

A. Ultraviolet radiations coming from the environment can affect the DNA of all cells. They can, for example, cause the formation of dimer between two successive thymines which blocks the duplication of the DNA (essential to mitosis).

We subject to ultraviolet radiations cultures of human cells taken from a normal person and from a person affected by a hereditary skin disease : *Xeroderma*.

Figure 1 shows the evolution of the percentage of modified thymines (found in dimer state) compared to the totality of the thymines of the DNA as a function of time.

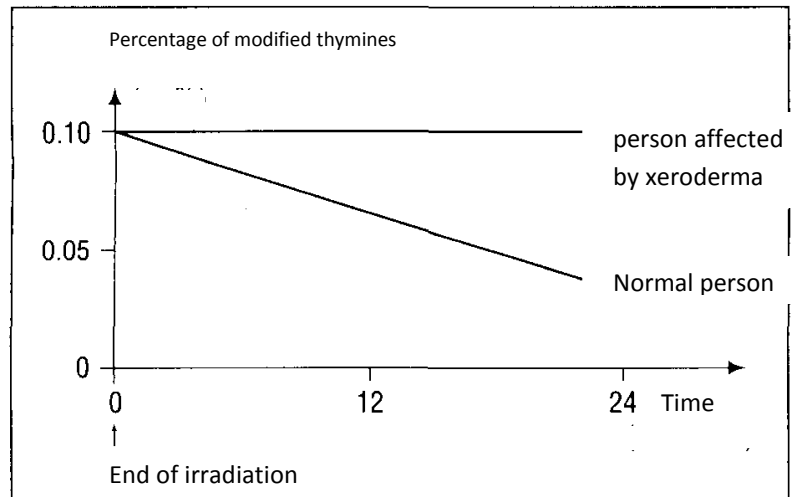


Fig 1. Evolution of the quantity of thymine in the dimer state.

1) Compare the influence of UV, at the end of irradiation, on the DNA of these two individuals.

2) Compare the evolution of the molecules of DNA as a function of time..

3) What difference could this provoke concerning the cells of these two subjects?

B. we propose to seek the origin of the difference observed in figure 1. For this purpose, we can use a biological model such as bacteria, whose DNA is free in the cytoplasm. Certain mutant bacterial strains present the same reaction to UV as the xerodermic cells.

We irradiate normal strains and mutant strains of these bacteria. Quickly, dimers of thymine are found in the cytoplasm of the normal cells, that continue then their multiplications, but we don't find dimers in the cytoplasm of the mutant cells, which stop multiplying.

4) Interpret these various results.

C. Other irradiations by ultraviolet rays are carried out on cultures of normal and xerodermic cells. We provide to these cells radioactive thymine and we measure the incorporation of the radioactivity (table 2). No cell retained for the study had time to duplicate its DNA.

normal epidermal cells non irradiated	normal epidermal cells after irradiation	Xerodermic epidermal cells after irradiation
no incorporation	all cells incorporate in varied places in their nuclei very small quantities of radioactivity	no incorporation

Table 2

5) From these results and those obtained thanks to the biological model, propose an explanation of the difference in the evolution of the DNA in table 2.

D. It was proven in experiments that the incorporation of radioactive thymine resumes again if we practice cuts on both sides of the dimers of DNA of the xerodermic cells.

6) What relation can we draw between the hereditary nature of this disease and the incapacity of the xerodermic cell revealed by the preceding experiments?

E. the mutated allele (noted -) responsible of this disease, is recessive with respect to the normal allele (noted +). A person +/- is normal.

7) How can you explain it from a molecular point of view and using your preceding answer?

8) Using the whole of the exercise, explain why each exposure to the Sun involves, in the xerodermic individuals, new and irreversible cutaneous lesions.

## CORRECTION

### II. A

- 1) At the end of irradiation ( $t=0$ ), the percentage of modified thymines in the DNA of both the normal person and the person affected with xeroderma is the same (0.1 %).  
PS: This means that the xerodermic cells are as sensitive to irradiation as the normal cells, they are not “more prone” to the formation of thymine dimers, but this is a question for another day...
- 2) In the xerodermic individual, the DNA is not evolving after the irradiation, the percentage of modified thymines remains constant at 0.1 %.  
In the normal individual, the percentage of modified thymines (thymine dimers) decreases from 0.1 % at  $t=0$  to 0.04 % at  $t=22$  hours. So the bottom line is that the modified thymines are being removed from the DNA of the normal person while they persist in the DNA of the xerodermic person.
- 3) The impact of this difference is that the cells of normal person could resume normal DNA duplication once they get rid of all the thymine dimers in their DNA while the cells of the xerodermic person will be incapable of duplicating their DNA because the thymine dimers are not removed from their DNA. Ultimately, this difference means that the cells of the normal person can resume their life cycles and undergo cell division while the cells of the xerodermic person can't and they will eventually die.

### B.

- 4) The irradiation of the two strains results in the formation of thymine dimers. The thymine dimers found, later on, in the cytoplasm of the normal strain mean that the normal bacteria were capable of cutting these dimers out of their DNA and, consequently, they resumed normal cycles and division. The absence of thymine dimers in the irradiated mutant strain shows that the mutant strain lacks the ability to cut out the dimers from its DNA which explains why they stopped multiplying.

Cutting out the thymine dimers from the DNA is the cause of the observed decrease in the percentage of thymine dimers (document 1, normal individual's case)

### C.

- 5) The non-irradiated normal cells did not incorporate radioactive thymines in their DNA while the normal cells that were irradiated with UV did incorporate radioactive thymines in their DNA.  
This means that incorporating new (radioactive) thymine in the DNA is part of a repair mechanism in normal cells. These normal cells probably cut out the thymine dimers (which explains why they appear in the cytoplasm) then replace them with fresh thymine which, in this case, happens to be radioactive.

Xerodermic cells are obviously incapable of repairing their DNA since they did not incorporate radioactive thymine and the thymine dimers persist in their DNA.

D.

6) The xerodermic cells can incorporate new thymine if the thymine dimers in their DNA were cut out (of course this “cutting out” doesn’t happen on its own, it needs the intervention of the experimenter). This shows that the xerodermic cells do have the required enzyme to incorporate new thymine in their DNA provided that the thymine dimers were cut out so their main disability is the lack of enzyme(s) that can remove the thymine dimers from the damaged DNA. Therefore the genetic defect involved is probably located in the gene coding for the enzyme that cuts out the thymine dimers.

7) The mutated allele is recessive with respect to the normal allele. From a molecular point of view, the mutated allele codes for a defective enzyme that cannot remove the thymine dimers while the normal allele codes for the functional enzyme that can remove these dimers.

A heterozygote individual thus has 50 % of the amount of the normal enzyme instead of having the full amount. It seems that 50 % of this amount is enough to repair the DNA up to an extent that allows resuming DNA duplication and cell division and thus having one copy of the mutated allele will not block cell division which explains why it is considered as recessive.

8) Sunlight contains UV radiations, exposure to this UV causes the formation of thymine dimers in both normal and xerodermic skin cells. The normal skin cells can easily remove these dimers, replace them with new thymines and resume normal DNA duplication and cell division, unlike the xerodermic cells.

The xerodermic cells fail to remove the thymine dimers, their DNA cannot replicate and the affected skin cell eventually dies which explains the cutaneous lesions.

Having that said, one question remains, what does this have to do with GLYCEMIA?

☺ Good bye everyone, you will be missed.