

國立中山大學九十三年學年度碩士班招生考試試題

科目：生物化學（生物醫學研究所碩士班）

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- (1) 請說明在酵素動力學研究工作中，(a) Hill plot (b) k_{cat}/K_m 能提供何種實驗結果 (10 分)
- (2) 請說明 Protein evolution 產生的可能機制為何？ (10 分)
- (3) 如果已知一蛋白質轉譯後修飾作用為 Myristoylation，並且會受 Ca^{2+} 的調控將此基團暴露於蛋白質表面進而與 Membrane protein 產生 Protein-Protein interaction，請問(a) Myristoylation 對此蛋白質之功能影響為何？ (b)如何分析 Ca^{2+} 對此蛋白質功能之調控 (10 分)
- (4) 某同學分析一蛋白質序列得知可能含有 Leucine-zipper motif 及 Zinc-finger motif，請問(a) 如何確認此 motif 所在位置；(b)如何分析其為 Functional motif (10 分)
- (5) Chymotrypsin 水解 Substrate 時可能產生 Acyl-enzyme complex，請問如何證明此 Intermediate 可能存在(10 分)
- (6) 請比較 cDNA microarray 及 Antibody microarray 所能提供的實驗數據，及其優劣點為何？(10 分)
- (7) 經由 Two-dimensional electrophoresis 及 Mass analysis 已知一蛋白質在癌細胞有大量表現，你如何進一步分析其和癌症發生的相關性？(10 分)

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(8) 下列為一科學論文之摘要，請說明其所使用實驗技術(劃線部分)

如何進行(10分)

Vitamin D₃ has been shown to upregulate p27^{Kip1} expression via Sp1 and NF- κ B binding sites in the p27^{Kip1} promoter. However, whether vitamin D₃ receptor (VDR) involves in this process is unclear. In this study, we demonstrated that expression of VDR in SW620 cells, which exhibited low level of endogenous VDR, increased vitamin D₃-stimulated p27^{Kip1} promoter activity. On the contrary, suppression of Sp1 expression by small interference RNA reduced the stimulation of p27^{Kip1} promoter activity by vitamin D₃ in LNCaP cells. DNA affinity precipitation assay and chromatin immunoprecipitation assay showed that VDR bound to the p27^{Kip1} promoter *in vitro* and *in vivo*. In addition, we also demonstrated that VDR interacted with Sp1 *in vitro* and in cells. Collectively, our results suggest that VDR is involved in the induction of p27^{Kip1} by vitamin D₃ and may interact with Sp1 to modulate the expression of target genes that lack VDR response element (VDRE) in their promoters.

解釋名詞 (每題 5 分，共 20 分)

- (a) Ramachandran plot
- (b) Humanized antibodies
- (c) Flip-flop of lipids
- (d) Sialic acid

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^{read}
Note: ~~read~~ all questions carefully. Write legibly. Answer all questions on the sheets provided.
A total of 50 questions, two points each, perfect score = 100 points.

