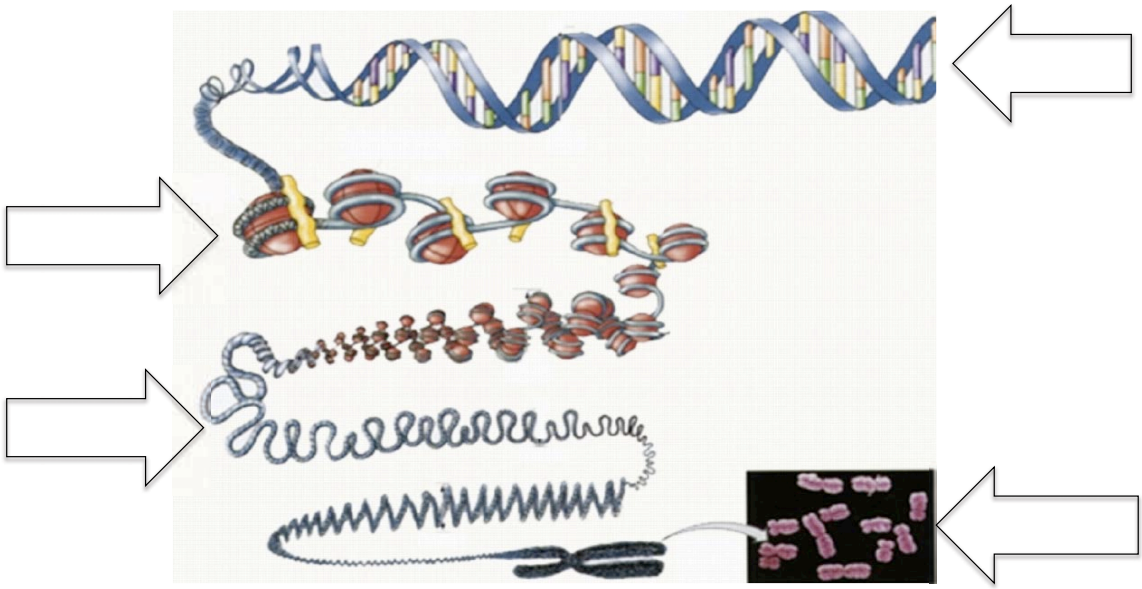
Name: _____ Date: _____

Each answer yields up to 2 points according to its correctness and completeness.

1. Assign names to the parts shown in this figure (chromatin; chromosome; DNA double strand; nucleosomes)



2. Name the nucleobases in DNA and explain how they bind.

3. Does a mutation in somatic cells affect the progeny as well as the individual? (explain)

4. What are the roles of stroma and parenchima? (explain)

5. Is it true that eukaryotic cells have internal membranes? (explain)

6. What is an oncogene? (explain)

7. Using the table below, find **a.** how many of hydrated electrons are produced, on average, when a 20-keV electron stops in water. And **b.** how many OH radicals are produced by a 500-eV electron that stops in water?

Table 13.3 *G* Values (Number per 100 eV) for Various Species in Water at 0.28 μs 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. What is the role of the enzyme *catalase*? (explain)

9. Why is the tumor microenvironment relevant to radiotherapy? (explain)

10. Provide a short derivation of the equation that gives the Surviving Fraction in the multitarget model.

11. How does the multitarget model differ from the Linear-Quadratic model?

12. Describe the Oxygen Effect and explain its importance in radiotherapy.

13. Draw a qualitative graph of the surviving fraction for both early-responding and late-responding cells.

14. Write the equation for the Biologically Effective Dose (BED) as a function $BED(D,N)$ of the **total** dose *D* and of the number of fractions *N*

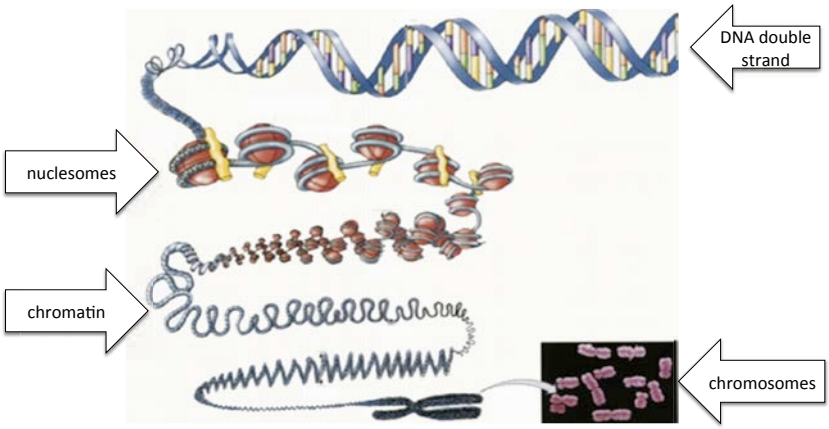
15. Consider the BED modified with the inclusion of total treatment time T in a fractionated radiotherapy

$$BED(D,N,T) = BED(D,N) - \frac{T - Tk}{\alpha Tp/\ln 2}$$

where N is the number of fractions, Tk is the kickoff time for tumor cell repopulation and Tp is the tumor population doubling time. Clearly, because of the time-dependent term, the longer we wait, and the less effective the treatment is;

