

**Directions:** Turn in the scantron form only. BE SURE TO WRITE YOUR NAME ON THE SCANTRON FORM. Guesses might be correct, blanks never are. Select the one best answer for each question.

**Part I. Passage on Prokaryotic Transcription.** Questions 1 - 7 are based on the following passage, taken from an advanced genetics text<sup>1</sup>. Answer the questions according to what is actually stated in the passage.

Positive and negative control systems are defined by the response of the operon when no regulator protein is present. The characteristics of the two types of control system are mirror images. Genes under negative control are expressed unless they are switched off by a repressor protein. Any action that interferes with gene expression can provide a negative control, but there is a uniformity in these mechanisms: a repressor protein either binds to DNA to prevent RNA polymerase from initiating transcription, or binds to mRNA to prevent a ribosome from initiating translation. Negative control provides a fail-safe mechanism: if the regulator protein is inactivated, the system functions and so the cell is not deprived of these enzymes. It is easy to see how this might evolve. Originally a system functions constitutively, but then cells able to interfere specifically with its expression acquire a selective advantage by virtue of their increased efficiency. For genes under positive control, expression is possible only when an active regulator protein is present. The mechanism for controlling an individual operon is an exact counterpart of negative control, but instead of interfering with initiation, the regulator protein is essential for it. It interacts with DNA and with RNA polymerase to assist the initiation event. A positive regulator protein that responds to a small molecule is usually called an activator. Other positive controls provide for the global substitution of sigma factors that change the selection of promoters, or antitermination factors that change the recognition of terminators. It is more difficult to see how positive control evolved, since the cell must have had the ability to express the regulated genes even before any control existed. Presumably some component of the control system must have changed its role. Perhaps originally it was used as a regular part of the apparatus for gene expression; then later it became restricted to act only in a particular system or systems. Operons are defined as inducible or repressible by the nature of their response to the small molecule that regulates their expression. Just as it is advantageous for a bacterium to induce a set of enzymes only after addition of the inducer substrate that they metabolize, so also it is useful to repress the enzymes that synthesize some compound if it is provided in adequate amounts by the medium. Thus inducible operons function only in the presence of the small-molecule inducer. Repressible operons function only in the absence of the small molecule corepressor (so called to distinguish it from the repressor protein). The terminology used for repressible systems describes the active state of the operon as derepressed; this has the same meaning as induced. The condition in which a (mutant) operon cannot be derepressed is sometimes called super-repressed; this is the exact counterpart of uninducible. Either positive or negative control could be used to achieve either induction or repression by utilizing appropriate interactions between the regulator protein and the small-molecule inducer or corepressor. Induction is achieved when an inducer inactivates a repressor protein or activates an activator protein. Repression is accomplished when a corepressor activates a repressor protein or inactivates an activator protein.

1. Repressor proteins may bind to:

1. either DNA or RNA polymerase
- \*2. either DNA or mRNA
3. either DNA or ribosomes
4. either RNA polymerase or ribosomes
5. DNA, RNA, ribosomes, or RNA polymerase

2. Once they are bound to their targets, repressor proteins may block initiation by:

1. either DNA or RNA polymerase
2. either DNA or mRNA
3. either DNA or ribosomes
- \*4. either RNA polymerase or ribosomes
5. DNA, RNA, ribosomes, or RNA polymerase

3. According to the passage, the evolution of which of the following is easiest to see:

- \*1. negative control of operons
2. positive control of operons
3. operons from single cistrons
4. antitermination
5. activator proteins

4. Which of the following may be a selective advantage for cells that have negative control:

1. immunity from viruses
2. lower mutation rates
- \*3. greater efficiency
4. more rapid response to environmental changes
5. all of the above.

5. Which of the following would always be an example of negative control:

1. An operon that lacks a normal promoter, and requires an additional protein for transcription initiation.
2. A gene that is only transcribed when an antiterminator is present.
3. An operon that is inducible.
4. An operon that is repressible.
- \*5. An operon that is constitutively expressed unless a repressor is present.

