國立中山大學生物科學系 99 學年上學期
博士班資格考試(筆試)

科目：細胞分子生物學

※請由 9 題中選 5 題做答並標明題號，每題配分為 20 分（答題超過 5 題者，以得分最低的 5 題計算成績）

1. Please describe how actin and actin binding proteins work together to drive cell migration in detail. (Rac, Rho, PI3K, Wasp, Arp2/3, profilin, gelsolin, caping proteins, cofilin, myosin and -----)

2. Please describe how mammalian cell cycle progression is regulated in detail (distinct phases, driving force, quality control, monitoring, initiation and termination----).

3. Please give an example of RTK (receptor tyrosine kinase) mediated signaling pathway and describe its importance in regulating physiological function.

4. Please define the term" post-translational modification ". How is protein function affected by post-translational modification?

5. Both Mass spectrometry and bioinformatic information are powerful tools in proteomics research. There are two types of soft ionization in mass spectrometry for proteins, please describe it. Protein primary structure can be determined by chemical methods and from gene sequences. How mass spectrometry data and two-dimensional polyacrylamide gel could be used to identify a protein expressed in cancer cells but not in normal healthy cells.

6. DNA damage is unavoidable and arise in many ways. It can be cause by spontaneous cleavage of chemical bonds in DNA, by environmental factors such as UV, radiation…etc. Actually, DNA damage occur at a low frequency ! Please, describe the possible molecular mechanisms of DNA repair.

7. Describe differences (synthesis, chemical structure, functions) between of glycoprotein and proteoglycans.

8. Up to present, with ~720 membranes in total, G-protein-coupled receptors (GPCRs) represent the largest protein family in the human genome. It already represent the largest class of target molecules for drugs available in clinical. What is GPCR ? Describe molecular mechanisms of GPCR signal transduction. How to predict or discover a new GPCR ?

9. Most cell types cannot be differentiated so easily. A flow cytometer identifies cells by measuring the light that they scatter and the fluorescence that they emit as they flow through a laser beam; thus it can quantify the numbers of cells a particular type from a mixture. Describe principles and applications of flow cytometry and cell sorting? What is fluorescence-activated cell sorter (FASC)?

國立中山大學生物科學系 99 學年上學期
博士班資格考試(筆試)

科目：神經科學

※請由 10 題中選 5 題做答並標明題號，每題配分為 20 分（答題超過 5 題者，以得分最低的 5 題計算成績）

1. Describe experimental methods that plot the 'receptive field' of a target sensory cell (visual neuron). Compare receptive fields that can be recorded in retinal ganglia cells and neurons in primary visual cortex of mammals.

2. List the tracts of pyramidal and extrapyramidal system and describe the functions of each system.

3. A neuroscientist has isolated a compound which he thought would be a novel neurotransmitter in the brain. Please list logical criteria to identify it.

4. Describe how sound waves in air within the external auditory meatus are transduced into movements of the basilar membrane in the cochlea, and explain how sounds of different intensities and pitches are distinguished by the cochlea?

5. Describe the location and functions of 'Limbic System" in mammals.

6. An agricultural worker accidentally swallows an insecticide that acts by blocking the transfer of a signal from nerves to muscles. Her skeletal muscles become limp, but her heart muscle continues to contract rhythmically. How can you explain those symptoms?

7. GABA plays as an inhibitory neurotransmitter in adult central nervous system. However, results from recent studies have suggested a totally different role, meaning excitatory effect, while GABAA receptor is activated during very early of development. Describe the physiological significance for this excitatory/inhibitory switch and its underlying mechanism.

8. Most of the ion channels in the cell membrane of a neuron are selectively permeable to certain ion. For example, voltage-dependent sodium channel is selectively permeable to Na+ ion. Describe the underlying molecular mechanisms that make ion channel selective.

9. Compare the relative advantages and disadvantages conferred by electrical synapses and chemical synapses. Could large, active, intelligent animals have evolved with only electrical synapses?

