Name: _____ Date: _____

*This exam consists of 18 questions.*
*Each answer yields up to 2 points according to its correctness and completeness.*

1. What's the approximate size of a prokaryote cell?

2. What's the approximate size of a human cell?

3. What is the cell cycle? (explain)

4. Do human cells proliferate all the time? (explain)

5. What is the genetic code? (explain)

6. What is the difference between stopping power and LET? (explain)

7. Using the table below, find **a.** how many of hydrated electrons are produced, on average, when a 10 keV electron stops in water. And **b.** how many $H_2O_2$ molecules are produced by a 1000 eV electron that stops in water?

**Table 13.3** *G* Values (Number per 100 eV) for Various Species in Water at 0.28 $\mu$s for Electrons at Several Energies

| | Electron Energy (eV) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Species** | **100** | **200** | **500** | **750** | **1000** | **5000** | **10,000** | **20,000** |
| OH | 1.17 | 0.72 | 0.46 | 0.39 | 0.39 | 0.74 | 1.05 | 1.10 |
| $H_3O^+$ | 4.97 | 5.01 | 4.88 | 4.97 | 4.86 | 5.03 | 5.19 | 5.13 |
| $e^-_{aq}$ | 1.87 | 1.44 | 0.82 | 0.71 | 0.62 | 0.89 | 1.18 | 1.13 |
| H | 2.52 | 2.12 | 1.96 | 1.91 | 1.96 | 1.93 | 1.90 | 1.99 |
| $H_2$ | 0.74 | 0.86 | 0.99 | 0.95 | 0.93 | 0.84 | 0.81 | 0.80 |
| $H_2O_2$ | 1.84 | 2.04 | 2.04 | 2.00 | 1.97 | 1.86 | 1.81 | 1.80 |
| $Fe^{3+}$ | 17.9 | 15.5 | 12.7 | 12.3 | 12.6 | 12.9 | 13.9 | 14.1 |

8. A 100 $cm^3$ sample of water is given a dose of 100 mGy from 1 keV electrons. Use the table in exercise 7 to find how many $H_2O_2$ molecules are produced in the sample.

9. What is a tumor-suppressor gene? (explain)

10. How does the probability of tumor onset change with age? (explain)

11. What is the multitarget model? What is the expression of the survival probability in the multitarget model?

12. What is the Relative Biological Effectiveness? (explain)

13. How does a radiosensitizer work? (explain)

14. What is the Tumor Control Probability (TCP)?

15. What is the Normal Tissue Complication Probability (NTCP)?

16. What is the isoeffect equation? (explain)

17. How does dose-rate affect radiotherapy and why?

18. How does the redistribution of cells in the cell cycle affect radiotherapy?

**Answers**

1. Prokaryotes are small. Their size is about 1-2 μm.

2. Eukaryotes are larger. A typical human cell has a diameter of about 15-20 μm.

3. The cell cycle is the sequence of different steps required to duplicate a cell. Each step is called *phase*. The main phases are G1, S, G2, M. The duplication of DNA takes place during the S phase, and mitosis takes place in the M phase. Phases have different durations: the shortest phase is the M phase.

4. Human cells do not proliferate all the time, but only when needed. Cell proliferation is driven by several molecular signals. An uncontrolled proliferation is one of the hallmarks of cancer.

5. The genetic code is the sequence of nucleotides in the DNA that encodes useful information (not all of DNA encodes information, a large part of it – about 90% – is just junk). Useful sequences form genes. There are about 25000 genes in the human genome, and they encode the sequence of amino acids that are the building blocks of proteins.

6. Stopping power applies to charged particles. LET (Linear Energy Transfer) applies both to charged and neutral particle beams.

7. 118 hydrated electrons; 19.7 $H_2O_2$ molecules.

8. On average 1.2e15 molecules of $H_2O_2$ are produced.

9. A tumor-suppressor gene belongs to the DNA-damage sensing network, and it works by triggering repair, or apoptosis in the case of unrepairable damage.

10. The probability of tumor onset usually behaves as a power law $\sim t^k$, where $k \approx 5$ or 6.

11. In the multitarget model we assume that a cell dies only when multiple targets are all hit. So, if the probability of not hitting a given target is $e^{-D/D_0}$, then the probability of hitting the same target *at least once* is $1 - e^{-D/D_0}$, and therefore the probability of hitting all of the $n$ targets at least once is $(1 - e^{-D/D_0})^n$, and finally the probability of NOT hitting all of them at least once is

$$S(D) = 1 - (1 - e^{-D/D_0})^n$$

12. Different types of radiation produce different amounts of ionization and of ROS. This changes the shape of the survival probability curve. The RBE is defined as the ratio

$$RBE = \frac{D_X}{D}$$

where $D$ is the dose of radiation that corresponds to the same survival probability as an equivalent dose $D_X$ of X-rays.

13. A radiosensitizer works by mimicking a nucleotide and substituting it in the DNA strand. It is however different from the original nucleotide, its chemical bonds are weaker and make the DNA easier to damage.

14. The TCP is the probability of killing 2re $N$ tumor cells, then the average number of surviving cells is $NS(D)$, and the probability that no cell survives is $e^{-NS(D)}$. When we use the linear-quadratic law, we find

$$TCP = e^{-NS(D)} = e^{-N(\alpha D + \beta D^2)}$$

If the density of tumor cells in the target is $\delta$ and the target volume is V, we can also write

$$TCP = e^{-\delta V(\alpha D + \beta D^2)}$$

15. The NTCP is the probability of complications in the normal tissue surrounding a tumor. The NTCP depend on dose in a way that produces a sigmoid curve similar to that of TCP. The strategy in many kinds of therapy consists in separating the two curves as much as possible in order to have a high TCP and a low NTCP.

16. The usual equation for the Biologically Effective Dose is

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

where $d$ is the dose delivered in a single fraction and there are in all $n$ fractions, and the total dose is $D = nd$. Two different fractionation strategies correspond to the same BED (isoeffect) when

$$D_1\left(1 + \frac{d_1}{\alpha/\beta}\right) = D_2\left(1 + \frac{d_2}{\alpha/\beta}\right)$$

In particular, it is common to carry out a comparison with $d$ = 2 Gy, and then the total equivalent dose at 2 Gy is given by the isoeffect equation

$$EQD_{2Gy} = D\left(\frac{d + \alpha/\beta}{2Gy + \alpha/\beta}\right) = nd\left(\frac{d + \alpha/\beta}{2Gy + \alpha/\beta}\right)$$

17. A small dose-rate allows repair to take place during irradiation, and therefore it is less effective than a high dose-rate.

18. Cells are more resistant in the S-phase, therefore the cells that survive an initial dose are mostly in the S-phase. If one allows cells to redistribute over the other phases, then they are again more sensitive to radiation.