Subtle damage from the sun

Sensor detects gene lesions caused by solar radiation

Carlos Fioravanti

When he was creating a sensor to detect lesions to DNA molecules at one of the laboratories of the Institute of Biomedical Sciences (ICB) of the University of São Paulo (USP), biologist André Schuch felt like he did as a boy back in his rural home town of Santa Maria, Rio Grande do Sul, taking apart model cars to remove their engines and make other toys. For the first three years, he designed, built and tested three prototypes that only showed him what he shouldn't do. He got it right with the fourth prototype, which has suggested that we have good reason both to worry about the excessive solar radiation that reaches our normally under-protected skin and not to rely so heavily on sunscreen when we go out to enjoy a summer day at the beach, especially those of us with light skin.

Initial tests with the sensor, or dosimeter, indicated that type A ultraviolet radiation (UV-A) – against which sunscreens afford much less protection than against the more energetic type B (UV-B) – can also induce lesions to DNA, the molecule that safeguards every living being's genetic material. Within each cell of the human body, DNA molecules are damaged and then fixed through protein repair thousands of times a day. When these lesions are not repaired, they can lead to undesirable genetic mutations. When those mutations produce defective cells that multiply nonstop, they can cause various types of cancer, mainly skin cancer, responsible for one in every four malignant tumors detected in Brazil. The National Cancer Institute (INCA) estimates that 134,000 Brazilians will be diagnosed with skin cancer in 2012.

It has also been found that the regions with the highest incidence of UV-B lie closer to the equator, not the poles, contrary to what would be expected given that the ozone hole in the upper atmosphere near the poles allows more type B ultraviolet radiation to pass there. In 2006, 2007 and 2008, Schuch exposed the sensors to natural light from 10 a.m. to 2 p.m., when solar radiation is most intense, at three locations: Punta Arenas, a city lying at a latitude of 55 degrees in the far south of Chile; Santa Maria, a city in São Paulo state (22° 34'); and Natal, capital of Rio Grande do Norte (05° 47').

Delicate skin: on hot days, sunscreen may not protect us as much as we'd like

MARTYN F. CHILLMAID/SCIENCE PHOTO LIBRARY

The surprising finding was that UV-B radiation was thirteen times more intense in Natal than in Punta Arenas – with a proportionate amount of DNA damage – even though the ozone layer was 50% thinner in Chile during three of the seven days in which measurements were taken. "We have to protect people's skin in Brazil, as they're now doing in Australia and Chile," says geneticist Carlos Menck, coordinator of the DNA repair laboratory at the ICB.

Menck states that he was very pleased to receive Schuch, who first came for a practicum in 2003. Since finishing his own doctorate in 1982, Menck has been studying DNA lesions and repair mechanisms. For many years he had wanted to find a way to measure molecular lesions but had met with failure. He sent samples to the Antarctic but that wasn't successful. When he began working with Schuch, he realized his basic mistake had been to use dry DNA, whose structure changes and does not precisely reproduce what happens with a molecule that is usually immersed in water.

As part of his doctorate, Schuch wanted to do something that would work in natural light, even though he didn't know how; the only experiments with cell, plant and animal lesions used artificial light. Furthermore, he wanted to do so more accurately than similar experiments in the United States and Japan. He in fact had experience measuring solar radiation using devices called radiometers, with which he had worked at the Santa Maria Regional Center for Space Research. Under a cooperation effort with researchers from Japan – the same ones who installed the equipment in the south – two radiometers are now perched on the roof of an ICB building. "We now have three years of monitoring," he says. "We're gathering a consistent database."

Having returned to Santa Maria with the hope of continuing the line of research begun during his doctoral studies, Schuch, 29, believes sensor readings can complement readings from specific radiometers, like the sensors that indicate the minimum doses of radiation capable of causing the skin burns known as *erythema*. He thinks the outlook is promising. "We've done more than create a dosimeter prototype," he says. "Now we can assess potential damage to DNA that is subjected to radiation

from outer space." His next step will be to measure lesions caused by sunlight directly in cell cultures and not just in DNA.