I. Transmission Genetics & Genomics (17 questions)

1. What is **not** the reason that Mendel succeed when others had failed? (1) Mendel used a plant in which he could control the matings (2) he repeated his experiments and obtained consistent results (3) he kept multilocus records and counted large numbers of progeny (4) he used continuous traits that were consistent within a strain.
2. A woman who is blood type A and a man who is blood type B have a child who is blood type O, what is the probability that a second child would be also be type O? (1) 1 (2) 1/2 (3) 1/4 (4) 3/4.
3. Bacteria that produce colonies containing a red pigment were distributed on nutrient agar and exposed to ultraviolet light for several days. The colonies that developed were red, with the exception of one colony that was white. The appearance of this white bacterial colony most likely resulted from (1) codominance (2) a mutation (3) synapsis (4) multiple alleles.
4. A genetic ratio of 2:1 is consistent with (1) complete dominance (2) recessive lethal (3) epistasis (4) co-dominant.
5. If there is one single pair of alleles that determine the number of toes for an animal species and homozygous dominant individuals have 8 toes, heterozygous ones have 7, and homozygous recessive ones have 6, the inheritance pattern would be referred to as (1) intermediate expression (2) genome imprinting (3) pleiotropy (4) maternal inheritance.
6. Two genes are 3.8 cM apart means (1) the physical distance between these genes is 3.8 Kb (2) the physical distance between these genes is 380 bp (3) the frequency of recombination between these two genes is 3.8% (4) the frequency of recombination between these two genes is 38%.
7. Punnett squares can be used to predict the probability of (1) being exposed to a contagious disease and contracting it (2) have an inherited disease or a genetically determined physical trait (3) both (1) & (2); (4) neither (1) or (2).
8. Pure-breeding long-fingered mice were bred to pure-breeding short-fingered mice. The F_1 were all long-fingered. The F_1 were crossed to obtain the F_2 . The F_2 data were: 9 long: 4 short: 3 stubby. How many genes controlling this trait? (1) one (2) two (3) three (4) four.
9. What are the goals of reproductive cloning with species other than Man? (1) to create new species (2) to

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save species facing extinction, such as the panda (3) to give birth to mythological creatures, such as Cerberus the three-headed dog (4) all of the above.

10. Scientists conducted a study of identical twins who were separated at birth and raised in different homes. They found that in some sets of twins the individuals showed a marked difference in intelligence. The most likely explanation for this difference is that (1) expression of inherited traits can modify the environment (2) environment can influence the development and expression of inherited traits (3) intelligence is a sex-linked trait (4) environment can not influence the expression of genes.
11. The function of "low-copy-number DNA" is (1) encoding most genes (2) encoding rRNA (3) encoding a single gene (4) encoding tRNA.
12. Which of the following are mismatches? (1) simple tandem array-repetitive sequence in the same orientation (2) compound tandem array-repetitive sequence in the same orientation (3) inverted repeats-repetitive sequence in the opposite orientation (4) single-copy gene sequence is not repeated.
13. A protein whose expression is needed in very large amounts for very short periods of time only, such as the oncogene product *c-Fos*, might be expected (1) to have a very unstable mRNA (2) to have a highly stable mRNA (3) to be encoded in multiple copies (4) to be present on a plasmid.
14. Why is a mapping function necessary for loci separated by more than about 7-10 map units? (1) double or even number of crossovers (2) single or odd number of crossovers (3) can not identify any crossovers (4) too many crossovers.
15. What functional class does most genes in a sequenced genome fall under? (1) unknown function (2) house-keeping (3) metabolism (4) cell cycle.
16. A highly variable gene variant or DNA sequence present in more than 1% of a population is called (1) polymorphism (2) VNTR (3) RFLP (4) STR.
17. What genetic information can be used to trace maternal lineage? (1) X-chromosome (2) Y-chromosome (3) nuclear genes (4) mitochondrial genes.

II. Cytogenetics (8 questions)

1. The gene-chromosome theory states that (1) chromosomes from both parents always have identical genes (2) homologous chromosomes do not have alleles (3) genes exist at definite loci in a linear sequence on chromosomes (4) Mendel's principles no longer apply to genetics.
2. Which of the statement is true (1) sex chromosome monosomy has worse phenotypic effects than somatic chromosome monosomy (2) polyploid plants often have smaller fruits, flowers and leaves (3) large scale inversions are more deleterious than large scale deletions (4) allopolyploidy results from hybridization

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between two species.

