

There are seven essays in this test. Each essay contains a text followed by few questions. Please answer these questions BRIEFLY according to the text provided to you.

**Assay I (15%):**

Osteoporosis is the most common bone disease, characterized by reduced bone density and an increased risk of fractures, affecting about 30% of women and 12% of men at some point during life. Osteoporosis occurs when the amount of bone removed from the skeleton by bone-resorbing osteoclasts exceeds that laid down by osteoblasts, the cells responsible for new bone formation. Restoring the imbalance between bone resorption and formation is therefore a key goal of pharmacological intervention in osteoporosis. Inhibitors of osteoclastic bone resorption, such as bisphosphonates, estrogen or selective estrogen receptor modulators, are already widely used in the treatment and prevention of osteoporosis. These agents reduce the occurrence of fractures but lack the ability to replace the substantial amounts of bone that have already been lost by the time osteoporosis has presented clinically. Drugs that stimulate new bone formation would therefore be a welcome addition to the therapeutic armamentarium in the treatment of established osteoporosis.

**Question:**

- I-1. Briefly describe the roles of osteoclast and osteoblast in osteoporosis? (5%)
- I-2. What agents have been used to treat osteoporosis? (5%) What are their shortcomings? (5%)

**Assay II (13%):**

Stem cells are cells with the capacity for unlimited or prolonged self-renewal that can produce at least one type of highly differentiated descendant. Usually, between the stem cell and its terminally differentiated progeny there is an intermediate population of committed progenitors with limited proliferative capacity and restricted differentiation potential, sometimes known as transit amplifying cells. Although a stem cell has high self-renewal capacity, it may actually divide relatively infrequently. Classically, mammalian stem cells have been studied in tissue such as blood and epidermis, where the differentiated cells do not divide and have a short life-span. However, stem cells are also present in tissues that normally undergo very limited regeneration or turnover, such as the brain and liver.

**Question:**

- II-1. What is stem cell? (5%)
- II-2. What are the major differences between stem cell and the differentiated cell? (5%)
- II-3. Where can you find stem cell? (3%)

**Assay III (10%):**

Body Worlds, traveling exhibition of skinned and preserved human bodies in lifelike postures, opened its doors in London last week. The revealing show is the brainchild of Gunther von Hagens, an independent anatomist who developed a "plastination" technique for preparing the specimens. Plastination replaces body fluid with special resins, making it possible to display whole bodies in dramatic poses. A pitcher, for instance, is frozen in midthrow, and a swimmer floats in midstroke. There are also disembodied spectacles, such as a complete human circulatory system. The exhibit, which has toured Europe and Japan in various forms since 1997, has been dogged by questions about how von Hagens obtain the specimens. He says some are the remains of friends, and that all donors approved the use of their bodies for education.

Ian Parkin, who runs a large-scale dissection facility for medical students at the University of Cambridge, says that exhibits are "very instructive" and that von Hagens is helping "return anatomy to the people and to demystify the inner workings of the human body." Body Worlds will be at London's Atlantis Gallery through the end of September.

**Question:**

- III-1. Please describe the plastination technique. (5%)  
III-2. How did von Hagens acquire his specimens? (5%)

**Assay IV (14%):**

Elephants in Africa inhabit two major vegetation types—savannah, bush and forest. Forest elephants differ in various aspects of size and morphology from savannah/bush elephants, but with some dissenting voice—most systematists have regarded them as members of a single species, *Loxodonta Africa*. Roca, Georgiadis, Pecon-Slatery and O'Brien compared the DNA sequences from two forms in four nuclear genes and found extensive genetic divergence between them and very little hybridization. The molecular data indicate that the two populations are as genetically distinct as lions are from tigers, and suggest that separate evolution for at least 2.5 million years and that the forest and savannah elephants should be classified as two distinct species that require individual attention in conservation programs. "The morphological evidence has been very, very strong," says conservation biologist Samuel Wasser of the university of Washington, Seattle. "When you see the genetic data, it seems almost a no-brained."

