This Week's Citation Classic®

Regan J D, Trosko J E & Carrier W L. Evidence for excision of ultraviolet-induced pyrimidine dimers from the DNA of human cells in vitro.
Biophysical J. 8:319-25, 1968.
[Biology Div., Oak Ridge Natl. Lab., TN and Dept. Natural Sciences, Michigan State Univ., East Lansing, MI]

Within 12 to 24 hours after human cells were irradiated with ultraviolet light, approximately 50 percent of the ultraviolet-induced pyrimidine dimers were lost from the DNA. Pyrimidine dimers were found in the trichloroacetic acid-soluble fraction of ultraviolet-irradiated cells at 24 hours. Excess thymidine, caffeine, or hydroxyurea had no effect on the loss of pyrimidine dimers from the DNA of ultraviolet-irradiated cells. [The *SCI*® indicates that this paper has been cited in over 290 publications.]

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I graduated from the University of Hawaii in 1964 and came to the Biology Division of Oak Ridge National Laboratory to postdoc with Ernie Chu. At the time everyone there was agog at the finding by Dick Setlow and Bill Carrier of excision of pyrimidine dimers in *Escherichia coli*. One of the most excited was Jim Trosko, a bright, enthusiastic researcher doing a postdoc with Shelly Wolff. "Think of it," Trosko would bubble, "DNA codes for enzymes to repair itself!"

I was supposed to be selecting for X-ray resistant human cells. Trosko and I got to wondering if X-ray resistant human cells could also be ultraviolet resistant, that is, dimer-excision proficient, as was the case with some of the *E. coli* strains. On the other hand we were loathe to spend any of our precious postdoctoral time on these experiments since there were already half a dozen papers around showing that mammalian cells didn't excise dimers (the hook was that all those experiments had been done with *rodent* cells).[1,2]

We talked with Carrier about all this and finally the three of us decided to go ahead and do it. Well, we got excision all right, but a lot of people didn't believe it at first, including us, because of the earlier rodent data and because we were only getting about half the dimers out. We did more experiments and still got the same answer, so we finally started to believe it ourselves.[3] Then, all of a sudden, Trosko moved to Michigan State University whereupon Alex Hollaender called me into his office and told me he hoped I wasn't entertaining any notions of going to any of "these universities" because there was "no one at these universities." "Everyone is here," he said. "You stay here." He knew we were getting dimer excision in human cells, and he didn't want *that* going anyplace.

Finally, I wrote the paper and, not without some trepidation, showed it to Setlow. The next morning he threw it on my desk and said, "Very impressive." (Wow!) "Where do you think I should publ—," I stammered. "*Biophysical Journal*," he snapped, "right away."

So anyway, that was that. Twenty years later Carrier and I are still here (I obeyed Hollaender's orders) on the fifth floor of Building 9207 in the office and laboratories that used to be Chu's when I was his postdoc. We are still studying human DNA repair. Do we have more answers now? A few, yes, but there are a lot more questions now, too. Like the late great comic Brother Dave Gardner used to say, "Well man, if you got it all nailed down, then what's that all around it?"[4]

1. **Trosko J E, Chu E H Y & Carrier W L.** The induction of thymine dimers in ultraviolet-irradiated mammalian cells. *Radiat. Res.* 24:667-72, 1965. (Cited 160 times.)
2. **Klimec M & Vlasinova M.** Thymine and uracil-thymine dimers and deoxyribonuclease acid synthesis in mammalian cells irradiated with ultraviolet light. *Int. J. Radiat. Biol.* 11:329-37, 1966.
3. **Carrier W L, Snyder R D & Regan J D.** Ultraviolet-induced damage and its repair in human DNA. (Regan J D & Parrish J A, eds.) *The science of photomedicine.* New York: Plenum Press, 1982. p. 91-112.
4. **Gardner D.** *Rejoice dear hearts.* RCA Victor LPM-2083, 1959. (Sound recording.)

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