請依題號順序於答案卷上作答，未依題序作答不予計分。

I. **Please fill out the specific terminology (Glossary) in each question.** (2% each, question 1-15)

1. An_____ is a viable DNA coding that occupies a given locus (position) on a chromosome.
2. _____ is the RNA splicing variation mechanism in which the exons of the primary gene transcript, the pre-mRNA, are separated and reconnected so as to produce alternative ribonucleotide arrangements.
3. The _____is a trinucleotide sequence in tRNA that is complementary to the codon in mRNA and enables the tRNA to place the appropriate amino acid in response to the codon.
4. _____ are proteins that assist the non-covalent folding/unfolding and the assembly/disassembly of other macromolecular structures, but do not occur in these structures when the latter are performing their normal biological functions.
5. A _____ site affects the activity only of sequences on its own molecule of DNA (or RNA); this property usually implies that the site does not code for protein
6. _____ describes a change in Ig gene organization in which the C region of the heavy chain is changed but the V region remains the same.
7. _____ describes the movement of a protein across a membrane as the protein is being synthesized. The term is usually restricted to cases in which the ribosome binds to the channel. This form of translocation may be restricted to the endoplasmic reticulum.
8. _____ is a reciprocal exchange of material between chromosomes that occurs during prophase I of meiosis and is responsible for genetic recombination.
9. A _____ mutation occurs when the gene product adversely affects the normal, wild-type gene product within the same cell. This usually occurs if the product can still interact with the same elements as the wild-type product, but block some aspect of its function. Such proteins may be competitive inhibitors of the normal protein functions.
10. _____ changes influence the phenotype without altering the genotype. They consist of changes in the properties of a cell that are inherited but that do not represent a change in genetic information.
11. _____ describes a type of repair system in which one strand of DNA is directly excised and then replaced by resynthesis using the complementary strand as template.

(背面仍有題目,請繼續作答)

12. A _____ is an intermediate structure in homologous recombination, for which the two duplexes of DNA are connected by the genetic material exchanged between two of the four strands, one from each duplex. A joint molecule is said to be resolved when nicks in the structure restore two separate DNA duplexes.

13. A _____ mutation is any change in DNA that replaces a codon specifying an amino acid with a translation-termination codon.

14. _____ describes the concept that two or more genes may fulfill the same function, so that no single one of them is essential.

15. The _____ hypothesis accounts for the ability of a tRNA to recognize more than one codon by unusual pairing with the third base of a codon.

II. Essay question (question 16-11)

16. In "Joomyeong Kim, et. el., Human Molecular Genetics, 2008, Vol. 17, No. 3 391–401", the authors tested the YY1 transcription factor that was predicted to control several domains, including the Peg3, Gnas and Xist/Tsix regions. They have used RNA interference strategies to generate transgenic mouse lines that express reduced levels of the cellular YY1 protein. They found that, in neonatal brains, lowering YY1 levels resulted in up-regulations of most genes within the Peg3 domain and down-regulation of Nespas gene within the Gnas domain, whereas three other transcripts were up-regulated, including Nesp, Gnasxl and Exon1A. In the Xist/Tsix domain, no obvious change was detected in the expression levels of the two genes in female mice. However, male mice showed low-level coordinated, up- and down-regulation of Xist and Tsix, respectively.

    a. What type of domains (genes) do you think Peg3, Gnas and Xist/Tsix regions belong to? (4%)

    b. In this particular type of genes, what kinds of transcriptional regulations do you think YY1 exerts? (6%)

    c. Two alternative terminologies specifically illustrating the regulatory sites (often displayed as tandem repeat sequence structures) within these regions. What are they? (6%)

    d. What is the most likely reason that the gender-specific outcome of Xist/Tsix domain was only **Low-Level**? (4%)

17. In the abstract of Bong-Gun Ju, et. al., Science, Vol 312, 2006, p1798-1802, they wrote: "Multiple enzymatic activities are required for transcriptional initiation. The enzyme DNA topoisomerase II associates with gene promoter regions and can generate breaks in doublestranded DNA (dsDNA). Therefore, it is of interest to know whether this enzyme is critical for regulated gene activation. We report that the signal-dependent activation of gene transcription by nuclear receptors and other classes of DNA binding transcription factors, including activating protein 1, requires DNA topoisomerase IIβ-dependent, transient, site-specific dsDNA break formation. Subsequent to the break, poly(adenosine diphosphate–ribose) polymerase–1 enzymatic activity is induced, which is required for a nucleosome-specific histone H1–high-mobility group B exchange event and for local changes of chromatin architecture.----------"

a. Please give a most appropriate title no more than 20 words for this paper. (10%)

b. In order to clarify the requirement of enzyme activity of TopoIIβ in the transcriptional activation in response to ERα–E2(17β-estradiol) interaction, they performed transient transfection assays in MCF7 cells using ERα reporter (β-galactosidase) activation system. In this system, they tried to employ (1) ERα ligand E2; (2) wild-type (WT) mouse TopoIIβ; (3) enzymatically inactive mutant mouse TopoIIβ (Pro723 Y Leu723); (4) human-specific TopoIIβ small interfering RNA (siRNA), and to measure the fold of β-galactosidase activity. Please draw a BAR FIGURE to apply the above listed 4 items and to exhibit your predicted results for the conclusion that enzymatic activity of TopoIIβ is indeed required for transcriptional activation in response to ligand treatment. (10%)

18. In "Ye V. Liu, et. al., Molecular Cell. 2007, Vol 25, p207–217", the authors found that Hypoxia-inducible factor 1 (HIF-1) regulates transcription in response to changes in O_2 concentration. O_2-dependent degradation of the HIF-1α subunit is mediated by prolyl hydroxylase (PHD), the von Hippel-Lindau (VHL)/Elongin- C/Elongin-B E3 ubiquitin ligase complex, and the proteasome. They have identified the receptor of activated protein kinase C (RACK1) as a HIF-1α-interacting protein that promotes PHD/VHL-independent proteasomal degradation of HIF-1α. RACK1 competes with HSP90 for binding to the PAS-A domain of HIF-1α in vitro and in human cells. HIF-1α degradation induced by the HSP90 inhibitor 17-allylaminogeldanamycin is abolished by RACK1 loss of function. RACK1 binds to Elongin-C and promotes ubiquitination of HIF-1α. Elongin- C-binding sites in RACK1 and VHL show significant sequence similarity.

a. What would be the best title (no more than 25 words) that you can give to summarize authors' works? (8%)

(背面仍有題目,請繼續作答)

b. Please draw a simple cartoon scheme to best represent this paper. (8%)

c. Although HIF-1α is either O_2-dependently or O_2-independently degraded, two players in addition to HIF-1α are commonly shared in the pathways. What are they? (4%)

d. In HIF-1α degradation pathways, what are the two proteins sharing the same or similar binding sites with RACK1? (4%)

e. According to authors' finding, what would you do to induce HIF-1α degradation during hypoxia? Please suggest three different treatments. (6%)