Reviewer's report

Title: Different Biological Effects of Two Major Types of UV-induced DNA Damage: CPD Causes Mutation and 6-4PP Induces Apoptosis.

Version: 1 Date: 29 June 2005

Reviewer: Thomas Berton

Reviewer's report:

General

1. The question posed by the authors is new but not well defined. The methods are somewhat appropriate but are well described and are there are sufficient details provided. The manuscript adheres to standards for reporting and data deposition and the writing is acceptable.

2. The title does not accurately convey what has been found in the manuscript. There is no data (except what has been published in the literature) that CPDs cause mutations. Here the authors do show that (6-4)PP causes apoptosis. The abstract does not convey what the authors found either. I was very surprised to find this out after I accepted to review the manuscript based on the abstract. I was under the assumption that there was going to be more experimental details regarding cell cycle arrest and mutations.

3. The data in Figure 1 and 2 are well controlled. Figure 3 and Table 1 contain the same data but in different formats. I am not sure about what UVB dose was used in Figure 3/Table 1. There are no histograms for Figure 3 as indicated in Figure 3 legend. Although Figure 4 and 5 provide experimental evidence for the role of CPD in not being able to induced apoptosis as well as (6-4)PP, these experiments seem to be out of context with the data from Figure 2 and 3. It seems topical application of these photolyases on mice could provide better data than a CPD mimic. What is the affect of removing either (6-4)PP or CPD by their respective photolyases on the repair of the remaining damage? It has been shown that p53 post-translational stability is required for an appropriate apoptotic response following UVB irradiation. How does the treatment of photolyases affect p53 expression and phosphorylation status?

4. The discussion is too short and not well balanced. There are other data that could help support the data that the authors failed to mention. It has been shown that transcription coupled repair (TCR) protects against UVB-induced apoptosis but not skin cancer. How does the removal of (6-4)PP or CPD by their respective photolyases affect TCR and / or global genome repair (GGR) for the remaining damage?

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Measurement of TCR or GGR after CPD-PL or (6-4)PP-PL treatment needs to be performed in order to determine if it is the type of damage or type of repair pathway or both that affects UVB-induced apoptosis. The authors need to remove the phrase, CPD causes mutations from the title because it is misleading unless the authors can show that removal of all (6-4)PP leads to mutations caused solely by CPDs. Remove either Table 1 or Figure 3 they convey the same thing.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
The expression and phosphorylation status of p53 needs to be assessed after UV-irradiation and photolyases treatment. What are the cell cycle profiles after photolyases treatment in Figure 3? Adding in vivo data showing that topical application of 6-4PP-PL and not CPD-PL on mice prior to treatment with UVB prevents apoptosis would strengthen the data.

Discretionary Revisions (which the author can choose to ignore)

None.

**What next?:** Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No

**Declaration of competing interests:**

I declare that I have no competing interests.