10. Richard Axel and Linda B. Buck were awarded jointly the 2004 Nobel Prize in Physiology or Medicine for their discoveries of "odorant receptors and the organization of the olfactory system". Describe their major contribution in detail.

國立中山大學生物科學系 99 學年上學期
博士班資格考試(筆試)

科目：生理學

※請由 10 題中選 5 題做答並標明題號，每題配分為 20 分（答題超過 5 題者，以得分最低的 5 題計算成績）

1. Draw an oxygen-hemoglobin dissociation curves representing blood sampled from a healthy normal subject.
    a. Indicate the location on the curve that represents systemic venous and systemic arterial blood.
    b. Describe how the curve can be altered if the pH value of the blood switches to 7.5; the temperature of the blood switch to 32 degree C; and the pCO_2 of the blood is at 60mmHg.

2. In an experimental animal, the sympathetic preganglionic fibers to the adrenal glands are cut. Compare the heart rate, blood pressure, and the concentration of epinephrine in the blood of this animal at rest and during stress.

3. It has been hypothesized that “pineal gland” in the brain serves as a major mediator of Biological Clock in mammals. Please propose reasonable experiments to test this hypothesis.

4. Clarify the meaning of the following terms used in describing ‘ Biological Rhythms’
    a. Circadian rhythm
    b. Free running rhythm
    c. ‘ jet lag’ or ‘ phase shift of a rhythm ‘
    d. Environmental cues

5. Assume that a tissue chamber was separated into two compartments by an epithelial membrane, and electric potential across the membrane (PD) was recorded continually.
    a. What would the initial PD be if both compartments of the chamber were filled with physiological solution (saline)?
    b. What would the PD be, after 30 minutes of saline application?
    c. What would happen if Ouaban (a potent ATPase inhibitor) be added to the chamber in question b?

6. It has been suggested that low-dose aspirin could be a supplementary therapy for prevention of cardiovascular disease. What's the rationale and describe your opinion.

7. How does the body's endocrine system do its job while stress strike in?

8. Describe anything you know about 2010 Nobel Prize in physiology or medicine.

9. What makes neuron in central nervous system "difficult" to regenerate?

10. What keeps the blood moving in a single direction in the heart, the arteries, and the veins?

國立中山大學生物科學系 99 學年上學期
博士班資格考試(筆試)

科目：生物化學

※請由 10 題中選 5 題做答並標明題號，每題配分為 20 分（答題超過 5 題者，以得分最低的 5 題計算成績）

1. What are structural motif and DNA-binding mode of transcriptional factors?

2. Please propose the experimental procedure for elucidating protein-DNA interaction from *In vitro* to *In vivo*.

3. Please state how to study protein-protein interaction using system biology manner.

4. Please describe physiological significance of post-translational modification of proteins? How many kinds of post-translational modification of proteins?

5. Please describe distribution of lipids and proteins on eukaryotic cell membrane.

6. Draw the chemical structures of (I) a phospholipid molecule; (II) a tripeptide molecule (Arg-Met-Leu); (III) a 4-base single strand DNA (A-T-C-G) molecule.

   Instructions: (I) In this phospholipid structure, use R1 and R2 to represent the alkyl groups, X to represent the polar group attached to the phosphate. You must show the ester bonds. (II) In this tripeptide molecule, use R-arg, R-met, and R-leu to represent the reactive groups of the three amino acids, respectively. (III) In this single strand DNA molecule, use Na, Nt, Nc, and Ng to represent the nitrogen bases, respectively.

7. List the **names of pathways** that can produce NADH and/or NADPH in a model eukaryotic cell such as yeast. Why does a model eukaryotic cell need so many pathways to generate NADH/NADPH? Do these pathways serve as backups for each other in case one pathway does not function? Why or why not?