3. What aspect of chromosome behavior most clearly accounts for Mendel's law of Independent Assortment? (1) movement of sister chromatids to opposite poles at anaphase II of meiosis (2) movement of homologous chromosomes to opposite poles at anaphase I of meiosis (3) crossing over between sister chromatids during prophase I of meiosis (4) independent alignment of different homologous pairs on the metaphase I spindle.
4. Which one statement is **not** true about polyploidy? (1) if all of the chromosome are involved in non-disjunction, the result would be a change in the ploidy level or a triploid (2) higher ploidy levels result in a higher number of gene copies which is an effective way to increase gene product production (3) for most animals, triploidy and higher level ploidy states are compatible with normal development (4) plants seems to be able to tolerate ploidy level changes and tend to be rely on ploidy differences.
5. In *Drosophila*, males are XY and females are XX. What is the sex determination system in the *Drosophila*? (1) a dominant factor on Y determines maleness (2) a dominant factor on X chromosome determines femaleness (3) balance of X chromosomes to the number of sets of autosomes, when ratio > 1 , the fly is female, when it is < 0.5 , the fly is male, hence XO is male but XXY is female (4) balance of X chromosomes to the number of sets of autosomes, when ratio > 1 , the fly is male, when it is < 0.5 , the fly is female, hence XO is female but XXY is male.
6. In a G-banding karyotype, where are the most likely localizations for genes? (1) dark bands (2) light bands (3) evenly distributed (4) nothing to do with banding patterns.
7. A _____ chromosome has its centromere near a tip so that it has one long arm and one very short arm (1) metacentric (2) submetacentric (3) acrocentric (4) none of the above.
8. Nondisjunction in which parent leads to the sex chromosome aneuploid XYY? (1) mother (2) father (3) either parent (4) both parents.

III. Molecular Genetics (17 questions)

1. Watson and Crick had the following pieces of evidence in mind when solving the structure of DNA (1) Levene's ratios, Franklin's X-ray picture, double-stranded nature, chemical components described by Levene (2) Chargaff's ratios, Franklin's X-ray picture, RNA template, chemical components described by Levene (3) Chargaff's ratios, Franklin's X-ray picture, proposed helical form, chemical components describe by Levene (4) Levene's ratios, Griffith's X-ray picture, chemical components described by Levene
2. The template strand refers to (1) the DNA strand which is read by RNA polymerase that is, the strand which is complementary to the mRNA (2) the DNA strand which is not ready by RNA polymerase (*i.e.*, the stand which is equivalent to the mRNA) (3) the DNA strand to which restriction enzymes bind (4) the DNA strand to which the tRNA anticodon loop binds.

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3. RNA polymerase III is involved in the synthesis of (1) mRNA (2) DNA (3) RNA viruses such as influenza virus (4) the transcription tRNA genes and 5S rRNA.
4. Frederick Sanger developed the Sanger method of DNA sequencing, also known as (1) cloning (2) DNA fingerprinting (3) the chain termination method (4) genomics.
5. Which of the following pharmaceutical products is not produced by genetically modified *E. coli* cells? (1) erythropoietin (2) insulin (3) clotting factor VIII (4) interferon.
6. A synthetic fragment of single stranded DNA that signals when it has located complementary DNA in cells is called (1) a DNA vaccine (2) a signal sequence (3) DNA fingerprinting (4) a gene probe.
7. In the work of McKnight and Kingsbury, the labeled primer they created (1) has the same sequence as the coding strand and works in primer extension by hybridizing to the template strand (2) has the same sequence as the template strand and works in primer extension by hybridizing to the coding strand (3) has the same sequence as the coding strand and works in primer extension by hybridizing to mRNA (4) has the same sequence as the template strand and works in primer extension by hybridizing to mRNA.
8. Introns which are spliced out of pre-mRNAs are not translated into polypeptides as (1) they do not contain open reading frames (2) they are not capped or polyadenylated or transported from the nucleus (3) they do not contain initiation codons, Kozak sequences or Shine-Dalgarno sites (4) all of the above.
9. In eukaryotic cells translation (1) takes place in the nucleus (2) is initiated by a ribosome binding to the Shine-Dalgarno sequence (3) takes place in the cytoplasm (3) is coupled with transcription.
10. The Meselson-Stahl experiment provided conclusive evidence for the semi-conservative replication of DNA. However, imagine if DNA replication were conservative and you are conducted the Meselson-Stahl experiment. What pattern of bands would you see in the sedimentation gradient? (1) 1st round of replication: 1 intermediate band, 2nd round: 1 light, 1 intermediate (2) 1st round of replication: 1 heavy band, 1 light, 2nd round: 1 intermediate (3) 1st round of replication: 1 heavy band, 1 light, 2nd round: 1 heavy, 1 light (4) 1st round of replication: 1 intermediate band, 2nd round: 1 intermediate.
11. The genetic code resides in _____ and is both _____ and _____ (1) pre-mRNA, commaless, overlapping (2) mRNA, commaless, non-overlapping (3) DNA, punctuated, non-overlapping (4) mRNA, punctuated, overlapping.
12. Choose the best description of template binding during transcription in eukaryotes (1) TBP and TFIIIF help RNA polymerase II bind to enhancers and the TATA box (2) many transcription factors facilitate binding of RNA polymerase II to the TATA box (3) the sigma subunit of RNA polymerase II binds to the TATA box (4) transcription factors and the sigma subunit bind to the poly-A tail region.

