Children of the Night in *The Others*

H. David Urquiza Hernandez
(Miami Dade College, USA)

Children of the Night, Children of the Moon or Children of the Dark are names used for referring to children suffering from xeroderma pigmentosum, a rare genetic disease in which the affected children cannot be exposed to sunlight, which can be fatal for them. This disease have been explored in a few films: *Children of the Dark* (a made-for-TV film), *Dark Side of the Sun*, a direct-to-DVD film and, finally, a mainstream film depicting children with this disease, *The Others*, an acclaimed and award-winning film directed by Alejandro Amenábar, starring Nicole Kidman as Grace, Fionnula Flanagan as Bertha and Alakina Mann and James Bentley as the children[1]. In *The Others*, Grace, the mother, and her two children Anna and Nicholas live in a big, dark, almost empty house. Later, we find out that the children cannot be exposed to the sun, so they only play inside the house, which has been emptied of superfluous furniture for the children to have more space in which to run around. The mother employs a new maid (Bertha) and two other new servants, and a series of events occur in such a way that the family, and the audience, begins to believe that the house is haunted. This article focuses on the depiction of children with xeroderma pigmentosum as represented in this film and how the film's approach and description of the disease match with the reality that families with affected children find every day.

"In this house, you must not open any door without first locking the previous one"

Grace (talking to Bertha): *You may not think that, once you have met the twins. They aren't like other children. Have you noticed what I am doing? (She locks the door) In this house, you must not open any door without first locking the previous one. It is vital that you remember this…*[2]

These enigmatic lines appears almost at the beginning of the film, after we have seen already the strange ritual of Grace, holding a bunch of keys in one hand and following precisely this principle: closing (locking, in fact) one door before opening another one.

A few minutes later, Grace explains her behaviour to Bertha.

Grace: *The doctors were never able to find a cure.*
Bertha: *To what?*
Grace: *Their condition. The children are photosensitive, or, in other words, they're allergic to light. They must never be exposed to light stronger than this (Grace is holding an oil lamp). Otherwise, in a matter of minutes, they'd break out in sores and blisters and would begin to suffocate. It would eventually be fatal*[2]

In this way, Grace describes the disease that the children suffer from, xeroderma pigmentosum. Clinically, the disease manifests as persistent skin redness, blisters and sores, as a result of even a very brief exposition to sunlight. It affects mainly the face, lips, eyes, scalp and other areas of the skin exposed to the sun. Ocular damage is very frequent. The signs of the disease normally appear in early childhood. Freckle-like pigmentation is common and around 25% of these children have neurological impairment[3,4]. These patients have up to 10 000-fold increased risk of some types of skin cancer, with a median age of onset of 8 years compared with 60 years in the normal population[4].

"The light has to be contained as if it were water"

Grace (talking to Bertha): *This house is like a ship. The light has to be contained as if it were water, by opening and closing the doors. The health of my children is at stake!*[2]

Grace made a brilliant comparison here. Light is a form of electromagnetic radiation (ER) and we are immersed in an ocean of ER. The ER that reaches us constantly can be produced as far away as distant galaxies and as near as microwave oven, TV receptors or mobile phones. The entire range of ER forms the electromagnetic spectrum[5] (Figure 1).

ER is a form of energy that has the duality of behaving both as waves and as particles. The particles of ER are photons. An important characteristic of ER is the wavelength (the distance between two successive peaks or troughs). Observe in Figure 1 that what we call light (or visible light) is just an extremely tiny part of the electromagnetic spectrum. Light is just this very small range of ER that is able to stimulate the receptors in

our retina. The wavelengths that we are able to visualize are approximately in the range of 700 nm (red) to 390 nm (violet). ER with a longer wavelength than that we perceive as red has lower energy than that required for stimulating our optical receptors, which is why we are not able to see IR radiation, whereas ER in the UV range is absorbed by the structure of cornea and lens, so usually they do not reach our retina (Figure 2).

In fact, because of the high energy of UV radiation, it can damage biological structures.

The main source of UV radiation is the sun. The atmosphere protects us from high-energy electromagnetic radiations such as gamma rays and most of the UV radiation[6].