8. Explain oxidative stress, including the sources of the stress, consequences to cells for long term exposure, and how cells cope with the stress. Is this stress a build-in (born to be) part of eukaryotic cells? Do the generation mechanisms of oxidative stress pose any effects on evolution?

9. Explain how to measure enzyme activity. Use a case to explain each situation if you can.

10. Use no more than 150 words in either Chinese or English to summarize the news below, which was posted on Nov 28, 2010 at Harvard. Grading criteria: Who, what, how, why.

"Scientists at Dana-Farber Cancer Institute say they have for the first time partially reversed age-related degeneration in mice, resulting in new growth of the brain and testes, improved fertility, and the return of a lost cognitive function.

In a report posted online by the journal Nature in advance of print publication, researchers led by Ronald A. DePinho, a Harvard Medical School (HMS) professor of genetics, said they achieved the milestone in aging science by engineering mice with a controllable telomerase gene. The telomerase enzyme maintains the protective caps called telomeres that shield the ends of chromosomes.

As humans age, low levels of telomerase are associated with progressive erosion of telomeres, which may then contribute to tissue degeneration and functional decline in the elderly. By creating mice with a telomerase switch, the researchers were able to generate prematurely aged mice. The switch allowed the scientists to find out whether reactivating telomerase in the animals would restore telomeres and mitigate the signs and symptoms of aging. The work showed a dramatic reversal of many aspects of aging, including reversal of brain disease and infertility.

While human applications remain in the future, the strategy might one day be used to treat conditions such as rare genetic premature aging syndromes in which shortened telomeres play an important role, said DePinho, senior author of the report and the director of Dana-Farber's Belfer Institute for Applied Cancer Science. "Whether this would impact on normal aging is a more difficult question," he added. "But it is notable that telomere loss is associated with age-associated disorders and thus restoration of telomeres could alleviate such decline." The first author is Mariela Jaskelioff, a research fellow in medicine in DePinho's laboratory.

Importantly, the animals showed no signs of developing cancer. This remains a concern because cancer cells turn on telomerase to make themselves virtually immortal. DePinho said the risk can be minimized by switching on telomerase only for a matter of days or weeks — which may be brief

enough to avoid fueling hidden cancers or cause new ones to develop. Still, he observed, it is an important issue for further study.

In addition, DePinho said these results may provide new avenues for regenerative medicine, because they suggest that quiescent adult stem cells in severely aged tissues remain viable and can be reactivated to repair tissue damage.

“If you can remove the underlying damage and stresses that drive the aging process and cause stem cells to go into growth arrest, you may be able to recruit them back into a regenerative response to rejuvenate tissues and maintain health in the aged,” he said. Those stresses include the shortening of telomeres over time that causes cells and tissues to fail.

The experiments used mice that had been engineered to develop severe DNA and tissue damage as a result of abnormal, premature aging. These animals had short, dysfunctional telomeres and suffered a variety of age-related afflictions that progressed in successive generations of mice. Among the conditions were testes reduced in size and depleted of sperm, atrophied spleens, damage to the intestines, and shrinkage of the brain along with an inability to grow new brain cells.

“We wanted to know: If you could flip the telomerase switch on and restore telomeres in animals with entrenched age-related disease, what would happen?” explained DePinho. “Would it slow down aging, stabilize it, or even reverse it?”

Rather than supply the rodents with supplemental telomerase, the scientists devised a way to switch on the animals’ own dormant telomerase gene, known as TERT. They engineered the endogenous TERT gene to encode a fusion protein of TERT and the estrogen receptor. This fusion protein would only become activated with a special form of estrogen. With this setup, scientists could give the mice an estrogen-like drug at any time to stimulate the TERT-estrogen receptor fusion protein and make it active to maintain telomeres.

Against this backdrop, the researchers administered the estrogen drug to some of the mice via a time-release pellet inserted under the skin. Other animals, the controls, were given a pellet containing no active drug.

