Mutated plant sheds light on DNA repair

If DNA mutations caused by excessive sunbathing can promote skin cancer in humans, how do plants manage to get away without harm? Rooted in place, many plant species take in much higher doses of ultraviolet (UV) radiation than human sun-lovers do during a tanning marathon.

Though plant cells are adept at mending the damage caused by UV-B, the most dangerous portion of sunlight, scientists have been in the dark about how they do it. Now, geneticists have created a mutant strain of cress that is unable to repair UV-induced DNA damage.

Ann B. Britt, a geneticist at the University of California, Davis, and her coworkers have pinpointed a gene in *Arabidopsis thaliana,* or mouse-eared cress, that in healthy plants is involved in clipping out marred DNA pieces, restoring the original genetic code. By displaying the way in which its DNA repair is hampered, this mutant strain of cress sheds light on how the repair process works in the wild-type plant.

Says Britt, "We know much about DNA repair and mutation in bacteria, some animals, even humans, but virtually nothing in flowering plants," largely because higher plants have stubbornly resisted scientists' attempts to generate DNA-repair-defective mutants. Her group's report in the Sept. 17 SCIENCE helps fill that gap and introduces a technique for breeding other mutant strains. "This study is taking the first step toward dissecting one pathway of DNA repair in plants," says Allen Smith, a Stanford University molecular biologist.

It may also help explain how plants are coping with the intensifying UV irradiation of Earth that accompanies the degradation of the planet's UV-absorbing ozone layer. "The ozone depletion has focused much interest on what increasing amounts of UV can do to crop plants and to the ecosystem in general. So it is time that we begin to understand how plants protect themselves from UV radiation," says Smith.

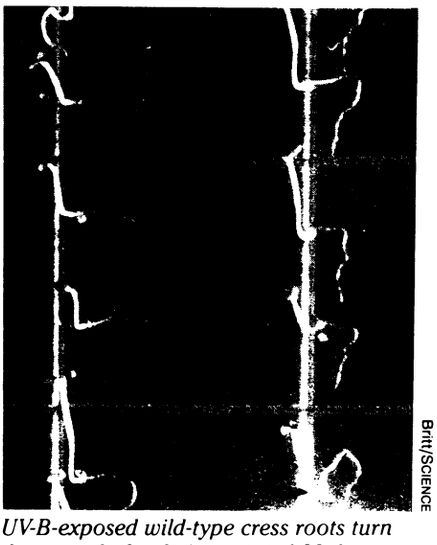
To create a plant impaired in its ability to repair DNA, Britt's group developed a "neat and clever technique," says Smith. The researchers treated seeds of *A. thaliana* with a chemical mutagen and grew them into stable lines. They placed seeds from these plants on round, vertical plates and allowed roots to emerge and grow downward along the plate for three days.

Next came the task of finding the needle in the haystack – spotting a UV-sensitive individual among the thousands of sprouting rootlets. To do that, the geneticists irradiated the baby roots with a short but intense dose of UV-B, strong enough to "give us a good sunburn in 30 seconds," Britt says. Then they rolled the plates 90 degrees. Wild-type roots continued to grow and, in response to gravity, took a sharp turn downward again. In contrast, the roots of the UV-sensitive mutants were no longer able to grow after the UV pulse. Thus, by never forming the right angle, they betrayed their genetic defect.

The mutant cress plants tolerate very little UV radiation, the researchers report. Although they develop normally in the absence of UV, the plants wither and turn black with dying tissue when exposed to even a small dose of UV, such as that emitted by the fluorescent lamps commonly used in offices. This sensitivity shows how crucial the DNA-repair gene is for the wild type to survive, Britt says.

Studies of this type might eventually help breed more UV-resistant crop plants, but Britt says she is more interested now in learning how DNA repair mechanisms can cause mutations in plants. "There are several DNA repair pathways," she says, "some that make no mistakes and some that are prone to make errors. These errors end up as DNA mutations in plants and thus may contribute to plant evolution."

The gene described in the current study belongs to the error-free group, but having identified it makes it easier to find other genes involved in DNA repair, including the error-prone ones. By mutating the mutant strain, Britt plans to knock out additional DNA repair genes and isolate strains that are even more vulnerable to UV. "This way we can gradually flesh out the repair pathways at work in higher plants," she says. – *G. Strobel*



Britt/SCIENCE

UV-B-exposed wild-type cress roots turn downward after being rotated 90 degrees (right). Mutated roots fail to turn, thus revealing their genetic defect (left).

Chicken cartilage soothes aching joints

An experimental therapy appears to offer significant relief to people suffering from the pain and swelling of rheumatoid arthritis.

Rheumatoid arthritis results when the immune system mistakenly attacks the body's own tissues – in this case, the inner lining of the joints. Although nobody knows for certain what causes the disease, some researchers think a virus combined with an inherited vulnerability triggers the autoimmune attack. As the disease progresses, it destroys the rubbery cartilage that cushions the ends of the bones.

Previous research suggested an unusual strategy against this disorder, one that relied on collagen, a fibrous protein found in cartilage. David E. Trentham and his colleagues at the Harvard Medical School in Boston knew that a collagen treatment blocked the development of an arthritic condition in rats. And the team's pilot study of 10 people suggested that this therapy could ameliorate and even eradicate clinical symptoms of the disease in humans.

So Trentham's team embarked on a clinical trial of collagen therapy in 59 people with severe rheumatoid arthritis. All volunteers were taken off the drugs they had been using to control their joint pain for the duration of the study. Each morning, 28 recruits drank a glass of orange juice containing collagen derived from purified chicken cartilage. The remaining 31 volunteers, who served as controls, drank orange juice containing a placebo. Neither the volunteers nor the researchers knew who received the active treatment and who got the placebo.

After three months, the team noticed a decrease in the number of swollen and tender joints reported by most people getting the collagen. Indeed, four of the 28 experienced a complete remission of their disease. "That was an unprecedented and surprising outcome of the study," Trentham says, adding that he doesn't know how long such a remission will last.

The researchers found no such improvement in the placebo group. Their report appears in the Sept. 24 SCIENCE.

Trentham admits his team doesn't know how the collagen therapy works. Perhaps it triggers the release of cytokines, powerful chemical substances that may dampen the revved-up autoimmune response to the body's cartilage and joints, he speculates. Much more work remains before they can determine the precise mechanism by which this treatment exerts its protective effects, he adds. – *K.A. Fackelmann*