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Please read the following paragraph and answer questions 1 to 4.

The strong epidemiological association between cigarette smoke (CS) exposure and respiratory tract infections is conventionally attributed to immunosuppressive and irritant effects of CS on human cells. Since pathogenic bacteria such as *Staphylococcus aureus* are members of the normal microbiota and reside in close proximity to human nasopharyngeal cells, we hypothesized that bioactive components of CS might affect these organisms and potentiate their virulence. Using *Staphylococcus aureus* as a model organism, we observed that exposure to cigarette smoke extract (CSE) decreased expression of the quorum-sensing *agr* system, which is involved in biofilm dispersal, and increased transcription of biofilm inducers such as *sarA* and *rbf*. CS contains bioactive compounds, including free radicals and reactive oxygen species, and we observed transcriptional induction of bacterial oxidoreductases, including superoxide dismutase, following exposure. Moreover, pretreatment of CSE with an antioxidant abrogated CS-mediated enhancement of biofilms. Exposure of bacteria to hydrogen peroxide alone increased biofilm formation. These observations are consistent with the hypothesis that CS induces staphylococcal biofilm formation in an oxidant-dependent manner. These observations indicate that the bioactive effects of CS may extend to the resident microbiota of the nasopharynx, with implications for the pathogenesis of respiratory infection in CS-exposed humans. (Modified from the abstract of an article published in Infection and Immunity, 2012 80:3804-3811)

1. Explain the following terms:
   a. Microbiota (6%)
   b. Quorum-sensing system (6%)
   c. Superoxide dismutase (6%)
2. Briefly describe the morphology and pathogenicity of *Staphylococcus aureus*. (8%)
3. List the experimental results mentioned in this study that support the hypothesis that cigarette smoke may induce staphylococcal biofilm formation by the oxidants it contains. (12%)
4. Design a research plan by which you can show to people that biofilm formation is important for the virulence (ability to cause diseases or kill the animals) of *S. aureus* in the mouse? (12%)

（背面仍有題目，請繼續作答）

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5. $CD8^+$ T lymphocytes are present in the brain of mice infected with enterovirus 71. $CD8^+$ T lymphocytes may damage neurons and cause death of infected mice. Alternatively, $CD8^+$ T lymphocytes may protect mice from infection. Please design experiments to address the arguments. (15%)

6. Herpes simplex virus type 1 (HSV-1) infection is the most common cause of sporadic, fatal encephalitis, but current understanding of how the virus interacts with cellular factors to regulate disease progression is limited. Here, we show that HSV-1 infection induced the expression of the cellular transcription factor early growth response 1 (Egr-1) in a human neuronal cell line. Egr-1 increased viral replication by activating promoters of viral productive cycle genes through binding to its corresponding sequences in the viral promoters. Mouse studies confirmed that Egr-1 expression was enhanced in HSV-1-infected brains and that Egr-1 functions to promote viral replication in embryonic fibroblasts. Furthermore, Egr-1 deficiency or knockdown of Egr-1 by a DNA-based enzyme greatly reduced the mortality of HSV-1–infected mice by decreasing viral loads in tissues. This study provides what we believe is the first evidence that Egr-1 increases the mortality of HSV-1 encephalitis by enhancing viral replication. Moreover, blocking this cellular machinery exploited by the virus could prevent host mortality.

A. How does HSV-1 infection affect Egr-1 expression? (5%)

B. How does Egr-1 affect HSV-1 infection in vitro (in cells) and in vivo (in mice)? (10%)

7. Please describe how the following viruses replicate their genomes (20%).

A. Adenovirus
B. Dengue virus
C. Human immunodeficiency virus
D. Hepatitis B virus