In their current version, the sensors – made of special transparent, rounded silicon, with two or three center holes, like buttons on an old coat – indicate the quantities of five types of lesions to the DNA molecule caused by UV-A or UV-B radiation. Sensor orifices are filled with a solution containing circular DNA, known as plasmid. When exposed to natural light, DNA absorbs the radiation that produces the lesions, which are later evaluated in a laboratory using reactions with DNA repair enzymes.

Menck and Schuch have been using the DNA lesion sensor to assess sunscreen efficacy. "Most sunscreens provide good protection against UV-B but do not do as well against UV-A," says Menck. They were surprised to find that one type of DNA lesion – pyrimidine (6-4) pyrimidone, one of the causes of mutations – can also be prompted by lower-energy UV-A and not just by UV-B, as previously believed. For this reason, they will probably suggest that the research and development team at an unnamed cosmetic manufacturer with whom they are collaborating reinforce the UV-A protection factor in its sunblocks.

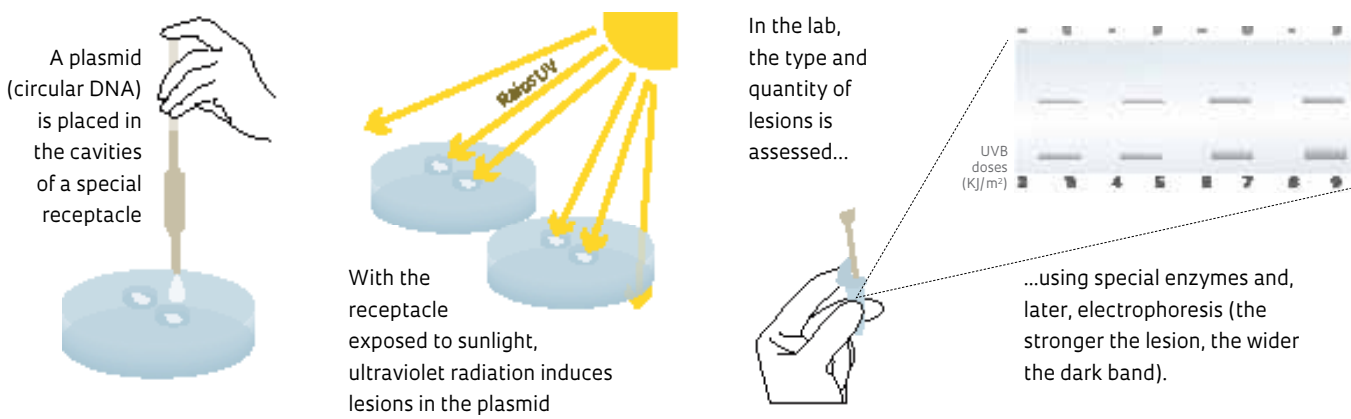
They also want to pinpoint the most appropriate protection factor for people with hypersensitivity to sunlight, like those with a condition called xeroderma pigmentosum (XP), caused by defects in DNA repair genes. People with XP run a hundred times greater risk of developing skin cancers than other people. To protect themselves, they must wear long-sleeved clothing even indoors, and apply sunscreen all over their bodies every day. To avoid the eye inflammation and tumors common in people with this genetic disorder, they have to wear sunglasses even to watch television.

In July 2010, Menck made his first visit to Araras, located 242 kilometers from Goiânia, capital of Goiás. This village presents a high number of people with XP: 22 have been diagnosed to date, out of a population of about 1,000 for the entire township of Faina, to which the village belongs. Over the past 50 years, about 20 people have died of the disorder, most likely so prevalent there because intra-family marriages are common. The total number of people with XP in Brazil is probably a thousand at most, scattered around the country. Schuch took his DNA sensors to Araras as well, where he recorded remarkably high levels of radiation and of lesions even among those without the disease, not a surprising finding considering the vast blue sky of the savannahs of central Brazil. Some members of the research team from his laboratory went to Araras as well and were amazed by the delicate skin of the residents with XP, who nevertheless continue working in the fields under the sun.