The damaging rays of the sun

Even with the atmospheric filter, the structural and functional integrity of DNA is constantly under the burden of UV radiation and other chemical and mutagen agents that can reach the cells. That is the reason that living beings have several mechanisms for monitoring, scanning and repairing damage in DNA. These mechanisms have collectively been called DNA-damage response[7]. The most ubiquitous environmental agent that damages DNA is UV light. It has been described that the residual UV in a strongly illuminated day can cause approximately 100 000 lesions per cell per hour. Nucleotide excision repair[8] (NER) is a particularly important mechanism in the repairing of lesions caused by UV light in DNA (so important that Aziz Sancar received recently the Nobel Prize for Chemistry in 2015 for his research on this topic). The NER system recognizes distortions in the helicoidal structure of DNA, caused by lesions in the nitrogen bases that form DNA. Damage caused by UV radiation in DNA is mainly the production of dimers of thymine and other adducts, i.e. the action of UV activate atoms in the DNA, producing abnormal bonds between the nitrogen base components of the nucleic acid or between photoproducts of these bases (Figure 3) (imagine a metallic ladder in which one step is melted by the action of an electrical ray and the melted step stays glued to the previous or following step in the ladder).

The distortion in the normal structure of DNA by the formation of these abnormal bonds appears as bulging lesions and they are detected by proteins that form part of this damage-scanning mechanism.

DNA damage and repair

NER operates through two pathways, and it is known that at least the products of seven different genes participate in repairing the DNA damaged by the UV light. These genes were characterized studying patients suffering from xeroderma pigmentosum, so they have been abbreviated *XPA*, *XPB*, *XPC*, *XPD*, *XPE*, *XPF* and *XPG*. These genes have the information required to form proteins that participate in NER.

The steps in repairing the DNA lesions include the following[8,9].

- Damage recognition: some proteins encoded in XP genes recognize the 'bulges' formed in DNA as a result of UV damage.
- DNA unwinding: since DNA is a helicoidal double-stranded molecule, it is necessary to unwind the molecule so the damaged areas are more accessible for repair.

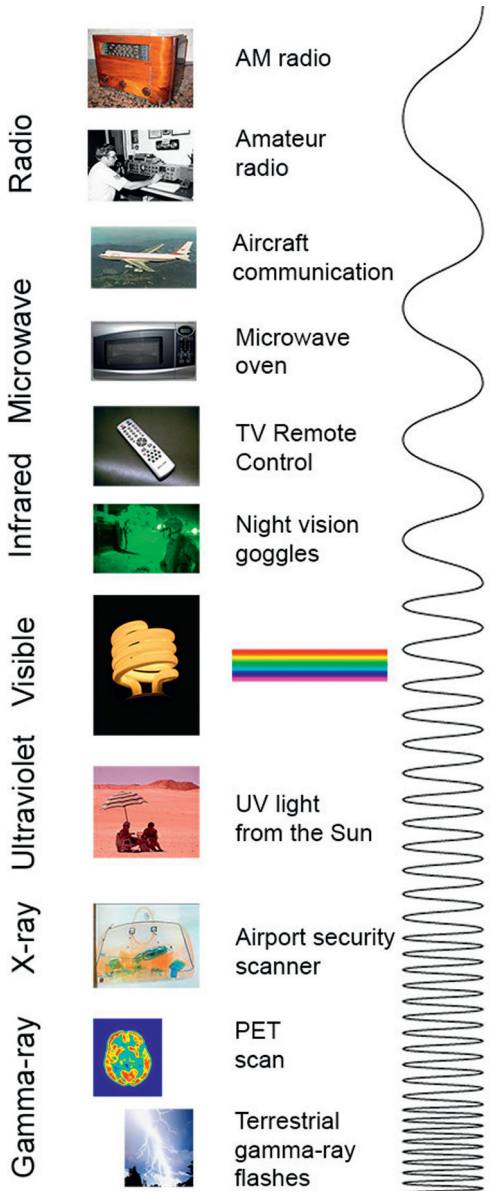

Figure 1: Electromagnetic spectrum (Image from NASA). Observe the multiple electromagnetic radiations that form the spectrum and the different wavelengths depending on the source.

