_____ _____

(Family Name, First Name) (Student No.)

FACULTY OF SCIENCE

FINAL EXAMINATION

BIOCHEMISTRY 507-454A

NUCLEIC ACIDS

Version 1

PLEASE MARK YOUR STUDENT NO. AND VERSION NO. ON YOUR COMPUTER SHEET.

Examiners: Dr. G. Shore (Coordinator)
Dr. N. Sonenberg
Dr. J. Pelletier
Dr. M. Tremblay
Dr. M. Park
Dr. C. Stanners

Monday, December 18th, 2000
09:00 hrs. - 12:00 noon

Answer all multiple-choice questions by blackening the corresponding number on the answer sheet. Your line must connect the brackets on either side of the number. If you change your mind, erase the mark completely, and then enter your new choice.

NOTE THE FOLLOWING FURTHER INSTRUCTIONS:

(l) Do not fold or bend the answer sheets.
(2) Blacken one space and only one for each question. If more than one space is blackened, the machine will reject your sheet.
(3) If you find it necessary to challenge a question, indicate the question challenged on the front page. Put your comments in the margin adjacent to the question.
(4) The mark values are given beside each question.
(5) This exam comprises 14 pages (does not include cover page, just the number of pages with questions).

Warning: Exam Security Monitor Program:

The examination Security Monitor Program detects pairs of students with unusually similar answer patters on multiple-choice exams. Data generated by this program can be used as admissible evidence, either to initiate or corroborate an investigation or a charge of cheating under Section 16 of the Code of Student Conduct and Disciplinary Procedures.

DO NOT TURN THIS PAGE
UNTIL YOU ARE TOLD TO DO SO.

NAME:_____STUDENT NO: _____
Course 507-454A Nucleic Acids:
Dr. N. Sonenberg's Section

Select the one which is best in each case, and mark the right answer on the computer score sheet.

1. DEAD box proteins function in splicing of pre-mRNAs:
(1 pt)

a) as kinases that phosphorylate splicing factors
b) as part of snRNPs (U1,U2...)
c) as helicases that destabilize secondary structure
d) by dephosphorylating splicing factors
e) by recognizing the 5N cap structure

2. Self-splicing of tetrahymena rRNA depends upon:
(1 pt)

a) generation of GTP
b) an exogenous guanosine
c) hydrolysis of ATP
d) hydrolysis of GTP
e) conserved consensus sequences

3. Nuclear tRNA splicing
(1 pt)

a) requires spliceosome formation
b) involves an ATP-dependent endonuclease
c) occurs in trans
d) depends upon lariat formation
e) requires the cap structure

4. 2,2,7-trimethylguanosine is found at the 5' end of
(1 pt)

a) eukaryotic mRNAs
b) U1 snRNA
c) U3 snRNA
d) 5S RNA
e) all small nuclear RNAs

5. U2-U6 pairing is required
(1 pt)

a) formation of the catalytic center
b) recognition of the 3' splice site
c) modification of RNA structure
d) dissociation of U2-U4 pairing
e) juxtaposition of the donor and acceptor splice sites

6. Thalassemia is caused (in some cases) by inappropriate splicing of
(1 pt)

a) U2 snRNA
b) plasminogen mRNA
c) immunoglobulin mRNA
d) globin mRNA
e) thalassemin mRNA

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Dr. N. Sonenberg's Section Cont.

Select the one which is best in each case, and mark the right answer on the computer score sheet.

7. Globin mRNA is spliced differentially (1 pt)

a) during development
b) in a tissue specific manner
c) in a species specific manner
d) to produce different proteins
e) globin mRNA is not spliced differentially

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Dr. N. Sonenberg's Section Cont.

For each of the statements below one or more are correct. Decide which answer(s) or completion(s) are correct and mark the correct answer on the computer score sheet:

1) if only a, b and c are correct
2) if only a and c are correct
3) if only b and d are correct
4) if only d is correct
5) if all are correct

8. Splicing of most nuclear pre-mRNAs requires:
(1 pt)
a) GU and AG at the 5N and 3N ends of introns
b) GTP
c) U4 and U6
d) A pyrimidine track downstream of the 3' splice site

9. U6 snRNP
(1 pt)
a) interacts with U2
b) is inactive when bound to U4
c) contains one RNA and several proteins
d) recognizes the branch site

10. SR proteins
(1 pt)
a) are involved in mitochondrial splicing
b) are components of the small nuclear RNPs
c) bind the 2,2,7-trimethylguanosine cap
d) contain serine/arginine-rich domains

11. Several forms of differential splicing have been reported. These include:
(1 pt)
a) optional exons
b) optional introns
c) mutually exclusive exons
d) internal splice sites

12. The yeast branch site intron sequence is
(1 pt)
a) UACUAAC
b) 100% conserved throughout evolution
c) critical for mRNA splicing
d) functions also in tRNA splicing

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Course 507-454A Nucleic Acids:
Dr. Sonenberg's Section Cont.