A priority for the DNA repair lab team now is helping the people with xeroderma pigmentosum who live in Araras

A series of reports published in the newspaper *Correio Braziliense* in October 2009 highlighted the plight of these people, who work all day in the fields even though they should not be out in the sun. The reports also recognized local leaders like Gleice Machado, president of the Goiás State Association of Carriers of Xeroderma Pigmentosum (Apoderma), and the work of doctors like dermatologist Sulamita Chaibub, who coordinates a project at Goiânia General Hospital to provide multidisciplinary care for XP carriers in Araras, and Rafael Souto, professor at the Pontifical Catholic University of Goiás (PUC/GO).

A method for measuring DNA damage



From left to right, Geni, Claudia and Vanda Jardim: many people in Araras, Goiás, are hypersensitive to light

Nine months ago, moved by the situation, pharmacist Evandro Tokarski, owner of a compounding pharmacy in Goiânia, started sending a highly potent sunscreen he developed himself to XP sufferers in Araras, free of charge. "I send some every month, so they won't run out," he says. "If we're able to help, why not do so?" He explains that he's developing a moisturizer to help treat dry skin in people with this genetic disorder and plans to present it soon to the physicians who treat this population.

For her part, Federal Senator Lúcia Vânia (Brazilian Social Democratic Party, or PMDB, Goiás) introduced a draft bill that would provide sickness benefits and a provision for retirement based on disability for XP sufferers in Araras. Approved by a Senate committee in November 2011, the bill should now move to the lower house. Likewise motivated by newspaper reports, university researchers in Goiás, the Federal District and São Paulo have stepped up their studies of ways to prevent the growth of tumors in XP carriers in Araras. Prevention includes adapting glass and other building materials used there to receive as little sunlight as possible, or even covering children's playground areas at school.

Incredible care must be taken, and often of a subtle nature. When Menck was there, he asked photojournalists not to use flash when they take pictures of XP sufferers, as it might harm them. He pledged to return in July with a set of DNA primers that can detect mutations in DNA repair genes in Araras residents. "They're almost ready," he explained with excitement in early March. "Helping these people and understanding why they have cancer and why they don't exhibit premature aging is our whole priority right now."

He and his team believe they can find new mutations in the genes that cause XP. "Describing a new mutation is a minor scientific contribution but each new mutation gives us a better understanding of why things happen in human beings," says Menck. Sometimes, he adds, DNA repair genes help make tumors resistant to the drugs meant to destroy them. In these cases, the goal is to intentionally curb the action of such genes so the drugs will be more effective. He is working to accomplish this as well, as part of a line of research expected to yield results in the longer run.

Menck recognizes that he has made considerable progress and has put together a productive, creative team that doesn't hesitate to take up challenges, like helping to alleviate suffering in Araras. Sometimes he goes back to his beginnings, taking down from his bookshelf a 95-page book with maroon covers and leafing through it; this is his doctoral dissertation, entitled "Survival and repair systems in mammalian cells," which got him started on the research path he continues following today. He observes that "there are things here that haven't been satisfactorily resolved yet." ■

PROJECTS

1. DNA lesion repair and its biological consequences – no. 1998/11119-7 (1999-2004)
2. DNA repair genes: functional analysis and evolution – no. 2003/13255-5 (2004-2009)
3. Cell response to lesions in the genome – no. 2003/13255-5 (2011-2014)

GRANT MECHANISM
1. 2. and 3. Thematic project

COORDINATOR
1. 2. and 3. Carlos Frederico Martins Menck – ICB/USP

INVESTMENTS
1. R$979,444.88
2. R$1,442,484.59
3. R$1,532,835.80

SCIENTIFIC ARTICLES

1. Schuch, A. P., Menck, C. F. The genotoxic effects of DNA lesions induced by artificial UV-radiation and sunlight. **Journal of Photochemistry and Photobiology B**. v. 99, n. 3, p. 111-16, 2010.

2. Menck, C. F. *et al.* Development of a DNA-dosimeter system for monitoring the effects of solar-ultraviolet radiation. **Photochemical & Photobiological Science**. v. 8, n. 1, p. 111-20, 2009.

FROM OUR ARCHIVES

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Issue no. 106 – December 2004

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Issue no. 82 – December 2002

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