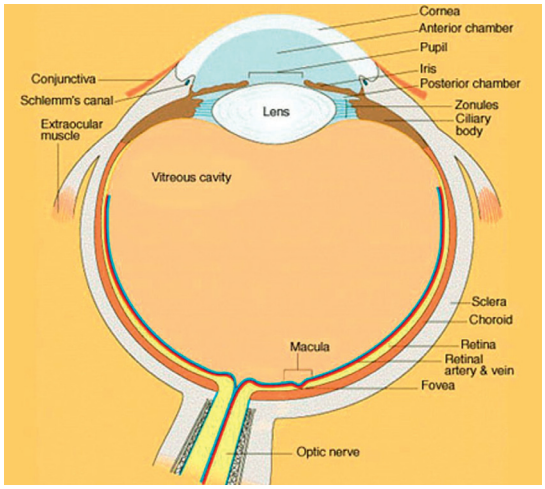

Figure 2. Structure of the Eye. Light should go through different eye structures for reaching the photoreceptors in retina. Only specific electromagnetic radiations can stimulate photoreceptors. UV radiation is absorbed by cornea and lens, which are very sensible to damage produced by UV (Image from University of Michigan Kellogg Eye center, Creative Commons 3.0)

- Damaged polynucleotide incision: it is necessary to cut the damaged DNA strand in order to separate it from the rest of the molecule.
- Damaged polynucleotide excision: once cut, the damaged strand is snipped out
- DNA synthesis *de novo:* the damaged strand is replaced by the correct DNA portion of the strand.

XPA, *XPC* and *XPE* encode proteins that participate in the recognition of the lesion, *XPB* and *XPD* encode products that show helicase function and participate in the unwinding of the DNA molecule, so specific enzymes can reach the lesion, *XPF* and *XPG* encode proteins that function as endonucleases. They cut the DNA by producing nicks in either side of the strand of the damaged DNA and releasing a region containing the damaged nucleotides. Polymerases are responsible for filling the gap with the appropriate complementary bases, using as template the remaining strand. A DNA ligase completes the process[8–10]. Figure 4 shows the process of repairing and different xeroderma pigmentosum gene products that participate in it.

A defective eighth gene, not related to the NER mechanism, can also cause the disease. It is called *XPV*, or Xeroderma Pigmentosum Variant. This gene encodes a polymerase involved in replication of oxidatively damaged DNA.

Patients with xeroderma pigmentosum have autosomal recessive mutations in any of these genes, so they are incapable of producing the proteins required for the detection or repair of DNA damaged by UV light.

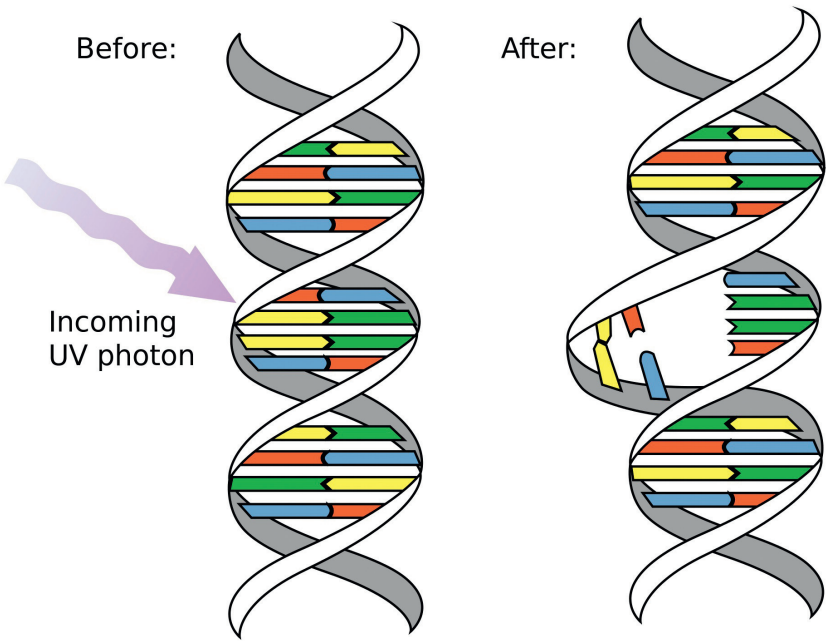

Figure 3. Action of UV light on DNA structure (Image from NASA/David Herring). The high energy of photons in UV light is absorbed by DNA and some of its components are strongly energized. They react among them, "sticking" together and forming abnormal structures.

