Name: ______________________________ Date: ________________

Part A: simple questions on basic biology, with multiple choice answer (cross or underline the correct answer, 1 point for each correct answer)

1. The main constituent of the cell membrane is
   A. a strong polymer
   B. hyaluronic acid
   C. ATP
   D. a phospholipidic bilayer
   E. DNA

2. Proteins are assembled by
   A. the Golgi apparatus
   B. the ribosomes
   C. the lysosomes
   D. the cytoplasm
   E. the nucleus

3. How big is a human cell (order of magnitude)?
   A. 10 nm
   B. 100 nm
   C. 1 μm
   D. 10 μm
   E. 100 μm

4. Mutations in stem cells affect
   A. the human organism only
   B. future generations only
   C. both the organism and future generations

5. DNA synthesis occurs during the
   A. G1 phase
   B. S phase
   C. G2 phase
   D. M phase

6. The human genome has the following number of base pairs
   A. $5 \cdot 10^4$
   B. $3 \cdot 10^7$
   C. $3 \cdot 10^9$
   D. $6 \cdot 10^9$
   E. $3 \cdot 10^{10}$

Part B: further simple questions on basic biology (provide a short written answer, up to 2 points for each correct answer)

7. What is the correct pairing of the four bases in DNA?

8. What is chromatin?

9. What is a double-strand break?

10. What is an exon?

Part C: basic questions on the interaction of radiation with cells (either mark the correct answer or provide a short written answer, up to 2 points for each correct answer)

11. Which is the correct formula for stopping power (from the elementary derivation, without the relativistic correction terms)?

A. $-\frac{dE}{dx} = Kz^2 \rho \frac{Z}{A} \beta^2 \ln \frac{m_e c^2 \gamma^2 \beta^2}{2\pi I}$

B. $-\frac{dE}{dx} = K\rho \frac{Z}{Az^2} \frac{1}{\beta^2} \ln \frac{m_e c^2 \gamma^2 \beta^2}{2\pi I}$

C. $-\frac{dE}{dx} = Kz^2 \rho \frac{Z}{A} \frac{1}{\beta^2} \ln \frac{m_e c^2 \gamma^2 \beta^2}{2\pi I}$

D. $-\frac{dE}{dx} = Kz^2 \rho \frac{A}{Z} \frac{1}{\beta^2} \ln \frac{m_e c^2 \gamma^2 \beta^2}{2\pi I}$

12. What is the difference between stopping power and LET?

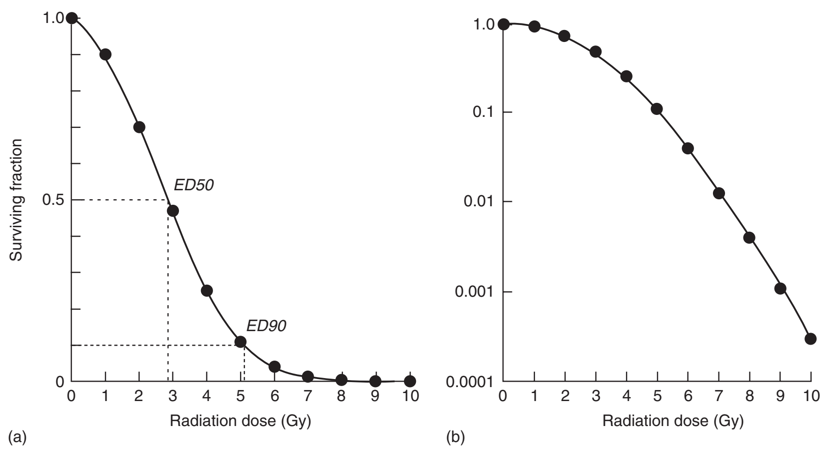
13. What is the difference between *direct* and *indirect radiation damage*?

14. What does the enzyme *superoxide dismutase* do?

15. What is the *oxygen effect*?

16. What is the role of the α and β coefficients in the linear-quadratic law? What does the α/β ratio mean?

17. A trivial question: consider the following figures, which represent survival curves. How do these survival curves differ? Motivate your answer.