6. Which of the following are proteins?

1. Repressors and corepressors
2. Activators and inducers
3. Corepressors and inducers
- \*4. Repressors and activators
5. Terminators and antiterminators

7. What is the difference between an inducible operon and a repressible operon?

- \*1. Whether the response to a small molecule is positive or negative.
2. Whether they are controlled by an activator or a repressor.
3. Whether they are regulated at the transcriptional or translational level.
4. Whether they respond to regulator proteins or sigma factors
5. Whether they are controlled by initiation or termination.

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## Part II. The following questions concern general aspects of transcription and translation.

8. Which of the following is true only of eukaryotic cells?

1. Their genes have promoters.
- \*2. Transcription and translation occur in separate parts of the cell.
3. RNA is transcribed by RNA polymerase
4. Transcription is regulated
5. RNA is synthesized in a 5' → 3' direction.

9. Under which of these conditions would the *lac* operon be transcribed at the highest rate?

- \*1. lactose present, glucose absent
2. lactose and glucose both present
3. lactose absent, glucose present
4. lactose and glucose both absent
5. allolactose and glucose both present

10. A mutant *lac* operon that lacked the operator would still respond to:

1. presence or absence of lactose
2. presence or absence of allolactose
3. the *lac* repressor
- \*4. presence or absence of glucose
5. the inducer

11. Which of the following phages is a temperate phage?

1. T2
2. T4
3. T7
4. SPO1
- \*5. lambda ( $\lambda$ )

12. This organelle removes introns

1. Ribosome
- \*2. Spliceosome
3. Primosome
4. Replisome
5. Centriole

13. Which of the following is **not** true of polyA tails:

1. they consist of 150-200 adenines
2. they are attached to the 3' ends of mRNAs
3. they prevent degradation of mRNAs
4. they are found in eukaryotes but not prokaryotes
- \*5. they are transcribed from long stretches of T's following coding regions

14. Which of the following are proteins?

1. TATA boxes
2. CCAAT boxes
3. GC boxes
- \*4. transcription factors
5. exons

15. The molecule that matches specific amino acids to codons is:

1. mRNA
2. rRNA
- \*3. tRNA
4. aminoacyl-tRNA synthetase
5. peptidyl transferase

16. The enzyme that charges tRNAs with specific amino acids is called:

1. peptidyl transferase
2. terminal transferase
- \*3. aminoacyl-tRNA synthetase
4. ligase
5. polynucleotide kinase

17. During transcription, at which end of the mRNA are new ribonucleotides added?

1. 5' end
- \*2. 3' end
3. carboxyl end
4. amino end

18. During translation, at which end of the peptide are new amino acids added?

1. 5' end
2. 3' end
- \*3. carboxyl end
4. amino end

19. The degeneracy of the genetic code implies:

1. Some codons can be translated as either of two different amino acids
2. There are more amino acids than codons
3. The genetic code in prokaryotes is different from the code in eukaryotes.
- \*4. Different codons can be translated as the same amino acid
5. Early in evolution the genetic code was precise, now it is sloppy

20. Which of the following is not recognized by a tRNA?

1. start codon
2. methionine codon
- \*3. stop codon
4. leucine codon
5. valine codon

**The diagram of phage  $\lambda$  on this page is provided to help you with questions 21-24.**

21. In phage  $\lambda$ , the first gene(s) expressed after infection are:

- \*1. immediate early genes
2. delayed early genes
3. late genes
4. the head and tail genes
5. *cI*, the gene that encodes the  $\lambda$  repressor