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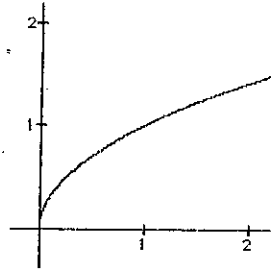
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13. Termination of transcription involves (1) hairpin loop formation of the poly-A repeat region (2) hairpin loop formation of the GC rich region (3) repair of telomeres in the GC rich region (4) repair of telomeres in the poly-A repeat region.
14. Select the correct order of action for the following list of enzymes during DNA replication (1) primase, ligase, polymerase I, gyrase, helicase (2) helicase, gyrase, polymerase III, polymerase I, ligase (3) polymerase I, polymerase III, gyrase, ligase, primase (4) ligase, helicase, primase, polymerase III, polymerase I.
15. DNA polymerase I is thought to add nucleotides (1) to the 5' end of primer (2) to the 3' end of the primer (3) in the place of the primer RNA after it is removed (4) on single-stranded templates without need for an RNA primer.
16. The activation process by which tRNA is bound to its corresponding amino acid is (1) changing (2) charging (3) coding (4) chargaff.
17. The bond between two amino acids is called a _____ bond and catalyzed by _____ (1) sulfide, aminoacyl synthetase (2) hydrogen, amino hydrogenase (3) phosphodiester, ligase (4) peptide, peptidyl transferase.

IV. Quantitative/Population Genetics & Bioinformatics (8 questions)

1. Breeders have developed a variety of chicken that has no feathers. Which methods were mostly likely used to produce this variety? (1) regeneration and incubation (2) artificial selection and inbreeding (3) grafting and hybridization (4) vegetative propagation and binary fission.
2. Assume that a cross is made between tall and dwarf tobacco plants. The F_1 generation showed intermediated height while the F_2 generation showed a distribution of height ranging from tall to dwarf, like the original parents, and many heights between the extremes. These data are consistent with which of the following mode of inheritance (1) polygenic inheritance (2) high frequency recombination (3) codominance (4) incomplete dominance.
3. For an organism with a diploid number of 10, what is the probability that all the chromosomes in a sperm cell will be derived from maternal homologs? (Assume no recombination) (1) $1/32$ (2) $1/64$ (3) $1/5$ (4) $1/10$.
4. Alcoholism is a trait that is often shared by members of the same family. This pattern (1) indicates that alcoholism has a high heritability (2) is explained by the fact that family members share many of the same genes (3) is explained by the fact that family members share similar environment (4) does not indicate the relative importance of genes or environment in determining the trait.
5. What factor is **not** likely to involve in evolution? (1) migration (2) genetic drift (3) carcinogen (4) mutation.

6. The data plotted here illustrate which relationship? (1) a normal distribution (2) an increasing, non-linear function (3) a decreasing linear function (4) an increasing, linear function.



7. The primary structure of a polypeptide means (1) the exact sequence of amino acids in the chain (2) the immediate structure of the chain, *e.g.*, and alpha-helix or beta-sheet (3) the overall three-dimensional structure of the protein (4) the exact structure as determined by X-ray crystallography.
8. Give an example of homology and similarity tool (1) PROSPECT (2) EMBOSS (3) RASMOL (4) BLAST.