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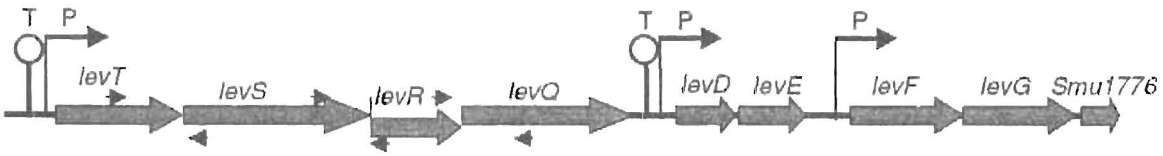
Section I

Please read the following paragraph and answer questions 1 to 3.

The *fruA* gene of *Streptococcus mutans*, the primary causative agent of human tooth decay, encodes for a secreted fructan hydrolase, which is a virulence determinant required for releasing D-fructose from levan- and inulin-type fructans. Expression of *fruA* is induced by growth in fructans. In *S. mutans* UA159, an operon (see the figure below) required for the expression of *fruA* was identified. This operon contained the genes (*levS and levR*) of a two-component system flanked by two genes (*levT* and *levQ*) predicted to encode the carbohydrate-binding proteins. These four genes were also essential for optimal growth of *S. mutans* on inulin-containing medium. In addition, this operon was shown to activate a four-gene cluster (*levD*, *levE*, *levF* and *levG*) located immediately downstream and encoding the Enzyme II (EII^{Lev}) complex for uptake of fructose and mannose, which was shown to negatively regulate the expression of *fruA*. Using transcriptional fusions, it was found that fructose could induce the *fruA* and *levD* operons through the two-component system/sugar-binding protein complex. Recombinant LevR protein was shown to bind to the promoter regions of *fruA* and *levD* in gel mobility shift assays. Thus, a 'four-component signal transduction system' activates fructan catabolism and the expression of an Enzyme II complex that functions in a feedback loop to sense the accumulation of the end-product of fructan degradation. (modified from "A novel signal transduction system and feedback loop regulate fructan hydrolase gene expression in *Streptococcus mutans* " published in in Molecular Microbiology. 2006; 62: 187–200)



P: promoter; T: transcription terminator.

1. Explain the following terms:
   a. Virulence determinant (7%)
   b. Operon (7%)
   c. Transcriptional fusion (7%)
   d. Gel mobility shift assays (7%)

(背面仍有題目,請繼續作答)

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2. What may be the role of LevR in production of secreted fructan hydrolase by *S. mutans* based on the observation described in this paragraph? (11%)

3. How would you demonstrate that the *levT-levS-levR-levQ* operon is required for growth of *S. mutans* on the inulin-containing medium? (11%)

Section II

4. (a) Describe the replication of herpes simplex virus (HSV). (5%)
   (b) What are the disease mechanisms of HSV? (5%)
   (c) Which antiviral drugs are available for the treatment of HSV infection? What are their targets and mechanisms of action? (6%)

5. (a) Describe the classification of retroviruses. (5%)
   (b) Describe the mechanisms of retrovirus oncogenesis. (5%)
   (c) Describe anti-HIV drugs and their modes of action. (6%)

6. What viruses can cause "common cold"? (6%)

7. WHO's 10-year campaign to eradicate smallpox started in 1966. The last naturally occurring case of smallpox was in Somalia in October, 1977. The eradication of smallpox was certified by WHO in 1980. For controlling polio infection, Global Polio Eradication Initiative (GPEI) was launched in 1988 by a collaboration led by WHO, Rotary International, UNICEF, and the US Centers for Disease Control and Prevention. The target date was set in the end of 2000. Despite significant advances, polio cases remained high in 4 countries, India, Pakistan, Afghanistan, and Nigeria. Why smallpox is easier than polio to be controlled in terms of viral characteristics, disease symptoms, vaccines, and other factors? (12%)