

This Week's Citation Classic®

Regan J D & Setlow R B. Two forms of repair in the DNA of human cells damaged by chemical carcinogens and mutagens. *Cancer Res.* 34:3318-25, 1974.
[Carcinogenesis Program, Biology Division, Oak Ridge National Laboratory, TN]

DNA repair in human cells takes one of two limiting forms, depending on the nature of the original insult to the DNA. Chemicals that damage DNA fall into two categories, those that result in the ionizing or "short" type of DNA repair and those that result in the ultraviolet or "long" type of repair. [The *SCI*® indicates that this paper has been cited in over 420 publications.]

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We were able to carry out these experiments mainly because we had developed a new method for assaying DNA repair, the bromodeoxyuridine (BrdUrd) photolysis method; the "BU-trick" we called it.¹ You trick the cells into repairing their DNA in BrdUrd, which is a thymidine analog. Then you irradiate the cells with a range of high doses of 313 nm light. This renders the bromouracil-containing repaired regions of the DNA alkali sensitive. You lyse the cells on top of an alkaline sucrose gradient

and centrifuge the DNA through the gradients for molecular weight determinations. Thus, you get in "one swell foop," as my physiology professor used to say, the number of repaired regions and the size of the average repair patch.

The first time we tried a BU-trick was over Labor Day weekend in 1969. On Labor Day itself, I was to meet with Dick Setlow in the lab so we could examine our results. Well, that day they were evacuating everybody from the lab who happened to be working. It seems that a couple of escaped murderers had hijacked an airliner, and these two clowns were threatening, were their demands not met, to crash the airplane into the Oak Ridge National Laboratory on the absurd notion that this would cause a nuclear explosion. Anyway, when I got to the lab, Setlow was already there. "Never mind the hijacking," he said. "This is important. This BU business works."

After that we went on to look at a bunch of different chemical carcinogens with this method, and they all turned out to be classifiable into the short patch (ionizing-type) or the long patch (ultraviolet-type) DNA repair mode. The long-patch repair pathway is nowadays more familiarly known as "bulky adduct" repair.² For further work in this field, see the recent reviews by R.J. Fram and D.W. Kufe³ and by P.A. Charp.⁴

Funny, I never did hear how that hijacking turned out.

1. Regan J D, Setlow R B & Ley R D. Normal and defective repair of damaged DNA in human cells: a sensitive assay using the photolysis of bromodeoxyuridine. *Proc. Nat. Acad. Sci. USA* 68:708-12, 1971. (Cited 250 times.)
2. Francis A A, Snyder R D, Dunn W D & Regan J D. Classification of chemical agents as to their ability to induce long or short patch DNA repair in human cells. *Mutat. Res.* 83:159-69, 1981. (Cited 50 times.)
3. Fram R J & Kufe D W. Inhibition of DNA excision repair and the repair of X-ray-induced DNA damage by cytosine arabinoside and hydroxyurea. *Pharmacol. Ther.* 31:165-76, 1985.
4. Charp P A. DNA repair in human cells—methods for the determination of calmodulin involvement. *Meth. Enzymology* 139:715-30, 1987.

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