**Question:**

- IV-1. Please give a title. (3%)  
IV-2. Has Roca's group described the morphological differences between elephants? (3%)  
IV-3. "The two populations are as genetically distinct as lions are from tigers...." Please explain how can Roca et al reach this conclusion? (8%)

**Assay V (20%):**

Anthrax is a disease caused by the bacterium *Bacillus anthracis*. It normally affects cattle, sheep, goats, etc. It is acquired from spores that remain viable in the environment (e.g. soil) for decades always able to germinate into active bacteria if they get into the body of a susceptible host. Humans can be infected by *Bacillus anthracis*, and if the spores enter by way of the lungs, the disease can be quickly fatal. These properties have made it one of the agents favored by bioterrorists. It is not the tissue-destructiveness of the active bacteria that is the problem but rather the toxin that they secrete. The bacteria are susceptible to antibiotics, but they must be given early before the toxin can produce symptoms. Once the toxin is in the system, it can be neutralized by giving antitoxin antibodies. Presently these are harvested from donors who had received anthrax vaccine in the armed forces. But there is hope that monoclonal antibodies can be manufactured that will be able to provide protection.

The anthrax toxin is composed of three different proteins (encoded by genes on one of the two plasmids in the organism):

- PA ("protective antigen") It gets this name because it provides the epitopes that elicit protective antibodies in the anthrax vaccine.
- LF ("lethal factor")
- EF ("edema factor")

**Infection:**

- PA molecules bind to receptors at the cell surface assembling in clusters of 7.
- LF and/or EF molecules then bind to these clusters.
- The complex is engulfed by receptor mediated endocytosis.
- The drop in pH in the endosome (endocytic vesicle) produces a change in the structure of the PA cluster enabling it to release its LF and EF into the cytosol.
- EF is an adenyl cyclase which raises the intracellular concentration of cAMP inhibiting phagocytosis by neutrophils.
- As its name implies, LF in the cytosol so disturbs the machinery of the cell that it dies.

**Question:**

- V-1. Why Anthrax is one of the agents favored by bioterrorists? (5%)
- V-2. How can one neutralize the Anthrax toxin? (5%)
- V-3. Please illustrate the relationships among PA, LF, and EF during Anthrax infection. (10%)

**Assay VI (13%):**

The immune system and the nervous system are both composed of complex networks of primary and accessory cells that are in constant communication with each other. In both systems, a record of a primary cell's encounter with a stimulus is preserved, such that upon reencountering the stimulus, the system remembers it and responds. Transmembrane signaling through surface receptors of both neurons and lymphocytes is regulated by clustering of these receptors with each other and other molecules. Information is transferred at points of contact between cells called synapses. In two systems, they have in common a number of molecules that required for synapse formation and operation. Recently, Khan and colleagues report that agrin—a well-characterized glycoprotein in neuromuscular junction, which is specialized synapses between motor neurons and muscle cells—is also present in the immune system. The authors propose that immune cell agrin may participate in the clustering antigen-specific T cell receptors and accessory costimulatory molecules at the I-synapse between T lymphocytes and antigen-presenting cells. The molecule is in reorganization of membrane lipid microdomains and setting the threshold for T cell signaling.

**Question:**

VI-1. What is “agrins” and where can you find it? (5%)

VI-2. What are the functions of agrin. (8%)

**Assay VII (15%):**

What is the definition of life? I remember a conference of the scientific elite that sought to answer that questions. Is an enzyme alive? Is a virus alive? Is a cell alive? After many hours of launching promising balloons that defined life in a sentence, followed by equally conclusive punctures if these balloons, a solution seemed at hand: “The ability to reproduce—that is the essential characteristic of life,” said one statesman of science. Everyone nodded in agreement that the essential of a life was the ability to reproduce, until one small voice was heard. “Then one rabbit is dead. Two rabbits—a male and female—are alive but either one alone is dead.” At that point, we all became convinced that although everyone knows what life is there is no simple definition of life.

**Question:**

VII-1. So, what is your definition of life? (15%)