22. After  $\lambda$  enters its dormant, lysogenic mode, the only gene(s) expressed is:

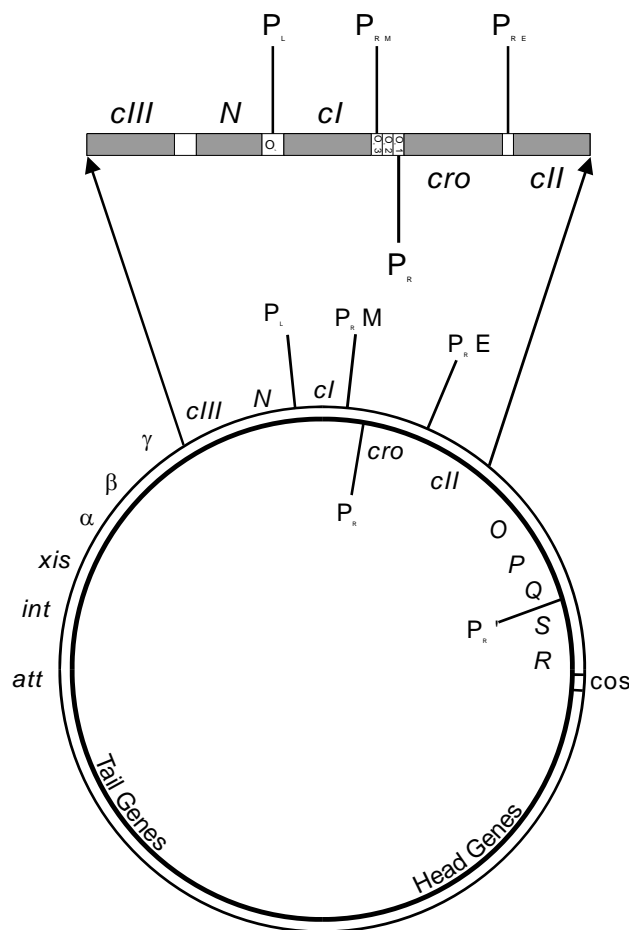
1. immediate early genes
2. delayed early genes
3. late genes
4. the head and tail genes
- \*5. *cI*, the gene that encodes the  $\lambda$  repressor

23. Before the lysis/lysogeny decision is reached, expression of genes to the left of *N* and to the right of *cro* requires:

- \*1. the antiterminator product of *N*
2. the antiterminator product *Q*
3. the product of the *cro* gene
4. the host protein RecA
5. the product of the *cI* gene

24. Why isn't the *cro* gene transcribed from the promoter  $P_{RE}$ ?

1. Transcription from  $P_{RE}$  goes to the right
2.  $P_{RE}$  is used only during lysogeny
- \*3. *cro* is not on the same strand of DNA as the promoter
4. a terminator blocks transcription from  $P_{RE}$
5.  $P_{RE}$  is blocked by the  $\lambda$  repressor



### Part 3. Passage on eukaryotic response elements.

Questions 25 - 30 are based on the following passage, taken from an advanced genetics text<sup>1</sup>. Answer the questions according to what is actually stated in the passage.

The principle that emerges from characterizing groups of genes under common control is that they share an element that is recognized by a regulatory transcription factor. An element that causes a gene to respond to such a factor is called a response element; examples are the HSE (heat shock response element), GRE (glucocorticoid response element), and SRE (serum response element). Response elements have the same general characteristics as upstream elements of promoters or enhancers. They contain short consensus sequences, and copies of the response elements found in different genes are closely related, but not necessarily identical. The region bound by the factor extends for a short distance on either side of the consensus sequence. The elements are not present at fixed distances from the startpoint, but are usually <200 bp upstream of it. The presence of a single element usually is sufficient to confer the regulatory response, but sometimes there are multiple copies. Response elements may be located in promoters or in enhancers. Some types of elements are typically found in one rather than the other: usually an HSE is found in a promoter, while a GRE is found in an enhancer. We assume that all response elements function by the same general principle. A gene is regulated by a sequence at the promoter or enhancer that is recognized by a specific protein. The protein functions as a transcription factor needed for RNA polymerase to initiate. Active protein is available only under conditions when the gene is to be expressed; its absence means that the promoter is not activated by this particular circuit. An example of a situation in which many genes are controlled by a single factor is provided by the heat shock response. This is common to a wide range of prokaryotes and eukaryotes and involves multiple controls of gene expression: an increase in temperature turns off transcription of some genes, turns on transcription of the heat shock genes, and also causes changes in the translation of mRNAs. The control of the heat shock genes illustrates the differences between prokaryotic and eukaryotic modes of control. In bacteria, a new sigma factor is synthesized that directs RNA polymerase holoenzyme to recognize an alternative -10 sequence common to the promoters of heat shock genes. In eukaryotes, the heat shock genes also possess a common consensus sequence (HSE), but it is located at various positions relative to the startpoint, and is recognized by an independent transcription factor, HSTF. The activation of this factor therefore provides a means to initiate transcription at the specific group of ~20 genes that contains the appropriate target sequence at its promoter. All the heat shock genes of *D. melanogaster* contain multiple copies of the HSE. The HSTF binds cooperatively to adjacent response elements. Both the HSE and HSTF have been conserved in evolution, and it is striking that a heat shock gene from *D. melanogaster* can be activated in species as distant as mammals or sea urchins. The HSTF proteins of fruit fly and yeast appear similar, and show the same footprint pattern on DNA containing HSE sequences.

