - Second AUG may be blocked because
      - Ribosome movement
b. mRNA structure terminates transcription = Attenuation
   - Controls the ability

   - An attenuator =

   - Two events are possible:
     i. if stem/loop forms at attenuator =
        - downstream genes
     ii. if protein binds attenuator =
        - downstream genes

2. **Intermolecular mechanisms of regulation**
   - Small RNAs
   - Can have trans-acting RNA

   - Small RNA binding can:
     a. Change
        - Binding to one region
        - May mask
b. RNA binding may affect activator protein

- activator protein

- endonuclease

3. Types of regulator RNAs
   a. Regulator RNAs in bacteria
      - sRNA =
      - Some are general =
      - Example: oxyS =

      • can activate
      • represses flhA gene by

A 3’ terminal loop in oxyS RNA pairs with the initiation site of flhA mRNA
b. MicroRNAs in eukaryotes
- Are small (10-30 bases) RNAs

- Widespread mechanism:
- MicroRNAs can
- Binding causes
- Double-stranded RNA may
- Way of regulating some messages
3. RNA interference (2006 Nobel Prize in Physiology/Med)
   - MicroRNA/mRNA binding
   - Method to specifically
   - Experimentally introduce into cell
   - Double stranded RNA will be
   - Mechanism looks like
   - Many eukaryotic viruses are composed of
   - Great way to test

![RNA interference diagram](image)
B. Phage Strategies for Controlling Gene Expression:
   - Phage =
   - Are two “lifestypes” possible
     • Lytic =
     • Lysogenic =

   - Phage use different strategies

   - Not all phages

A phage may follow the lytic or lysogenic pathway

- Phage can sense

- Led to the first
C. Gene Cascades of Phage Lambda (\(\lambda\)):
- \(\lambda\) has both
- Circuit for lytic development
- When \(\lambda\) enters,
- Has
- If late genes get expressed =
- If Repressor gets expressed =

1. Gene sets
   a. Immediate-early genes
      - Has only
        i. \(N\) gene =
           - antitermination allows
        ii. \(cro\) gene
           - prevents synthesis of Repressor =
           - turns off
           - early genes
b. Delayed-early genes
   i. 2 replication genes =
   ii. 7 recombination genes
       - some needed
       - some needed
   iii. 3 regulator genes with opposing functions
       - \(cII\) and \(cIII\) =
       - \(Q\) = Antitermination factor

c. Late genes
   - 2 genes
   - 21 genes for heads and tails =
2. The lytic cycle
- Phage DNA enters as linear molecule,
- Immediate-early genes
  • \(N\) is expressed
  • \(cro\) is expressed
- N product (pN) allows antitermination=
  • \(N\) transcript
  • \(cro\) transcript
- All late genes transcribed
  • \(P_R^+\) expressed
  • when pQ made (as part of delayed-early extension from \(cro\)),

![Diagram](image-url)
3. Lysogeny is maintained by cI Repressor
   - Lytic cycle put in motion
   - Each also has an
   - Between $P_L O_L$ and $P_R O_R$ is
   - if cI Repressor binds
4. Other aspects of Repressor binding
   a. The operator regions of PL and PR have
      - Binding of cI at operator is cooperative =

      ![Diagram of Repressor protein and RNA polymerase binding](image)

b. Repressor binding is needed for cI transcription
   - Octomers of cI are
     - When bound as octomer
       • bends
       • facilitates
   - When bound as 12-mer
     • RNA pol
   - Autogenous circuit =

      ![Diagram of Repressors binding and transcription](image)
5. Establishing lysogeny
- When λ first enters host cell,
  - Thus, $P_L$ and $P_R$ are
  - $N$ is
  - $cro$ is
  a. $cII$
     - Classic activator protein
     - $P_{RE}$ is
     - RNA pol
     - Once $P_{RE}$ recognized =
  b. $cIII$
     - $cII$ protein
     - $cIII$ helps
6. The Cro repressor is needed for the lytic cycle
   - Lysogeny is established when
     - Cro is produced
     - *cro* encodes
     - Cro is a dimer that binds to $O_L$ and $O_R$
     - Cro has highest affinity for $O_R^3 =$
     - Cro can then bind to $O_R^1$ and $O_R^2$ with equal affinity (no cooperativity) =
     - By the time early genes are turned off,
7. Determining lytic or lysogenic pathways
   - Once infected,
   - The fate of the phage depends on

   a. Initial event in entering lysogenic phase =
      i. Cooperative
      ii. Shuts off
      iii. Starts up
b. Initial events entering lytic phase =
- Stops
- Leads to more
- cII and cIII quickly degrade =

c. cII is the critical switch
- If cII active =
- If cII inactive =

d. Stability of cII
- When bacteria growing well =
- Phage uses
8. Immunity
   - Occurs when λ is integrated into host genome =

   - Occurs because

9. Release from lysogeny
   - Recall that
     i. DNA binding
   -
     ii. Dimer binding
   - used for
   - When prophage undergoes damage

   - Get expression from