After four weeks, the scientists observed remarkable signs of rejuvenation in the treated mice. Overall, the mice exhibited increased levels of telomerase and lengthened telomeres, biological

changes indicative of cells returning to a growth state with reversal of tissue degeneration, and increase in size of the spleen, testes, and brain. “It was akin to a Ponce de León effect,” noted DePinho, referring to the Spanish explorer who sought the mythical Fountain of Youth.

“When we flipped the telomerase switch on and looked a month later, the brains had largely returned to normal,” said DePinho. More newborn nerve cells were observed, and the fatty myelin sheaths around nerve cells — which had become thinned in the aged animals — increased in diameter. In addition, the increase in telomerase revitalized slumbering brain stem cells so they could produce new neurons.

To show that all this new activity actually caused functional improvements, the scientists tested the mice’s ability to avoid a certain area where they detected unpleasant odors that they associated with danger, such as scents of predators or rotten food. They had lost that survival skill as their olfactory nerve cells atrophied, but after the telomerase boost, those nerves regenerated and the mice regained their crucial sense of smell.

“One of the most amazing changes was in the animals’ testes, which were essentially barren as aging caused the death and elimination of sperm cells,” recounted DePinho. “When we restored telomerase, the testes produced new sperm cells, and the animals’ fecundity was improved — their mates gave birth to larger litters.”

The telomerase boost also lengthened the rodents’ life spans compared to their untreated counterparts — but they did not live longer than normal mice, said the researchers.

The authors concluded, “This unprecedented reversal of age-related decline in the central nervous system and other organs vital to adult mammalian health justifies exploration of telomere rejuvenation strategies for age-associated diseases.”

Other authors include members of the DePinho research group and Eleftheria Maratos-Flier, an HMS professor of medicine at Beth Israel Deaconess Medical Center.

The research was supported by grants from the National Institutes of Health and the Belfer Foundation.”

國立中山大學生物科學系 99 學年上學期
博士班資格考試(筆試)

科目：免疫學

※請由 10 題中選 5 題做答並標明題號，每題配分為 20 分（答題超過 5 題者，以得分最低的 5 題計算成績）

1. 何謂株落選擇理論(clonal selection theory)？這項理論對免疫學的研究領域具有何種影響？

2. 佐劑是疫苗的重要成分，疫苗與佐劑相互配合方可增強免疫反應，故佐劑的開發及運用亦是疫苗製備的重點之一。根據目前的相關研究，可依照佐劑的作用機制將佐劑分為兩大類，即為 vaccine delivery systems 和 immunostimulatory adjuvants，請分別說明這兩大類佐劑如何增強免疫反應。

3. 體內非專一性免疫反應(non-specific immune responses)與專一性免疫反(specific immune responses)構成應付外來病原的兩大機制，請說明這兩大機制如何相互協調以清除外來病原？

4. 接種疫苗是目前對抗疾病的有效方法之一，請依照疫苗的製成成分將疫苗分類，並說明各類疫苗的製作過程？並請以引發有效的免疫反應為基礎提出疫苗的設計應注意哪些重點？

5. 專一性免疫反應具有四個特性，即antigen specificity、diversity、immunologic memory、self-nonself recognition，請分別**詳細解釋**這四個特性的意義。

6. 免疫學中的補體(complement)、抗體(antibody)及細胞免疫(cellular immunity)共同組成免疫學中的三大系統。請以 C3b 為例說明三者之間內在關聯的分子機制。

7. 某病人的皮膚具有片狀紅斑(sheet erythema)及點狀紅斑(point erythema)。血液檢查發現該患者的血小板為 10×10^9/L(正常值為 $100\sim300\times10^9$/L)並具有抗核抗體(ANA)。試分析該患者的免疫病理原因。