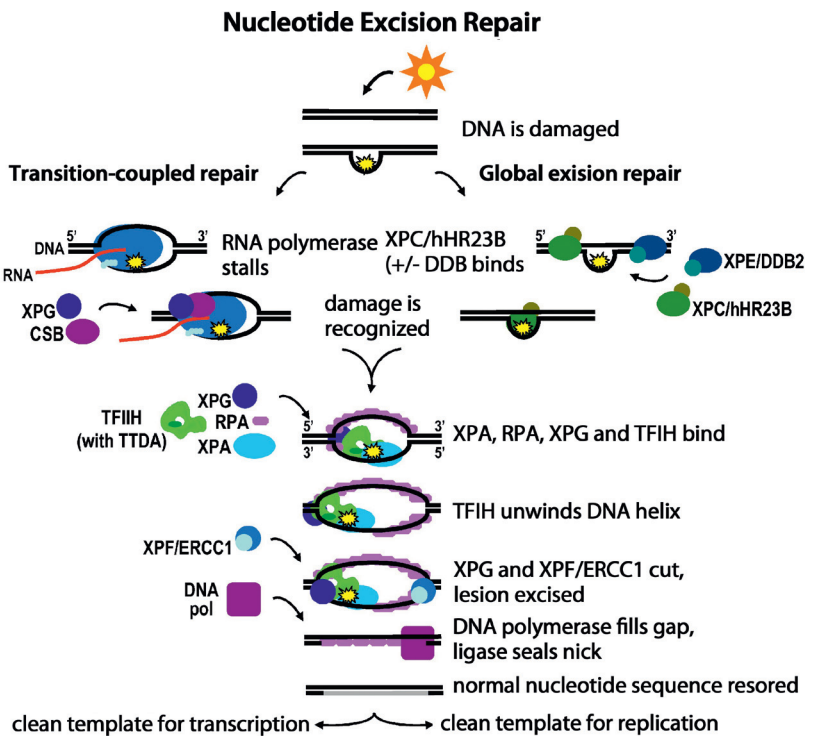

Figure 4. Reparation process of UV-damaged DNA. Observe different products of XP genes participating in the repairing of UV-damaged DNA.(Image from Fuss and Cooper[10] ; Creative Commons Public Domain)

Autosomal meaning not located in sexual chromosomes, so males and females can suffer the disease in equal proportion; recessive means that it is necessary to inherit the same defective gene from each parent for the disease to appear.

"Whatever you do, don't open the curtains[2]"

The most important goal in the treatment is to protect the patient from the sunlight and other sources of UV radiation[3,9,11]. Some artificial lighting such as halogen lamps and other fluorescent lamps can also produce UV light. The UK Xeroderma Pigmentosum Support Group recommends LED lightbulbs as the safest.

All windows should be covered. Luckily, there are commercial UV-protective films nowadays that can be used at home, in the car, in the school or in the workplace.

The use of UV meters is strongly recommended by the UK Xeroderma Pigmentosum Support Group. It will allow the patient to monitor indoor lighting and light coming through windows. It can also be used to check whether the clothes the patient is going to use will protect him/her from UV light. The UV meter can be put under the clothes in the sunlight, and, after a while, the meter should be read.

It is advisable that the person with xeroderma pigmentosum wears long trousers, long sleeves, gloves and a hat with a wide brim. UV protection for the face and the eyes is essential. It is recommended to use UV protective full-face visors and or appropriate sunglasses.

