

※ 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. Homeostasis is essential for health and survival. Moreover, stress is a situation in which there exists a threat to homeostasis. When we are under stress, it is important to maintain blood pressure, to provide extra energy sources in the blood and to temporarily shut down nonessential functions. Please illustrate how our body responds to stress and returns to homeostasis. (12 points)
2. Please describe the events occurring during chemical synaptic transmission in a nervous system. (12 points)
3. “A prolonged, tetanic contraction is occurred in the skeletal muscles but not observed in the cardiac muscles.” Do you agree this statement? Why? (12 points)
4. When you first stand up after getting out of bed in the morning of cold winter, how does your pressure detected by the baroreceptors change? (12 points)
5. Hypoxia is defined as a deficiency of oxygen at the tissue level. Please describe the four categories of hypoxia, explain their causes and give an example for each category. (12 points)
6. If you are an excellent physiologist who is invited by National Institutes of Health (NIH) of USA to develop a new contraceptive, what would you do? Please describe the action mechanism of this contraceptive, which you are planning to develop. (12 points)
7. Please read the following abstract and answer questions (A) and (B).
(A) Please describe the aim and main results of the abstract of article. (12 points)
(B) Based on the results and conclusion of this article, what will be the next question that you are interested to investigate and what are the experiment(s) that you will design for answering this question? (16 points)

Title: Photo-releasable ligands to study intracrine angiotensin II signalling.

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Abstract:

Several lines of evidence suggest that intracellular angiotensin II (Ang-II) contributes to the regulation of cardiac contractility, renal salt reabsorption, vascular tone and metabolism; however, work on intracrine Ang-II signalling has been limited to indirect approaches because of a lack of selective intracellularly-acting probes. Here, we aimed to synthesize and characterize cell-permeable Ang-II analogues that are inactive without uncaging, but release active Ang-II upon exposure to a flash of ultraviolet light, as novel tools to study intracrine

Ang-II physiology. We prepared three novel caged Ang-II analogues, [Tyr(DMNB)⁴]Ang-II, Ang-II-ODMNB and [Tyr(DMNB)⁴]Ang-II-ODMNB, based upon the incorporation of the photolabile moiety 4,5-dimethoxy-2-nitrobenzyl (DMNB). Compared to Ang-II, the caged Ang-II analogues showed 2-3 orders of magnitude reduced affinity toward both angiotensin type-1 (AT1R) and type-2 (AT2R) receptors in competition binding assays, and greatly-reduced potency in contraction assays of rat thoracic aorta. Following ultraviolet irradiation, all three caged Ang-II analogues released Ang-II and potently induced contraction of rat thoracic aorta. [Tyr(DMNB)⁴]Ang-II showed the most rapid photolysis upon ultraviolet irradiation and was the focus of subsequent characterization. Whereas Ang-II and photolysed [Tyr(DMNB)⁴]Ang-II increased ERK1/2 phosphorylation (via AT1R) and cGMP production (AT2R), caged [Tyr(DMNB)⁴]Ang-II did not. Cellular uptake of [Tyr(DMNB)⁴]Ang-II was 4-fold greater than that of Ang-II and significantly greater than uptake driven by the positive-control HIV TAT(48-60) peptide. Intracellular photolysis of [Tyr(DMNB)⁴]Ang-II induced an increase in nucleoplasmic Ca²⁺ ([Ca²⁺]_n), and initiated 18S rRNA and NF-κB mRNA synthesis in adult cardiac cells. We conclude that caged Ang-II analogues represent powerful new tools to selectively study intracrine signalling via Ang-II.