8. 某病人身上出現紫癜(purpura)。以下是該患者的血液檢查報告：

代號	檢查項目	結果	參考值
WBC	白細胞	7.13	$4\sim10\times10^9$/L
RBC	紅細胞	5.59	$3.5\sim5.5\times10^{12}$/L
PLT	血小板	15	$100\sim300\times10^9$/L
WPV	紅細胞平均體積	78	86~100fL
MPV	血小板平均體積	4.20	6.8~13.6fL
Anti-PLT	抗體	+++	陰性

試分析其中的致病機制。

9. 已知 C1 inhibitor 的缺失可導致血管神經性水腫，但 c1q 的缺失可導致系統性紅斑狼瘡。試分析 c1 inhibitor 及 c1q 缺失的免疫病理基礎。

10. 試分析 X 染色體連鎖的淋巴細胞增生症候群(X-linked lymphoproliferative syndrome，XLPS)的免疫機制。

國立中山大學生物科學系 99 學年上學期
博士班資格考試(筆試)

科目：植物生理學

※請由 10 題中選 5 題做答並標明題號，每題配分為 20 分（答題超過 5 題者，以得分最低的 5 題計算成績）

1. Describe how plants absorb water and minerals.

2. Describe how plants use sun energy to gain chemical energy.

3. Describe how light (blue and red) affect the morphogenesis during the growth and development.

4. Describe the molecular action of the plant hormones, give one example.

5. Describe how plants deal with the biotic and abiotic stress.

6. (a) Imdole-3-acetic acid (IAA) is the main plant growth regulator responsible for phototropism of stem. Please explain the possible mechanism. (b) Gibberellin (GA) is the most important plant growth regulator in the promotion of seed germination. Please use wheat seed as an example to explain how GA affects seed germination.

7. (a) Abscisic acid (ABA) is the plant growth regulator that regulates stomata opening. Please explain how ABA can regulate stomata opening under water stress? (b) Ethylene is the plant growth regulator that causes seedling triple response in Arabidopsis during seed germination. Please explain the possible mechanism how ethylene can cause seedling triple response during seed germination.

8. (a) Plants generally require appropriate photoperiod, light wavelength and phytochrome for transition from vegetative to reproductive growth. Please explain how the photoperiod, the wavelength of light (red light and far-red light), and phytochrome (Pr and Pfr forms) affect the flowering of short day and long day plants, respectively. (b) There are day-neutral plants, which their transition from vegetative to reproductive is much less influenced by environmental conditions. Use tobacco plant as an example to explain how the day-neutral plants make transition from vegetative to reproductive growth.

9. (a) Phenolics, terpenes, and alkaloids are the three major plant secondary metabolites. Please list the possible metabolic pathways for phenolics and terpenes biosynthesis in plants. (b) The basic structures of phenolics are C6-C1, C6-C3, (C6-C3)n, C6-C3-C6, and (C6-C3-C6)n. The terpenes can be divided further into monoterpene、sesquiterpene、diterpene、triterpene、tetraterpene and polyterpene. Please classify the following compounds to particular type of phenolics or terpenes.

   “Gibberellin, rubber, coumarin, anthocyanins, salicylic acid, squalene, lignin, condensed tannin, pyrethroids, lycopene, limonene.”

10. Please explain the following terms: host and nonhost resistance, gene-for-gene hypothesis, vertical resistance (major gene resistance) and horizontal resistance (polygene resistance), hypersensitive response, plant immunity, local and systemic acquired resistance, pathogen-derived resistance in plant-microbe interactions.

國立中山大學生物科學系 99 學年上學期
博士班資格考試(筆試)

科目：生態學

※請由 10 題中選 5 題做答並標明題號，每題配分為 20 分（答題超過 5 題者，以得分最低的 5 題計算成績）

1. 共域分布棲地重疊的物種可能以何種途徑達到共存(co-existence)並降低競爭?

