

※ 考生請注意：本試題不可使用計算機。請於答案卷(卡)作答，於本試題紙上作答者，不予計分。

1. Please read the abstract and answer the following questions:

The recognition of microbial patterns by Toll-like receptors (TLRs) is critical for activation of the innate immune system. Although TLRs are expressed by human CD4<sup>+</sup> T cells, their function is not well understood. Here we found that engagement of TLR7 in CD4<sup>+</sup> T cells induced intracellular calcium flux with activation of an anergic gene-expression program dependent on the transcription factor NFATc2, as well as unresponsiveness of T cells. As chronic infection with RNA viruses such as human immunodeficiency virus type 1 (HIV-1) induces profound dysfunction of CD4<sup>+</sup> T cells, we investigated the role of TLR7-induced anergy in HIV-1 infection. Silencing of TLR7 markedly decreased the frequency of HIV-1-infected CD4<sup>+</sup> T cells and restored the responsiveness of those HIV-1+ CD4<sup>+</sup> T cells.

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- a. What are anergic T cells? In general, how T cells become anergic? (6%)
- b. TLR7 is one of important pattern recognition receptors to defense pathogen infection. What is the ligand of TLR7? (4%)
- c. How does infection by HIV lead to AIDS? (10%)
- d. In your opinion, what are the contributions of this research? (10%)

2. Enterovirus 71 (EV71) is a single-strand non-enveloped RNA virus. EV71 infection can cause from mild hand-foot-mouth disease to severe meningitis or fatal pulmonary edema in young children. Several serious EV71 endemic have occurred in Taiwan in recent years. Immune responses to EV71 are important to control the disease.

- a. One of the most important antiviral immune responses is to induce production of type-I interferons (IFN- $\alpha/\beta$ ). Please describe how IFN- $\alpha/\beta$  suppresses virus replication. (10%)
- b. To establish EV71 virus-specific adaptive immunity, processing of viral antigens to activate T cells is crucial. Please describe how the EV71 viral antigens been processed to CD4<sup>+</sup> and CD8<sup>+</sup> T cells. (15%)

3. Please describe what you know about hypersensitivity. (15%)

4. What are features of effective vaccines? (15%)

5. The 2014 Tang Prize in Biopharmaceutical Science is awarded to Dr. James P. Allison and Dr. Tasuku Honjo for the discoveries of CTLA-4 and PD-1. What are the functions of CTLA-4 and PD-1 in immune regulation and how to apply to cancer immunotherapy? (15%)