The metallothionein (MT) gene provides an example of how a single gene may be regulated by many different circuits. The metallothionein protein protects the cell against excess concentrations of heavy metals, by binding the metal and removing it from the cell. The gene is expressed at a basal level, but is induced to greater levels of expression by heavy metal ions (such as cadmium) or by glucocorticoids. The control region combines several different kinds of regulatory element, and suggests the principle that when a promoter is regulated in more than one way, each regulatory event depends on binding of its own protein to a particular sequence. The two 'constitutive' promoter elements are the TATA box and GC box, located at their usual positions fairly close to the startpoint. Also needed for the basal level of constitutive expression are the two basal level elements (BLE), which fit the formal description of enhancers. Although located near the startpoint, they can be moved elsewhere without loss of effect. The inductive response to metals is conferred by the multiple MRE sequences. These function as promoter elements. The presence of one MRE confers the ability to respond to heavy metal; a greater level of induction is achieved by the inclusion of multiple elements. The response to steroid hormones is governed by a GRE, located 250 bp upstream of the startpoint, which behaves as an enhancer. Deletion of this region does not affect the basal level of expression or the level induced by metal ions. But it is absolutely needed for the response to steroids. The regulation of metallothionein illustrates the general principle that any one of several different elements, located in either an enhancer or promoter can independently activate the gene. The absence of a element needed for one mode of activation does not affect activation in other modes. The variety of elements, their independence of action, and the apparently unlimited flexibility of their relative arrangements, suggest that a factor binding to any one element is able independently to increase the efficiency of initiation by the basal transcription apparatus, probably by virtue of protein-protein that stabilize or otherwise assist formation of the initiation complex.

25. According to the passage, which of the following statements is true:

1. Heat shock responses are controlled by the same elements in both prokaryotes and eukaryotes.
2. Response elements that are found in promoters are never found in enhancers.
3. Eukaryotic RNA polymerase binds to response elements.
4. Response elements always must be present in multiple copies to be effective.
- \*5. The sequence of a functional response elements does not need to exactly match the consensus sequence for that element.

26. It is assumed that response elements regulate transcription at this step:

- \*1. initiation
2. elongation
3. intron splicing
4. polyadenylation
5. termination

27. Which of the following is/are proteins?

1. HSE
- \*2. HSTF
3. HSE and HSTF
4. HSE, GRE and SRE
5. GRE and SRE

28. Which of the following possible regulatory mechanisms is not mentioned as part of the heat shock response in eukaryotes?

1. increased transcription of some genes
2. decreased transcription of some genes
3. changes in translation of mRNAs
- \*4. changes in stability of mRNAs

29. Which of the following DNA sequences would you expect to bind the same proteins?

- \*1. HSE's from fruit flies and mice
2. Heat shock gene promoters from yeast and bacteria
3. BLE's and MRE's from the same metallothionein gene
4. MRE's and GRE's from the same metallothionein gene
5. BLE's and GRE's from the same metallothionein gene

30. Which of these changes would you expect to produce the largest change in the level of constitutive expression of the MT gene?

- \*1. Moving the TATA back 100 bases upstream.
2. Moving the BLE elements 200 bases upstream
3. Complete removal of the MRE element
4. Complete removal of the GRE element
5. Moving the MRE sequence 100 bases upstream.