2. 試述能量流轉與物質循環對食物網的重要性。

3. 試述棲地保育與物種保育這兩種策略所根植的科學基礎與政策執行上的差異。

4. 生物的分布如何受何環境與歷史因子影響？請各以一種區域特有性、孑遺分布性、全球廣布性以及間斷分布性生物說明之。

5. 請敘述一種群聚生態學領域的研究方法。

6. 請敘述土壤的分類。（可以用主要土綱類別敘述之）

7. 何謂假重複（pseudoreplication）？又如何在取樣時避免之。

8. 請敘述存在於熱帶地區平地的生物群落（biomes）以及它們之間的區別。

9. 依光合作用的三個主要途徑（C_3, C_4 和 CAM）分類之植物物種對於 CO_2 增加會有如何反應？

10. 植物生態學家 P. Grime 將植物的生活史策略分為 R, C 和 S 三類，請敘述此三類生活史策略以及在不同演替階段之優勢度。

國立中山大學生物科學系 99 學年上學期
博士班資格考試(筆試)

科目：行為生態學

※請由 10 題中選 5 題做答並標明題號，每題配分為 20 分（答題超過 5 題者，以得分最低的 5 題計算成績）

1. Three hypotheses were proposed to explain why male care in fishes is commonest with external fertilization. Please describe these hypotheses.

2. Explain how communication signals originate and how they are modified during evolution?

3. Describe the handicap hypothesis and Fisher's hypothesis related to the elaborate male sexual displays.

4. Animals compete for resources by exploitation or by territoriality. Please compare these strategies and explain when it pays to compete by means of territorial defense rather than exploitation.

5. Define or explain TEN of the following terms:

a. war of attrition	b. economics of prey choice	c. harem
d. ethology	e. evolutionary stable strategy	f.. polyandry
g. promiscuity	h. behavioral ecology	i. lek
j. hawk-dove model	k. ideal free distribution	l. ritualization
m. resource value	n. mutualism	o. game theory

6. 請詳述何謂 parental care? 其對非真社會性動物(eusocial animals)的意義為何？

7. 個體間的敵對行為對於群聚動物的利弊為何？試申論之。

8. 請問如何判斷生物行為乃由本能或個體學習而來？

9. 何謂 honest signalling？

10. 試述雌性動物以何種策略防止性騷擾？

國立中山大學生物科學系 99 學年上學期
博士班資格考試(筆試)

科目：族群生物學

※請由 10 題中選 5 題做答並標明題號，每題配分為 20 分（答題超過 5 題者，以得分最低的 5 題計算成績）

1. Why is Earth "just right" for life? What does problem happened in past 100 years? Please use the viewpoint of biodiversity and conservation biology to explain it.

2. In past 50 years, several International Conventions and Protocols are focused on conservation biology and biodiversity. Please figure out what Conventions and Protocols in past 50 years.

3. To evaluate the inbreeding or outcrossing, please use data below to estimate the population genetics and give suggestion to manage this species.

Pop	**Locus**	**No. of alleles**	**No. of effective allele**	H_O	H_E
Crest Line 1	primer5	8.000	3.991	0.000	0.749
	primer49	6.000	3.749	0.000	0.733
	primer69	18.000	7.416	0.060	0.865
	primer107	11.000	5.681	0.000	0.824
	primer172	8.000	5.470	0.000	0.817
	primer195	16.000	7.017	0.190	0.857

4. Based on conservation genetics, please discuss the factors that affect the island endemic species more than continental endemic species, why?

5. IUCN Red List Categories classify species into different levels by different rule, please clear to describe the criteria to define the level of endangered species.

6. Discuss the three distribution patterns of individuals within a population and explain the conditions that give rise to each pattern.

7. Describe several approaches used by ecologists to establish age structure for plant and animal populations.

8. Contrast the density-dependent and density-independent mechanisms of population regulation.

9. Why do some species have a larger home range than others? Explain why a carnivorous mammal requires a larger home range than an herbivorous mammal of similar body size.

10. Explain how the outcome of competition between two species is a function of both species and environmental characteristics.