For each of the statements below one or more are correct. Decide which answer(s) or completion(s) are correct and mark the correct answer on the computer score sheet:

1) if only a, b and c are correct
2) if only a and c are correct
3) if only b and d are correct
4) if only d is correct
5) if all are correct

13. The U11 splicing system of some nuclear pre-mRNAs requires:
(1 pt)

a) GU and AG at the 5' and 3' splice junctions
b) U4 ATAC and U6 ATAC snRNAs
c) GTP
d) U12 snRNP

14. U3 and U1 RNAs have what in common?
(1 pt)

a) they possess a monomethylated cap structure
b) they are components of small nuclear RNPs
c) they both participate in splicing in ribosond RNA biogenesis
d) they both have nuclear functions

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Please answer briefly the following questions.

3.

A. Describe the optimal conditions needed for designing a gene targeting vector in the production of a knock-out animal.

(4 pts.)

B. The cloning of the sheep Dolly was extraordinary for which reason?

(3 pts.)

C. List the different embryo manipulations that are possible in the early stages of mammalian development.

(3 pts.)

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Dr. Morag Park's Section:

4. You have been hired by a pharmaceutical company to run their gene discovery program. Your goal is to identify new oncogenes in human tumors.

You have frozen tissue from a number of human tumors.

Describe the experiments you would perform to:-

A) Identify if this tumor harbored an active oncogene.

(3 marks)

B) If you show that there is an oncogene, describe experimentally how you would isolate it.

(3 marks)

C) Once you isolate your oncogene describe the approaches that you would undertake to understand its mechanism of activation.

(4 marks)

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Dr. C. Stanners' Section:

5.

a) You have a cell mutant that is resistant to drug X. Outline a method for cloning the full-length functional cDNA in the mutant that is responsible for this drug resistance.

(**8 marks**)

b) Suggest a plausible molecular model for the drug resistance and for the nature of the mutation.

(**4 marks**)

c) Using diagrams, assuming that your model in b) is correct, show what you would expect on Southern, Northern and Western blots using your cloned cDNA and appropriate antibody as probes. Provide brief explanations.

(**4 marks**)

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Dr. Stanners' Section

6. Tumor cells from a cancer patient are subjected to a genome scan and show at least 10 deletions relative to corresponding normal cells. How would you proceed to demonstrate which of these deletions could have been instrumental in causing the cancer?

(**6 marks**)

7. A dangerous virus from Africa is found to have a DNA genome consisting of 100 genes. Two of these are believed to be responsible for the virulence of the virus in that their functions are required to kill infected cells by integration into and inactivation of certain essential cellular genes. Outline one method for identifying them and cloning them, and identifying and cloning the cellular genes that are inactivated.

(**10 marks**).

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8. If your oligonucleotide synthesizer was capable of making nothing longer than 12mers, how large a genome library (consisting of lambda virus clones with inserts of 20 kb average in length) could be screened using these oligonucleotides as probes?

(**4 marks**).

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Dr. G. Shore's Section

9. A DNA microarray analysis of genes responsive to p53 during p53-induced apoptosis identified an mRNA transcript that was repressed by 10-fold. The corresponding cDNA contained an open reading frame encoding a novel protein of 281 amino acids. Computer-generated analysis of the protein sequence revealed the presence of sequence motifs typical of a transcription factor. You name the protein prp30 (p53-repressed protein of 30 kDa).

Suggest 2 models to explain how prp30 might function in p53-induced cell death. For each model give experimental approaches to elucidate the apoptosis signaling pathway(s) that is (are) influenced by prp30; this should include examples of known regulators of apoptosis as well as approaches that will identify new regulators of cell death.

(20 marks; 36 min)

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