The damage provoked by the sunlight can be attenuated using a wide-spectrum sunscreen (blockers of UVA and UVB), e.g. SPF 50, and also a protective lipbalm. Since the patient is not producing vitamin D from precursors in the skin (sun is required for this process), complements of vitamin D need to be prescribed as well. Regular visits to the dermatologist, oculist, and neurologist are also necessary.

"Don't they ever play outside?"

Grace has organized the house in such a way that the children have some space to play inside: most of the furniture, big adornments, mirrors etc. have been stored in a specific (and kind of scary) room. This house disposition gives more space for the children to play inside instead of the forbidden, during daytime, outside. They can go out at night, however.

Fortunately, it is not the situation nowadays. XP societies, formed by families, friends and other sponsors, are making important contributions for the socialization of the children with this disease. They support families and educate society about this rare disease. Some of these societies have created camping facilities for children with photosensitivity, such as Camp Sundown Xeroderma Pigmentosum Society, USA (www.xps.org) and Owl Patrol Night Camp XP Support Group, UK (www.xpsupportgroup.org.uk). The French XP Society (www.enfantsdelalune.org) has developed a partnership with speleological clubs, in such a way that '*les enfants de la lune*' ('children of the moon') can participate in explorations and visits to caves. Other societies in Germany (www.xerodermapigmentosum.de), South Africa (www.xpsociety.co.za), Tunisia and other countries have developed several initiatives for increasing society's awareness in relation to this disease, helping in the development of new devices for UV protection, and raising funds for patient treatment and UV damage prevention.

Next time that you enjoy a beautiful summer's day, recall that there are families that cannot appreciate it, and consider that may be there is a way in which you can contribute to help these children of the night to become children of the day. ■

David Urquiza graduated with an MD with specialization in Clinical Biochemistry from the ISCM-SC, Cuba. He later obtained a PhD in Biological Science (ISCM-Havana, Cuba), based on his research on amniotic fluid. During several years, he organized and advised in prenatal and neonatal screening in different countries. Results of his research have been presented and published in Brazil, Cuba, China, Italy, Spain and Russia. He has taught Medical Biochemistry in universities in Cuba, Africa and the Dutch Caribbean. Nowadays, he works as an Instructional Advisor and Adjunct Faculty at the Miami Dade College, Miami, FL, USA. His Biochemistry blogs in Spanish (temasdebioquimica.wordpress.com/) and English (biochemistryquestions.wordpress.com/) have had more than 4 million visitors. Email: hhernan2@mdc.edu

References

1. *The Others* Official Site: http://www.miramax.com/movie/the-others/
2. *The Others* screenplay: http://screenplayexplorer.com/?tag=the-others-movie-script
3. Xeroderma pigmentosum at Medscape: http://emedicine.medscape.com/article/1119902-overview#a5
4. Bradford, P.T., Goldstein, A.M., Tamura, D. et al. (2011) Cancer and neurologic degeneration in xeroderma pigmentosum: long term follow-up characterizes the role of DNA repair. J. Med. Genet. **48**, 168–176
5. NASA Imagine the Universe! The Electromagnetic Spectrum: http://imagine.gsfc.nasa.gov/science/toolbox/emspectrum1.html
6. Allen, J. (2001) Ultraviolet Radiation: How It Affects Life on Earth: http://earthobservatory.nasa.gov/Features/UVB
7. Jackson, S.P. and Bartek, J. (2009) The DNA-damage response in human biology and disease. Nature **461**, 1071–1078
8. Sancar, A. and Tang, M.-S. (1993) Nucleotide Excision Repair. Photochem. Photobiol. **57**, 905–921
9. Kraemer, K.H., DiGiovanna, J.J. (2003) Xeroderma Pigmentosum. In GeneReviews® (Internet) (Pagon, R.A., Adam, M.P., Ardinger, H.H. et al., eds), University of Washington, Seattle
10. Fuss, J.O. and Cooper, P.K. (2006) DNA repair: dynamic defenders against cancer and aging. PLoS Biol. **4**, e203
11. Lehmann, A.R., McGibbon, D. and Stefanini (2011) Xeroderma pigmentosum, Orphanet J. Rare Dis. **6**, 70