Part D: this part contains discussions on a radiobiology argument highly relevant to radiotheraphy. Provide answers as requested in the text. (up to 2 points for each correct answer)

18. We begin with the Biologically Effective Dose (BED) as defined during the course: find the BED for a treatment 40F x 1.5Gy/8 weeks, both for early ($\alpha/\beta \approx 10$) and for late responding tissues ($\alpha/\beta \approx 3$).

19. Now we consider the effects of repopulation, i.e., tumor cell regrowth, in a treatment with a total dose D that takes a total time T and such that repopulation does not begin until time Tk (k stands for "kickoff", i.e., "kickoff time" in this case)

- write down the explicit expression for the surviving fraction after a total dose D

- after the kickoff time, the population of tumor cells restarts its growth: write down the expression of the exponential growth factor, assuming a population doubling time Tp

- combine the two factors to obtain an overall factor

- take the logarithm and divide by α, to obtain a new definition of the BED that takes into account tumor cell repopulation

Answers

Part A

1. D; 2. B; 3. D; 4. A.; 5. B; 6. C

Part B

7. A-T, G-C
8. It is a packaged form of DNA that consists mainly of DNA and proteins
9. It is a break in both strands of DNA
10. It is a coding (meaningful) part of DNA. This is in contrast to introns, which are the noncoding parts of DNA.

Part C

11. The correct answer is C. This can be inferred from the dependence on the parameters in front of the logarithm.

12. Stopping power works for charged particles only, while LET is defined for any particle beam, and this includes photons and neutrons.

13. Radiation can act on molecules – like DNA and proteins – directly, by breaking chemical bonds. It can also produce radiochemical species that act as mediators, and attack cellular components – and again DNA and proteins are among the targets.

14. SOD transforms the superoxide anion O_2^- into hydrogen peroxide.

15. The *oxygen effect* is the enhancement in the killing action of radiation due to the presence of oxygen.

16. The alpha coefficient corresponds to the linear dependence on total dose of the exponent in the survival probability. The beta coefficient is related instead to the quadratic dependence. The higher the ratio α/β, the greater the importance of the linear term. Since the quadratic term is associated to the probability of repeated damage, and this is smaller for cells with short proliferation times, then we observe smaller values of this ratio for cells with slow proliferation, and higher values for cells with fast proliferation. Since cells with slow proliferation also display the adverse effects of radiation on longer timescales, they are called "late responding". Likewise, cells which proliferate fast are called "early responding".

17. The curves represent the same data, but the curve on the right has a logarithmic vertical scale.

18. Starting from the linear-quadratic model

$$S = \exp\left(-\alpha D - \beta D^2\right)$$

we define a Biologically Effective Dose for fractioned treatments of *N* doses *d* and total dose *D* = *Nd*:

$$BED = D\left(1 + \frac{d}{\alpha/\beta}\right)$$

In this case N = 40; d = 1.5 Gy; so that the total dose is D = 60 Gy, and it is delivered over 8 weeks (7.5 Gy/week). Then

$$BED = 60\,\mathrm{Gy}\left(1 + \frac{1.5\,\mathrm{Gy}}{3\mathrm{Gy}}\right) = 90\,\mathrm{Gy} \qquad \text{(late responding)}$$

$$BED = 60\,\mathrm{Gy}\left(1 + \frac{1.5\,\mathrm{Gy}}{10\,\mathrm{Gy}}\right) = 69\,\mathrm{Gy} \qquad \text{(early responding)}$$

19. The surviving fraction is, as above

$$S = \exp\left(-\alpha D - \beta D^2\right)$$

After the kickoff time, the tumor cell population grows and is amplified by the exponential factor

$$\exp\left(\frac{T - Tk}{Tp/\ln 2}\right)$$

Therefore at the end of the total time T, we find that the tumor cell population has been multiplied times the factor

$$\exp\left(-\alpha D - \beta D^2\right)\exp\left(\frac{T - Tk}{Tp/\ln 2}\right) = \exp\left(-\alpha D - \beta D^2 + \frac{T - Tk}{Tp/\ln 2}\right)$$

and after easy passages we find a modified definition of BED, that takes into account the total treatment time

$$BED = D\left(1 + \frac{d}{\alpha/\beta}\right) - \frac{T - Tk}{\alpha Tp/\ln 2}$$