- let Δt be the time between fractions and write the total time as a function of N and Δt
- use the previous result to rewrite the expression $BED(D,N,T)$ as a function $BED(D,N,\Delta T)$
- what is the rationale behind this formula? How is it related to the 4R's (or 5R's) of Radiobiology?

Answers



1.

2. Adenine-Thymine; Cytosine-Guanine

3. Mutations in somatic cells only affect the individual and not the progeny. Mutations in germ cells affect the progeny.

4. The stroma is that part of a tissue that has connective and structural role. The parenchima is made up of cells that perform the action of a given tissue or organ.

5. Unlike prokaryotes, eukaryotic cells have several internal membranes, like the nuclear membrane, the endoplasmic reticulum, and the Golgi apparatus.

6. Oncogenes stimulate cell growth. In tumors they are activated even in the absence of growth signals.

7. a. 226 hydrated electrons; b. 2.3 OH radicals

8. Catalase is a fast enzyme that transforms hydrogen peroxide – a dangerous Reactive Oxygen Species that can damage both DNA and other delicate cellular structures – into water.

9. The tumor microenvironment has high acidity, is hypoxic and has a high intracellular fluid pressure. It also has an irregular vascularization and no lymphatics. All this means that it is difficult to diffuse chemotherapic drugs into the tumor microenvironment, and hypoxia makes it difficult to kill the cells deep inside the microenvironment, because of the Oxygen Effect.

10. The probability of missing a target inside the cell must be given by the probability

$$P(0) = e^{-a}$$

where *a* is proportional to the dose, i.e.,

$$P(0) = e^{-D/D_0}$$

which also means that the probability of at least one hit is

$$1 - P(0) = 1 - e^{-D/D_0}$$

If there are multiple targets, say *n* targets, all of which must be hit to kill a cell, then the probability of hitting all of them at least once is

$$\left(1 - e^{-D/D_0}\right)^n$$

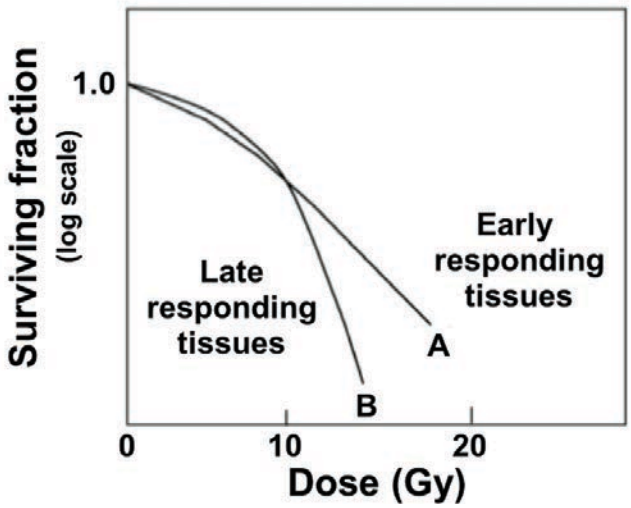
and therefore the probability of NOT hitting all of them at least once – i.e. the probability of surviving – is

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

11. The multitarget model has the wrong derivative for very low doses, but it has the correct curvature for very high doses, unlike the linear quadratic model.

12. The surviving fraction depends on the partial pressure (or concentration) of oxygen. It is found that for not too high LET's the surviving fraction is lower when the partial pressure of oxygen is high. Therefore tumor cells in hypoxic conditions are more resistant to radiation, and in radiotherapy it is important to reoxygenate tumor tissues as far as possible.

13.



and alpha/beta ≈ 10 Gy for early responding tissues, alpha/beta ≈ 3 Gy for late responding tissues.

14. $BED(D,N) = D\left(1+\frac{D/N}{\alpha/\beta}\right)$

15. The total time is $T = (N-1)\Delta t$. This means that

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

This expression has two terms: the first is positive and becomes larger for smaller *N*, the second becomes more negative for larger *N*. This means that the BED is largest for *N*=1.

This result is mathematically correct, but it is not acceptable in practice. Indeed the total dose in a regular treatment is of the order of several tens of Gy's, and this means that damage to healthy tissues in a non-fractionated treatment could be excessive. Thus, to optimize we should include at least one term that takes into account the normal tissue complication probability (NTCP).
Importantly, the modified BED formula includes repopulation.